This presentation

- Hierarchical clustering
- Linkage methods
- ***Note for BiBC Master students: this presentation is exactly equal to the Essentials course one except for 4 slides at the end. If you feel comfortable with hierachical clustering, feel free to tune out and start on the short practical!***

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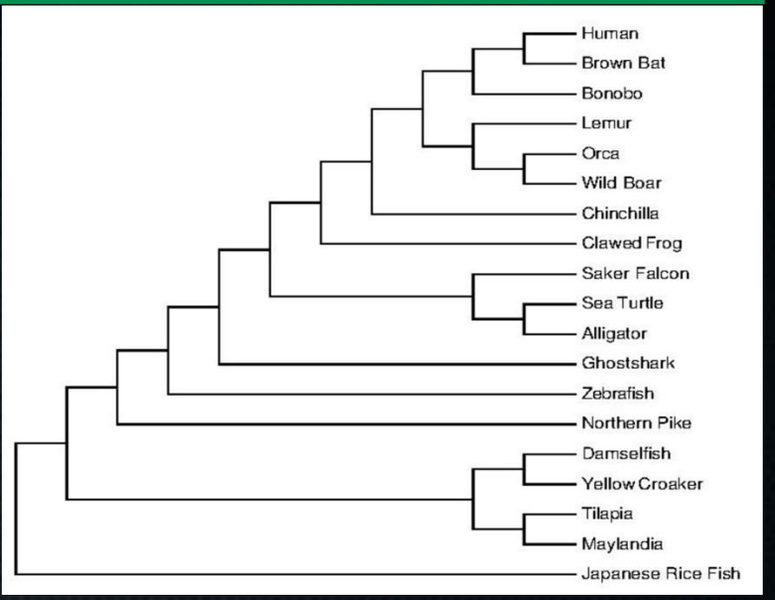
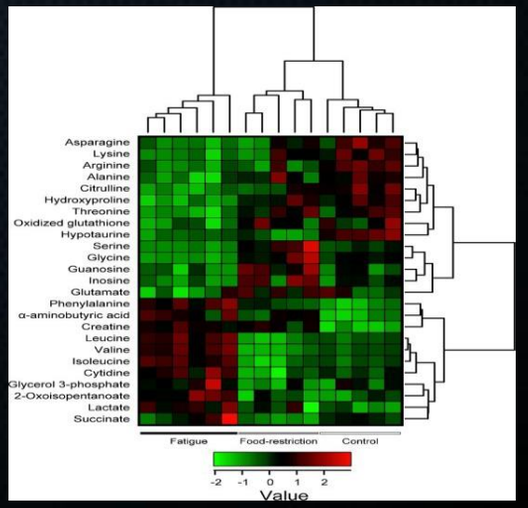
Agglomerative or hierarchical clustering

- Make a tree connecting all samples, which you can separate into clusters at any level you like
- Start from clusters containing individual samples, stop when you‘ve agglomerated all clusters into one big clustering.



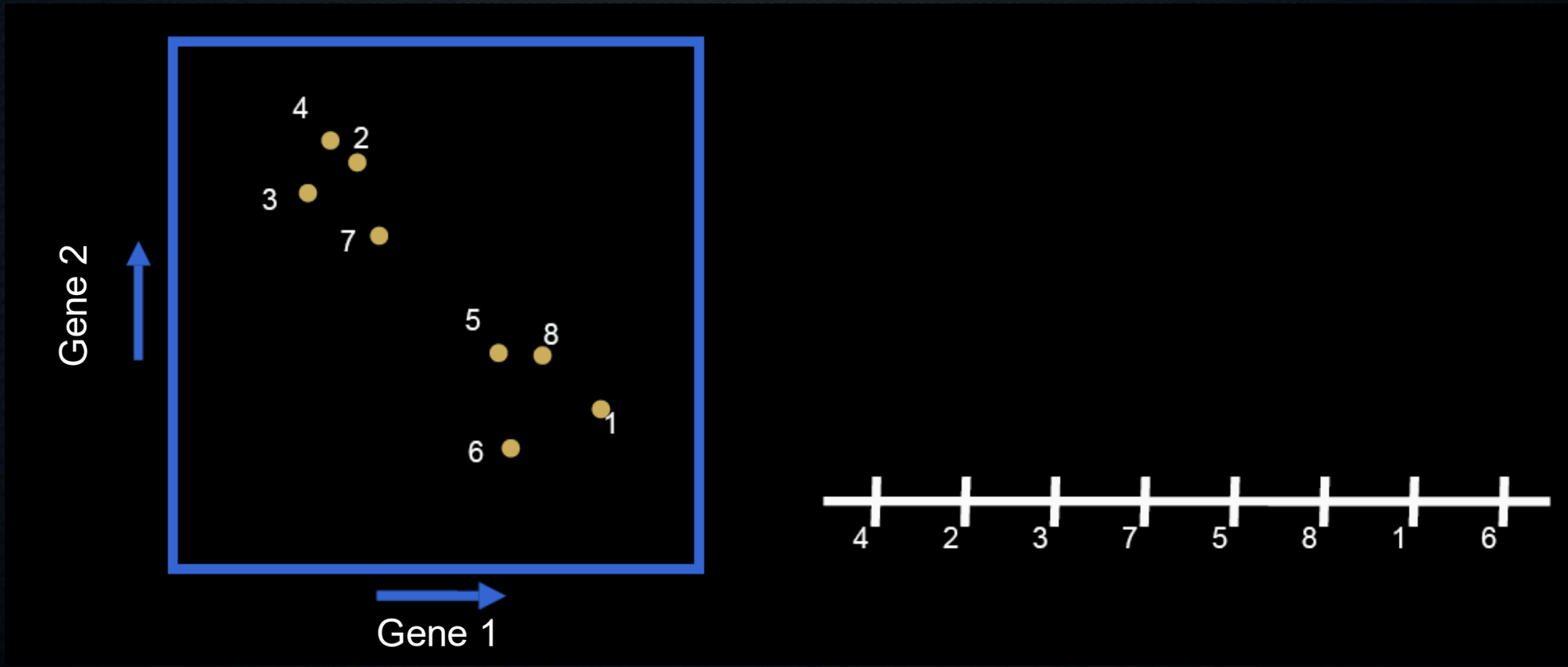
Source: https://commons.wikimedia.org/wiki/File:Phylogenetic_Tree.pdf



Source: Kume, S., Yamato, M., Tamura, Y., Jin, G., Nakano, M., Miyashige, Y., ... & Kataoka, Y. (2015). Potential biomarkers of fatigue identified by plasma metabolome analysis in rats. PloS one, 10(3), e0120106.

Agglomerative or hierarchical clustering

- Let‘s look at an example: find most similar objects and group them



Source: Jeroen de Ridder

Agglomerative or hierarchical clustering

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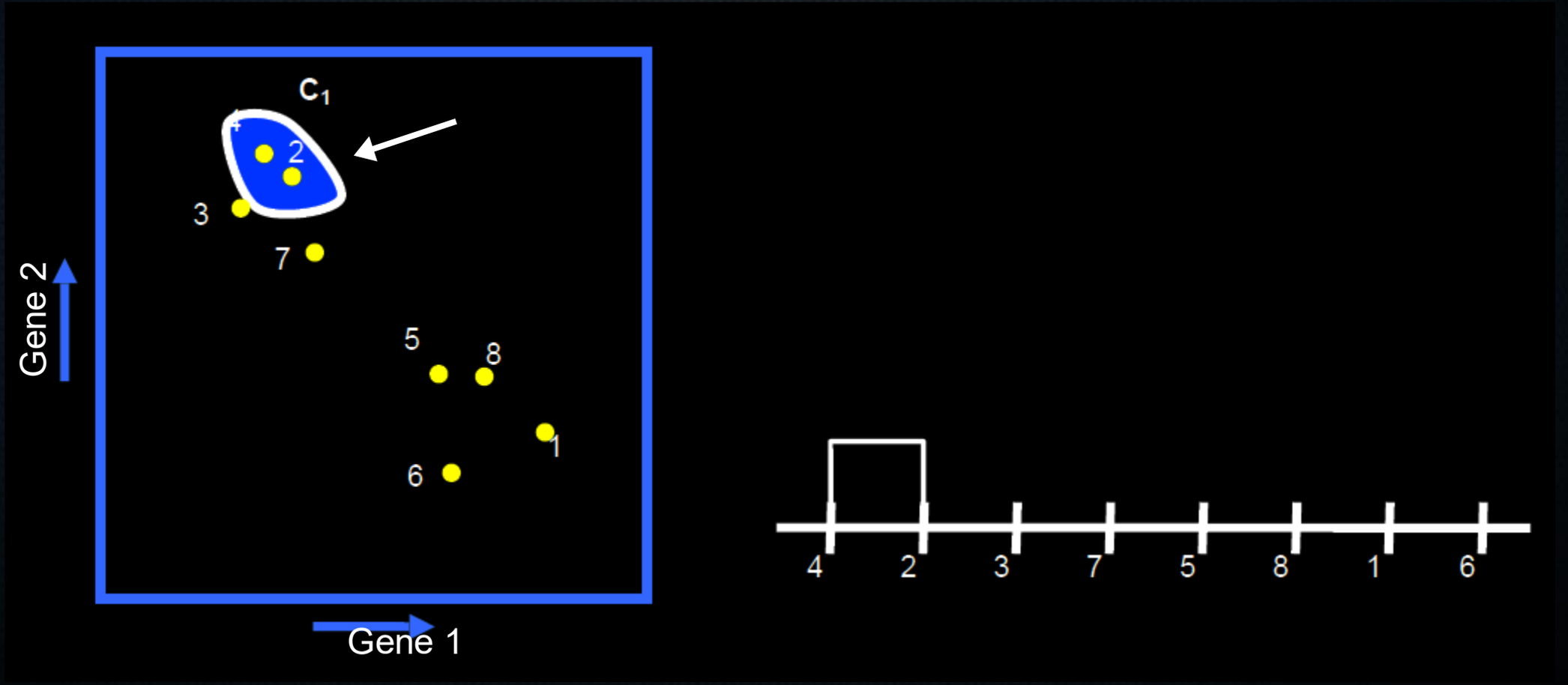

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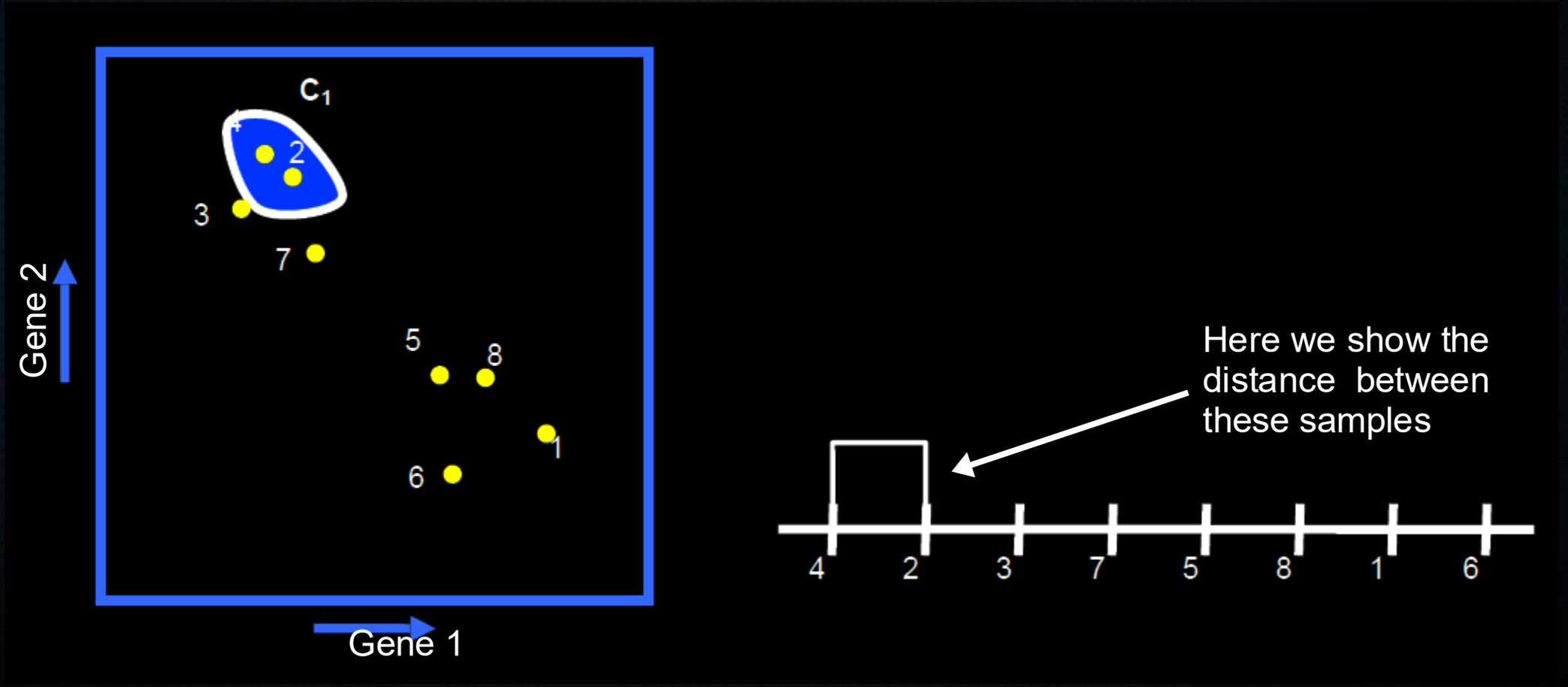
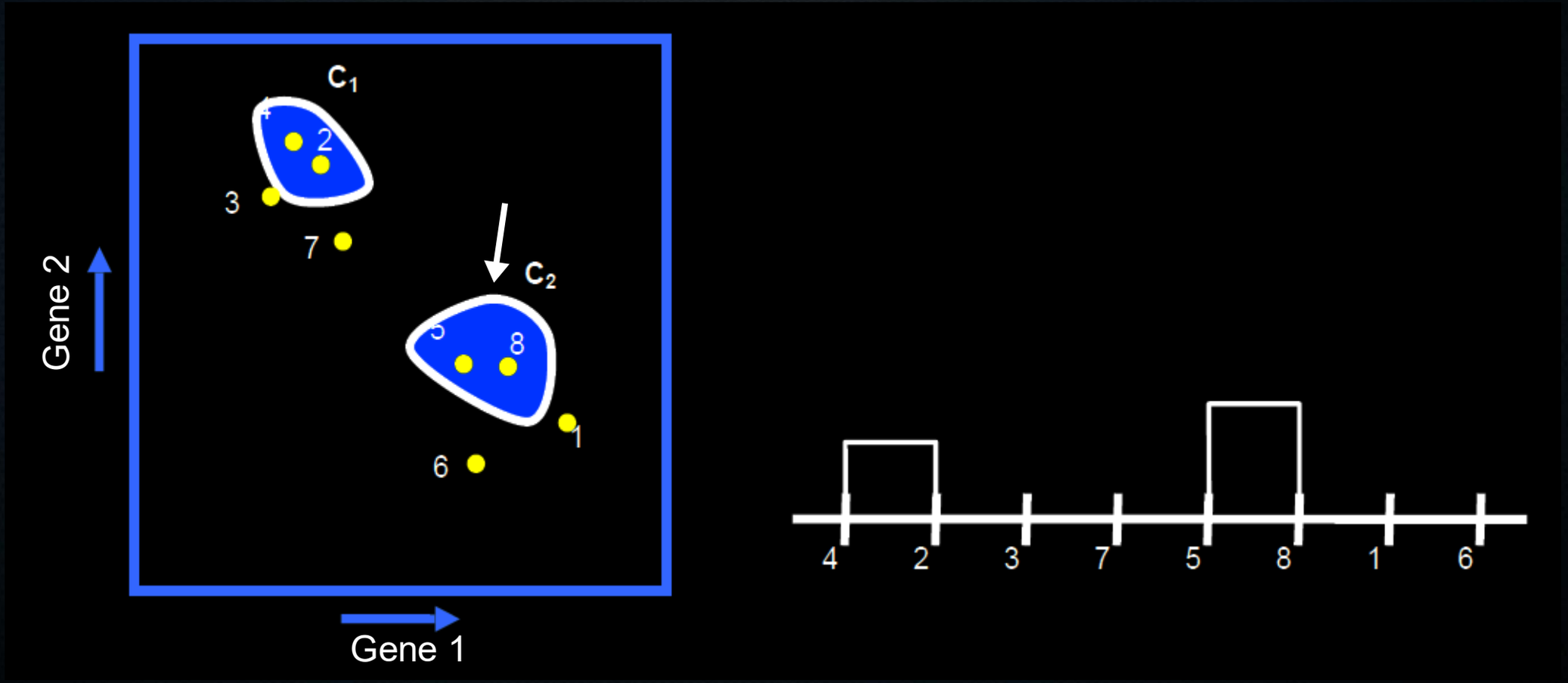


Source: Jeroen de Ridder

Agglomerative or hierarchical clustering

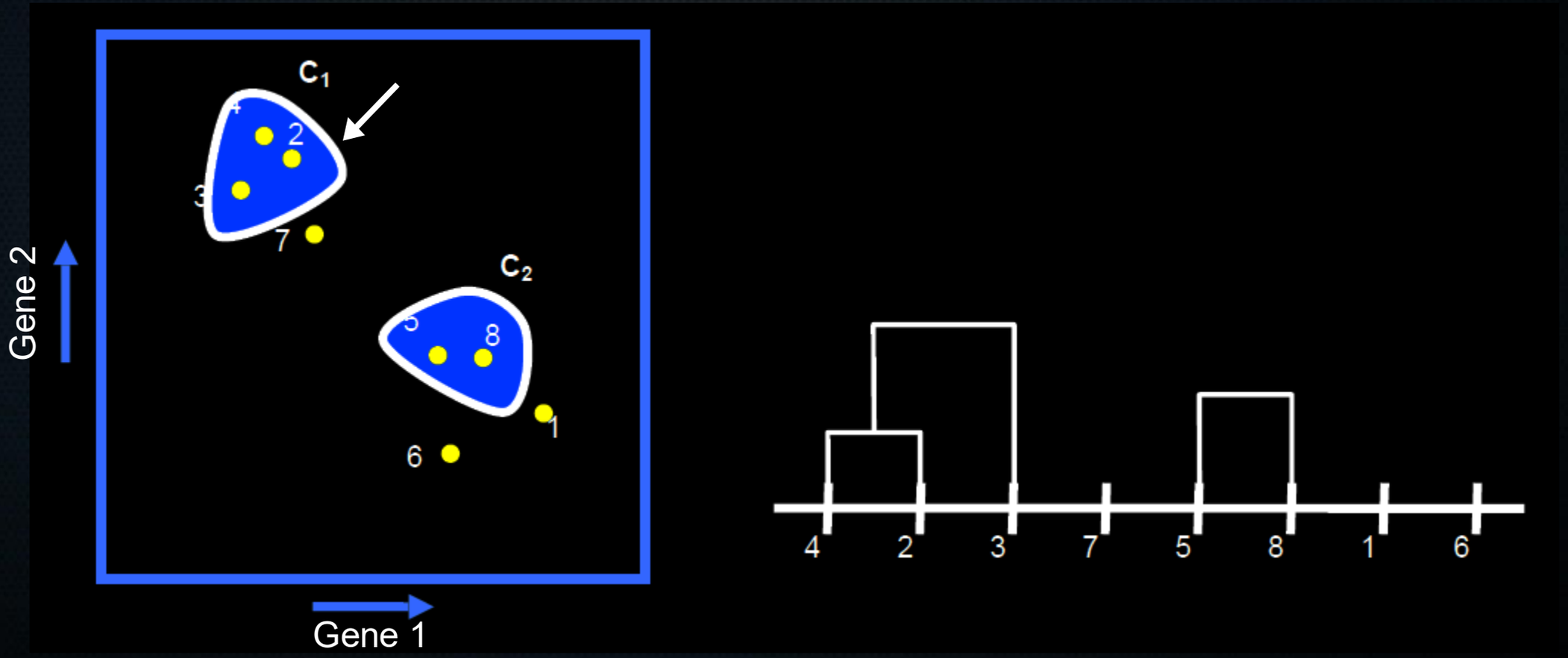
- Again, find most similar objects and group them



Source: Jeroen de Ridder

Agglomerative or hierarchical clustering

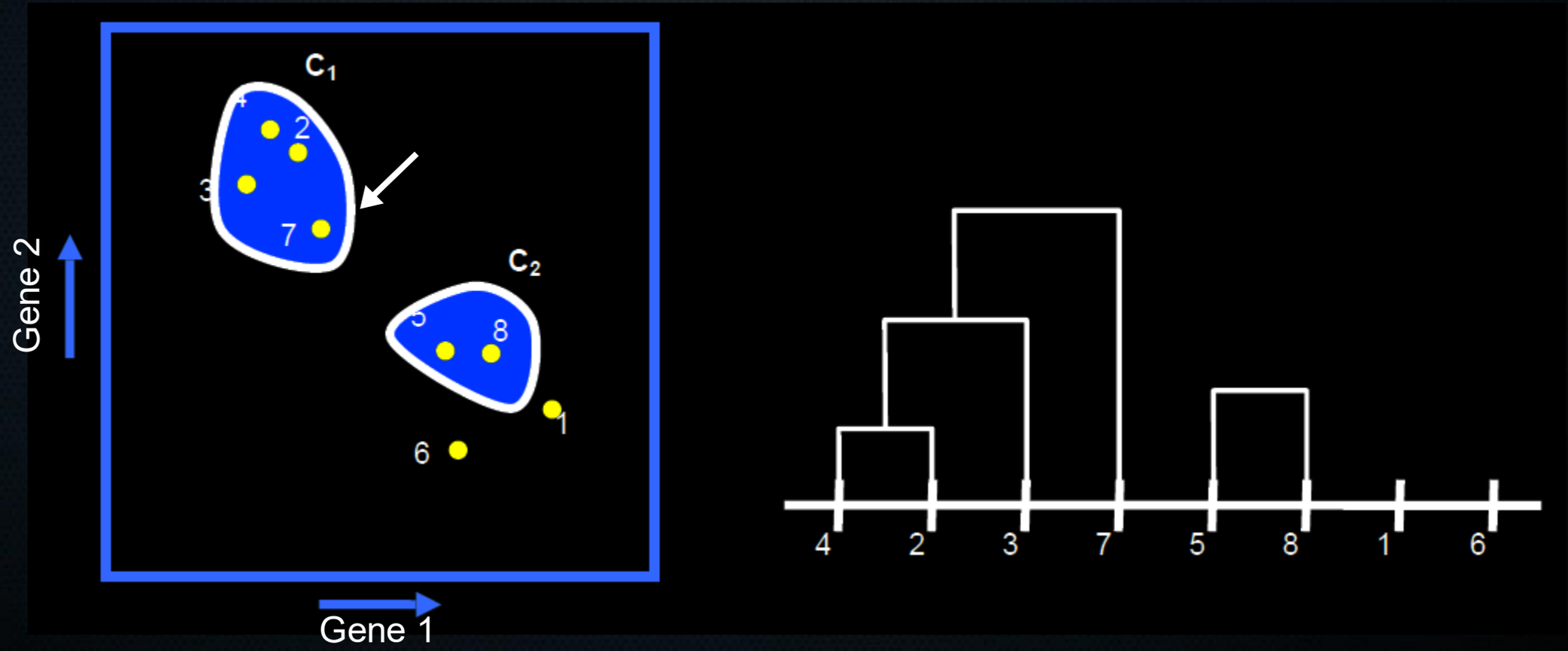
- Now: closest distance between cluster 1 and point 3!



Source: Jeroen de Ridder

Agglomerative or hierarchical clustering

- Keep iterating until everything is clustered together



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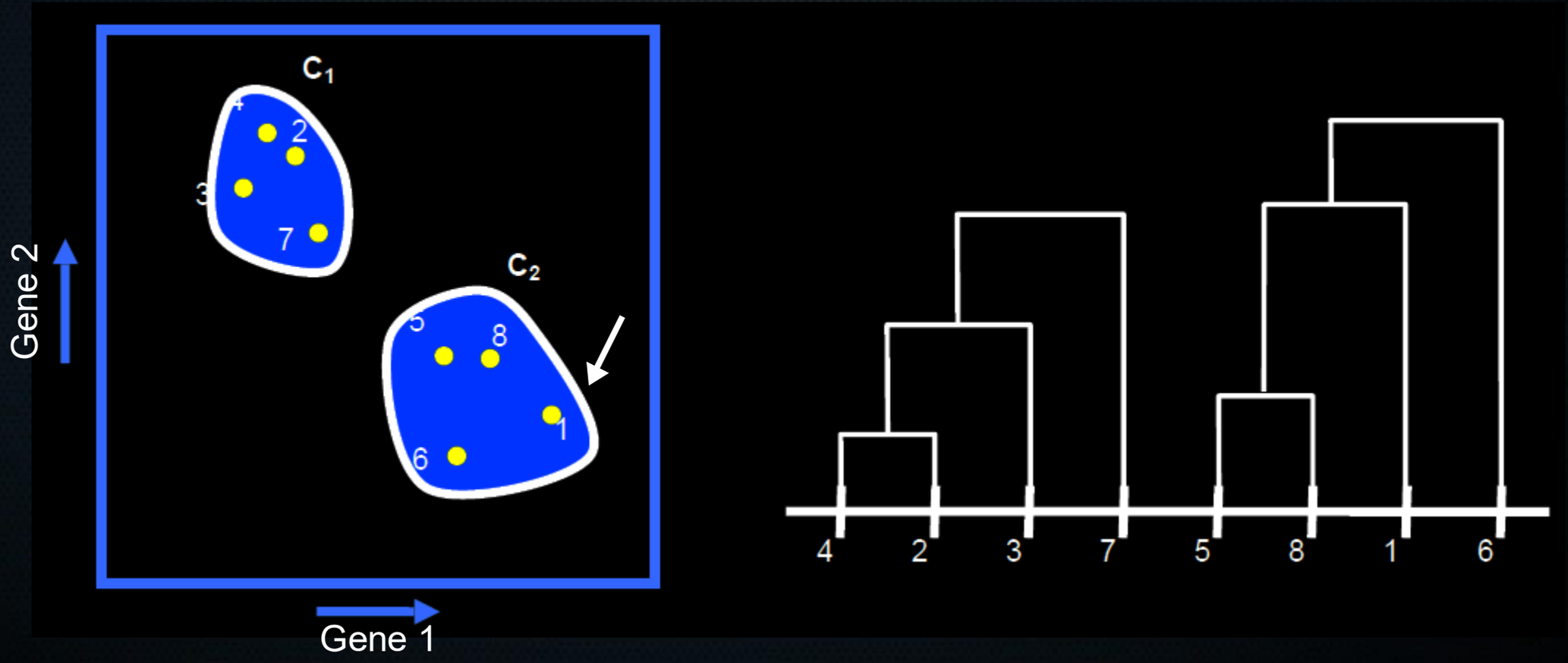

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Agglomerative or hierarchical clustering

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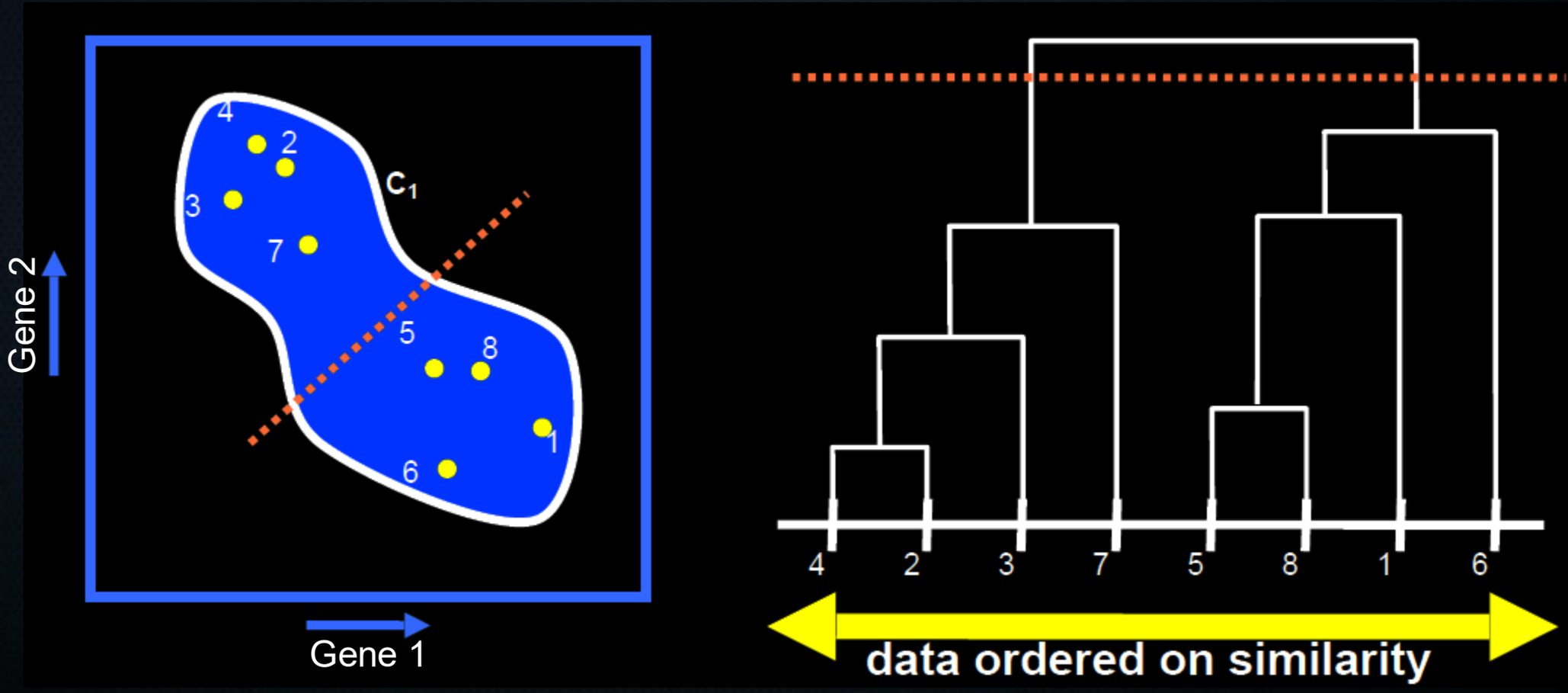

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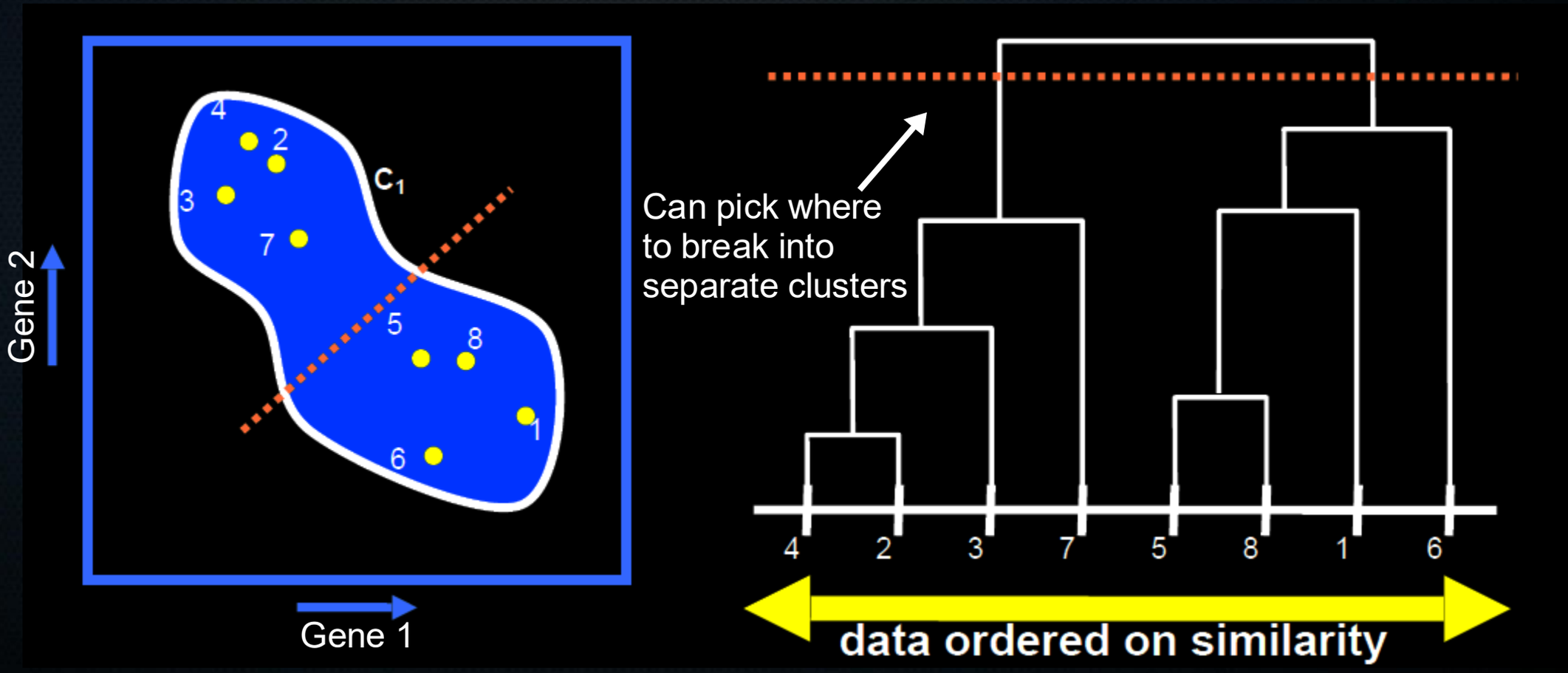
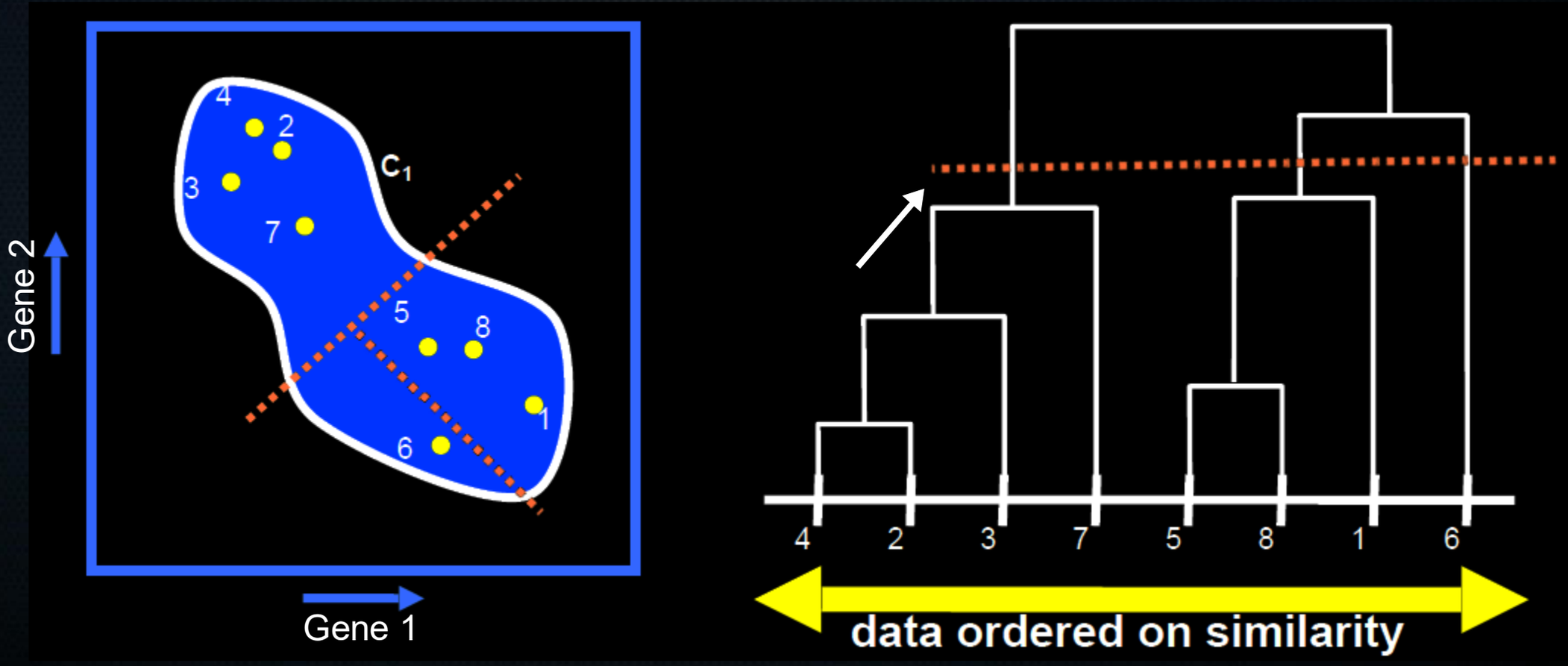


Source: Jeroen de Ridder

Agglomerative or hierarchical clustering

- Make clusters by cutting the tree at any position



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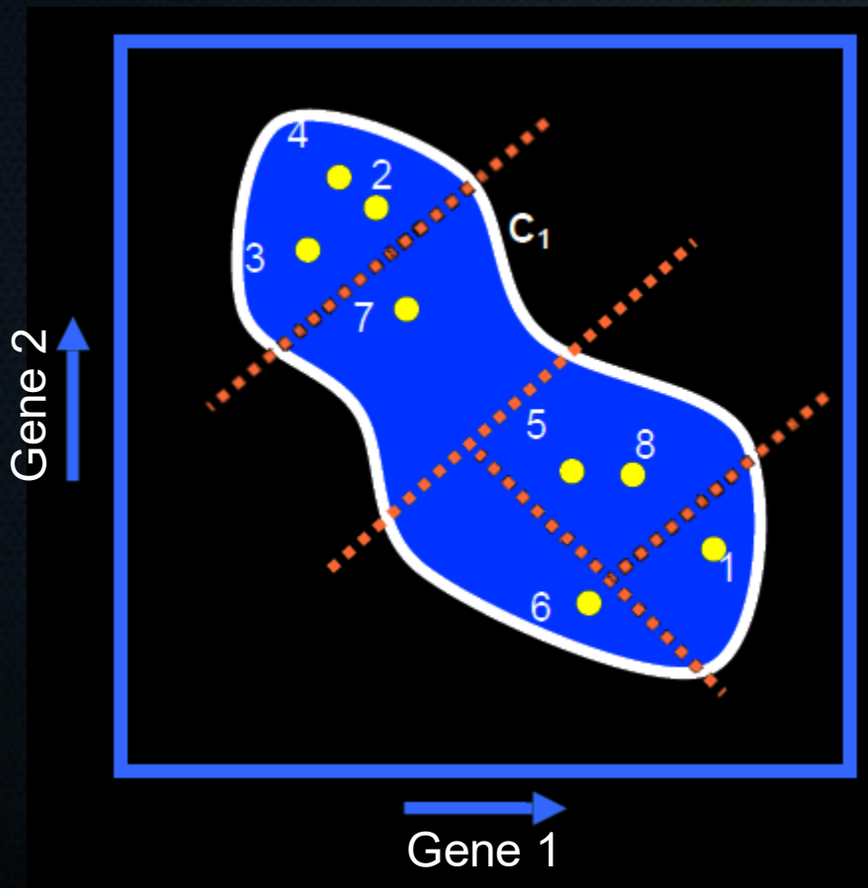

Dendrogram

Source: Jeroen de Ridder

Agglomerative or hierarchical clustering

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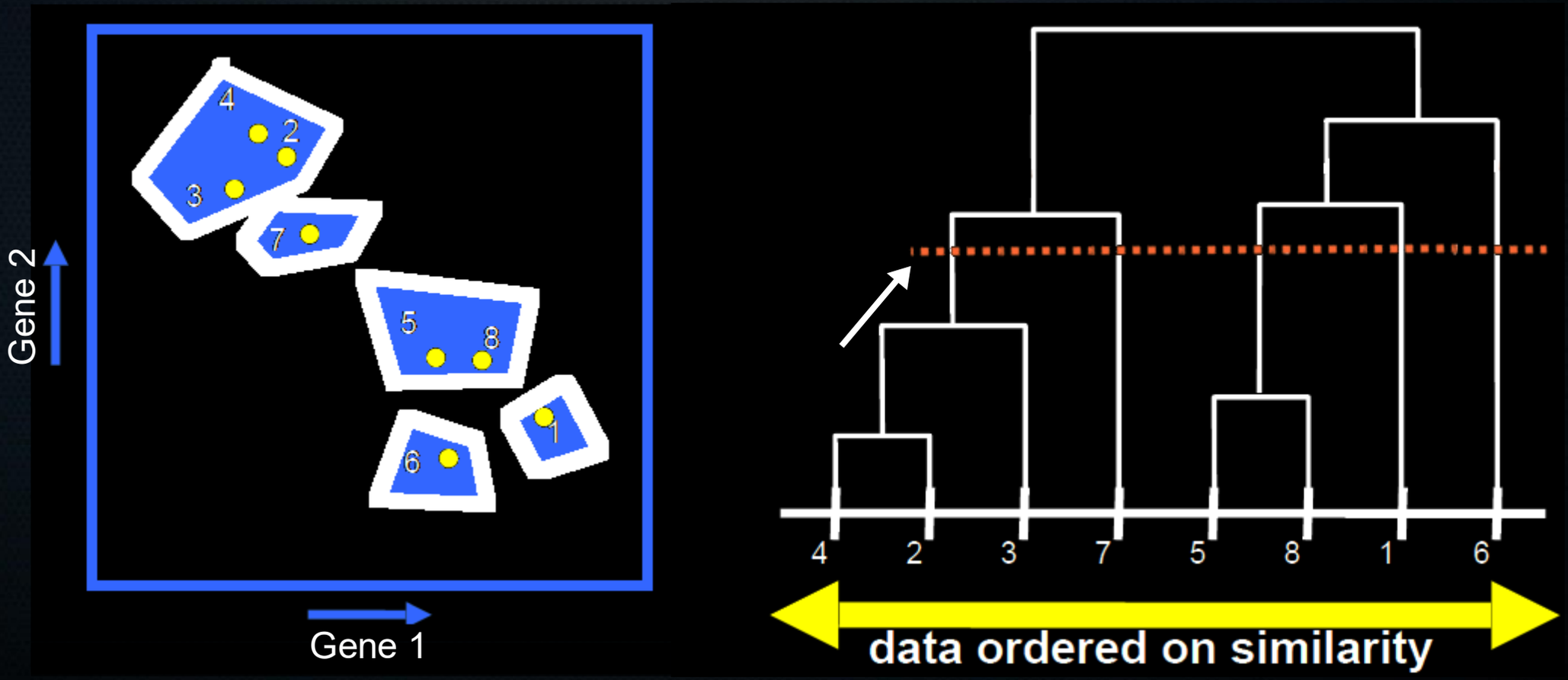

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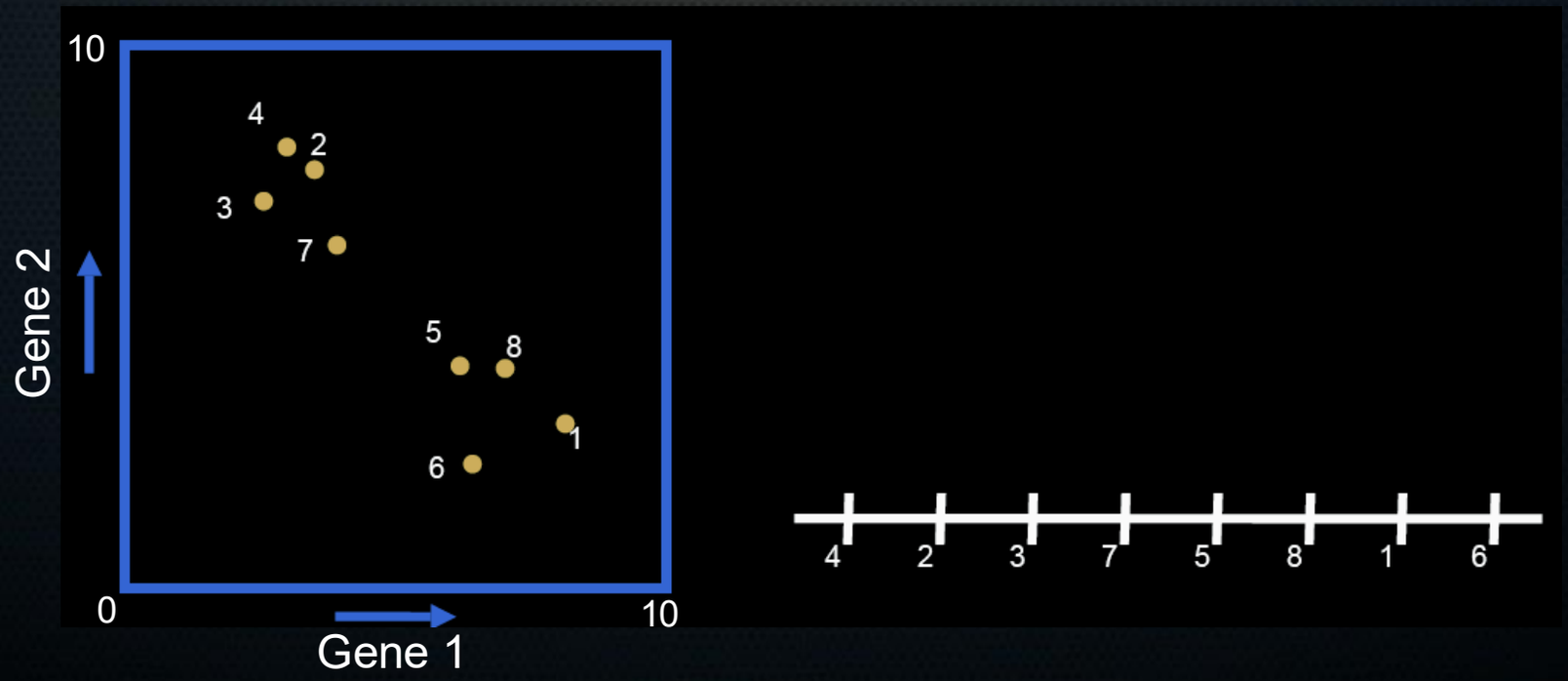
How do we define cluster similarity?

Cluster	Gene 1	Gene 2
1	8	3.5
2	3.2	7.6
3	2.5	7
4	2.9	7.8



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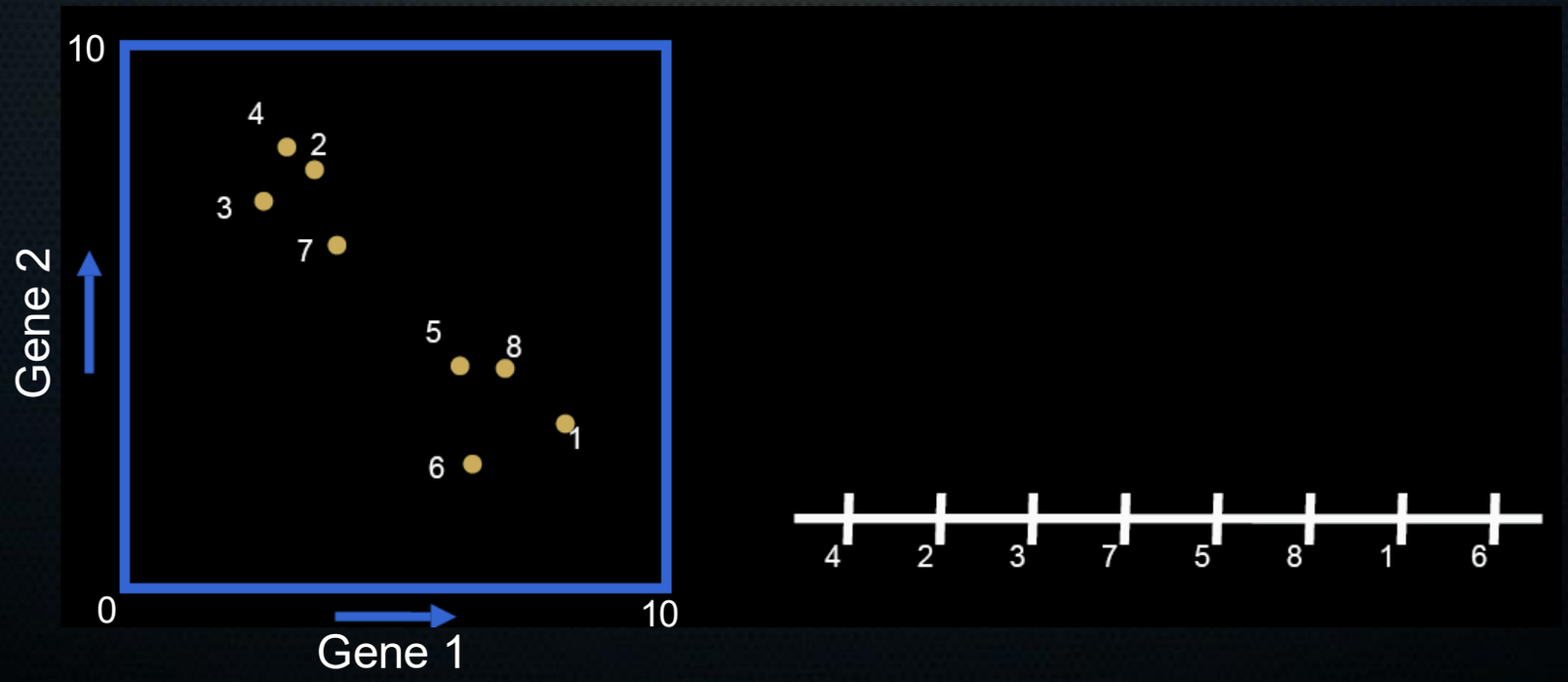
Distance	1	2	3	4
1	0			
2		0		
3			0	
4				0



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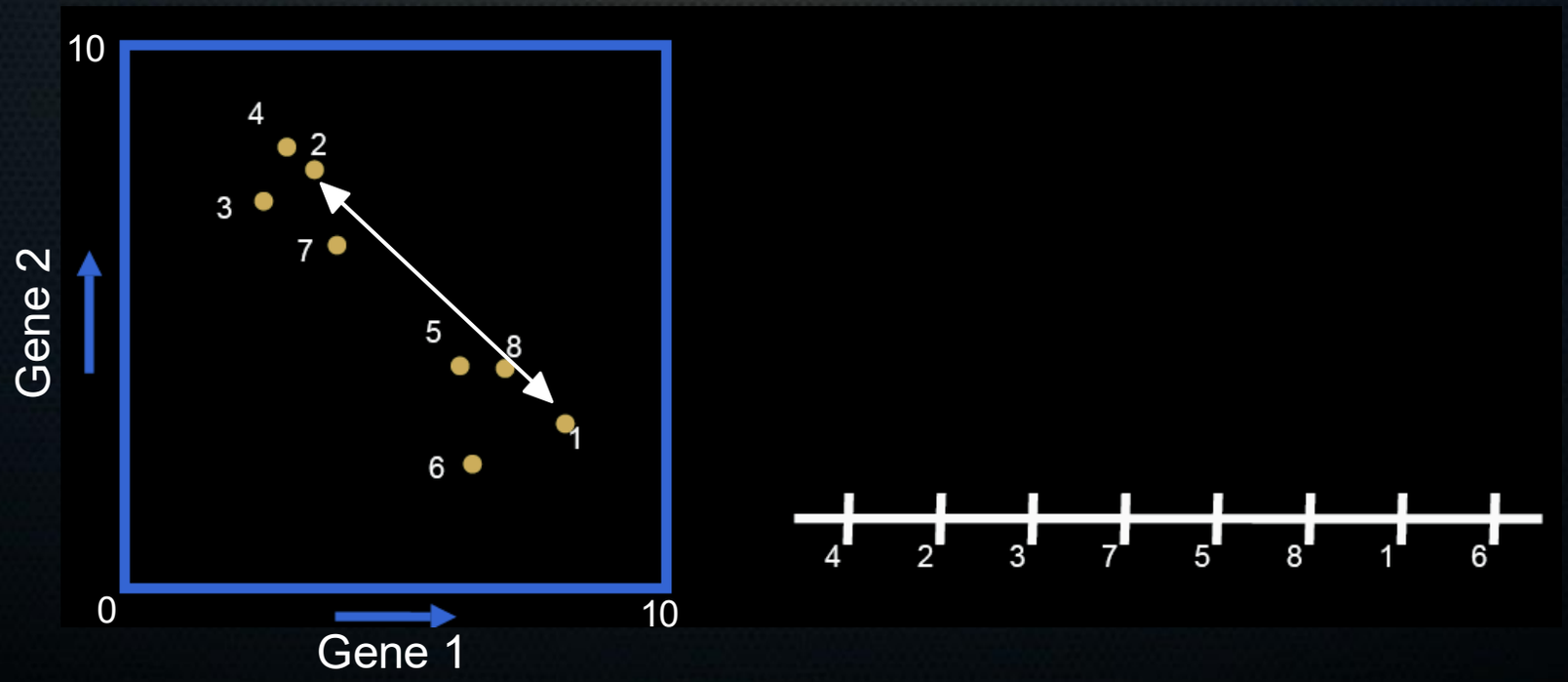

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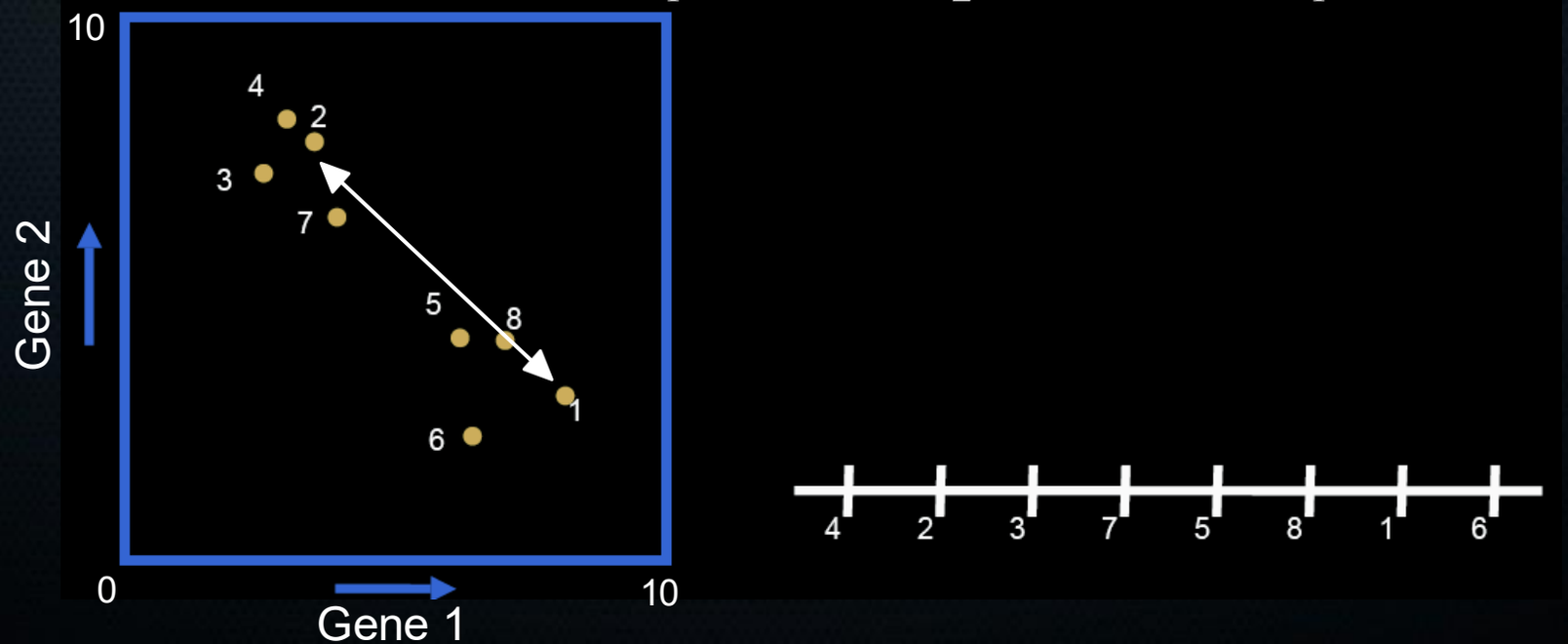
$$distance = \sqrt{(Gene1_1 - Gene1_2)^2 + (Gene2_1 - Gene2_2)^2}$$



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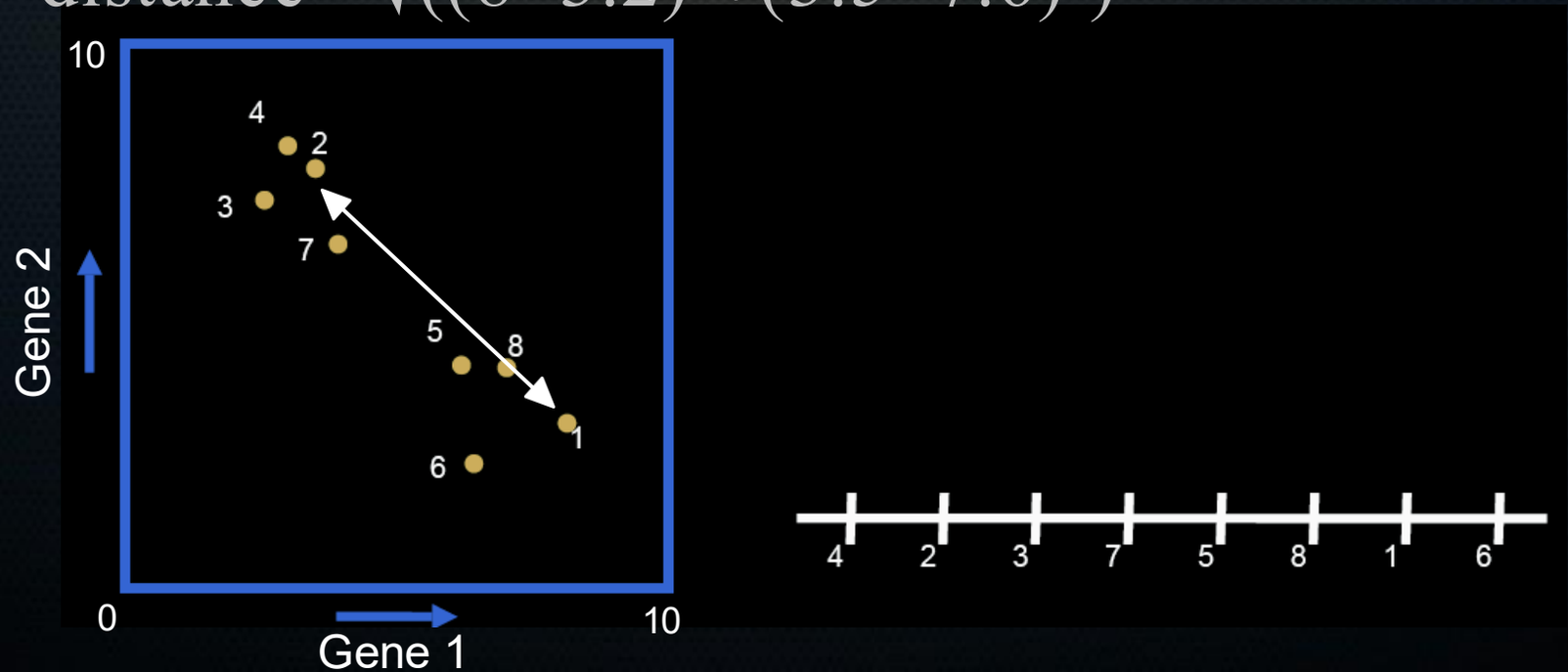
$$distance = \sqrt{((8-3.2)^2+(3.5-7.6)^2)}$$



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Distance	1	2	3	4
1	0	6.31		
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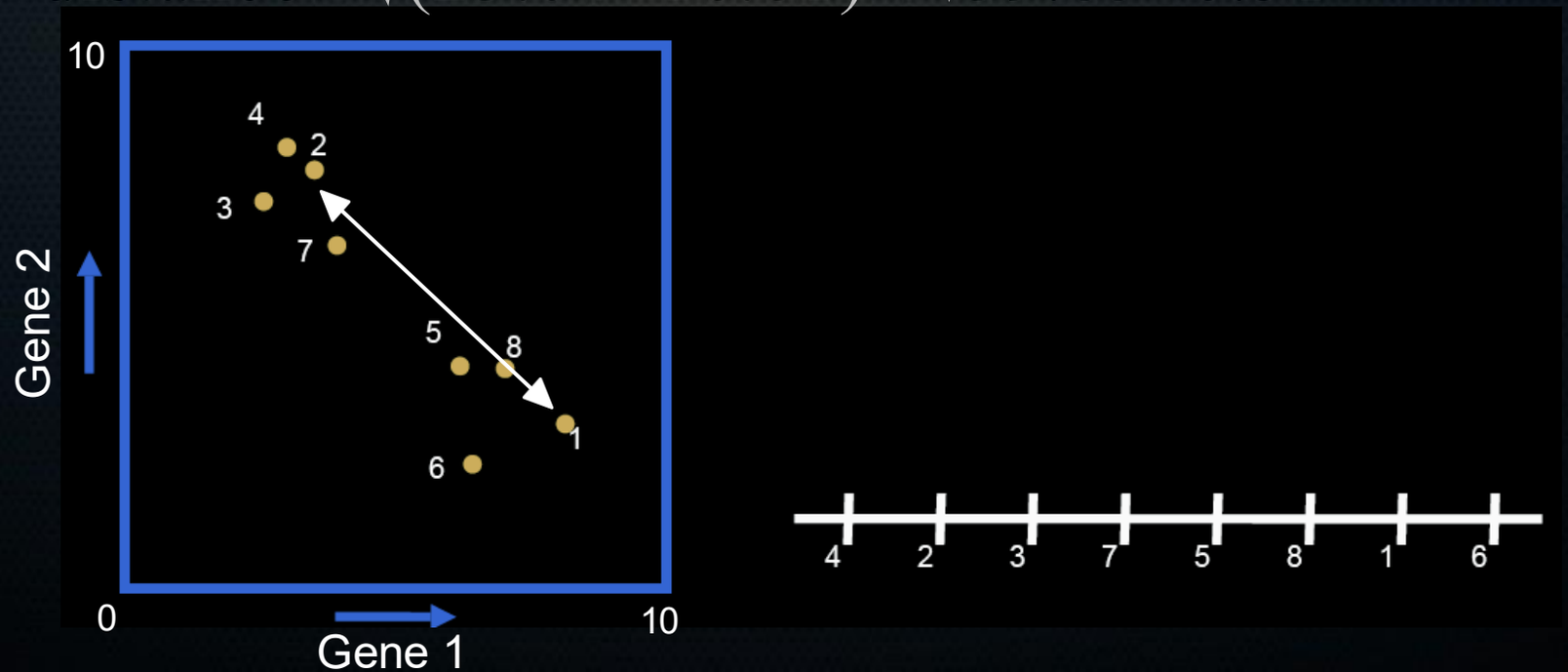
3			0	
4				0

$$\text{distance} = \sqrt{(23.04 + 16.81)} = \sqrt{39.85} \approx 6.31$$



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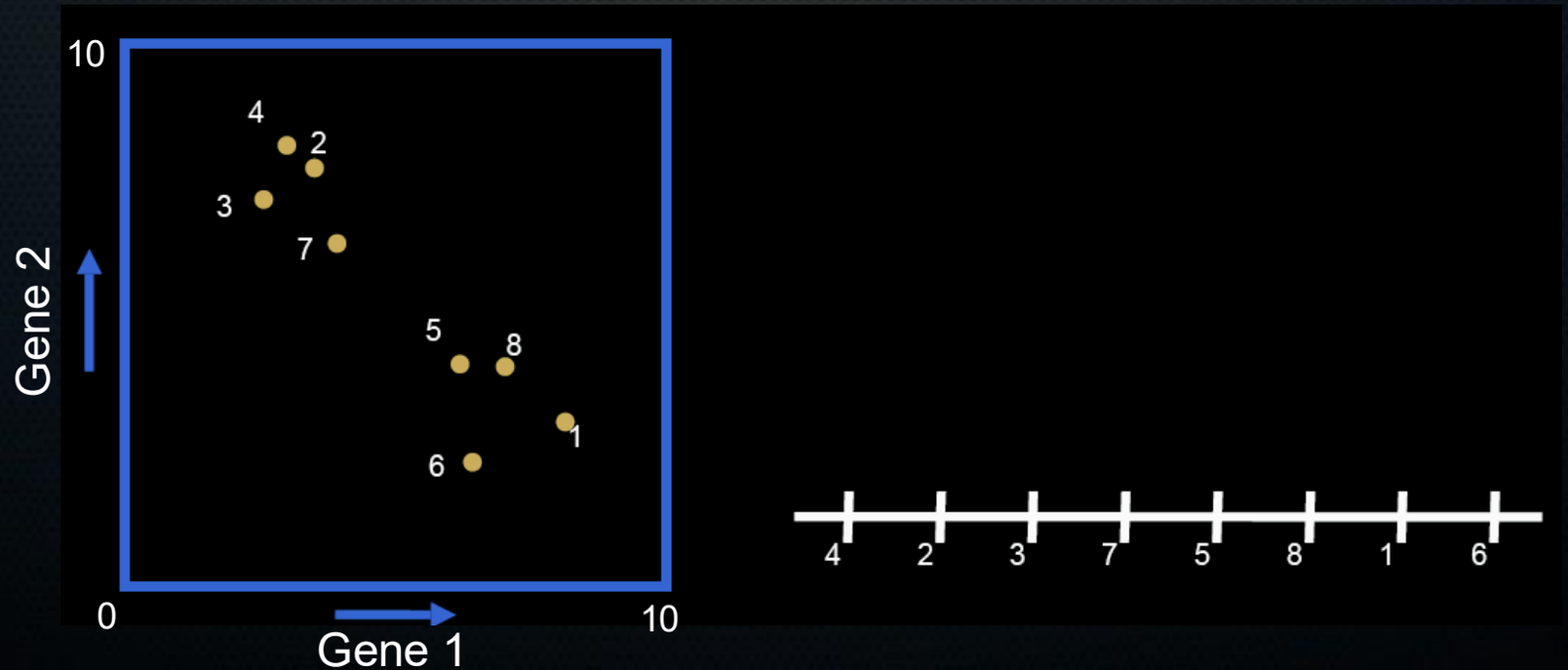

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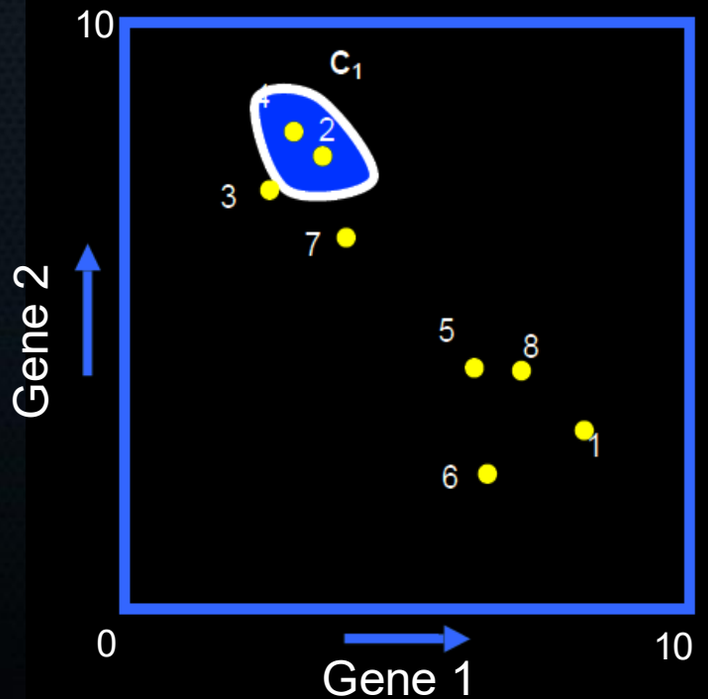
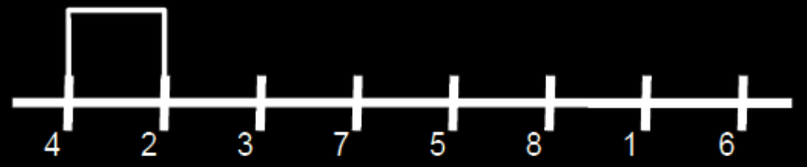
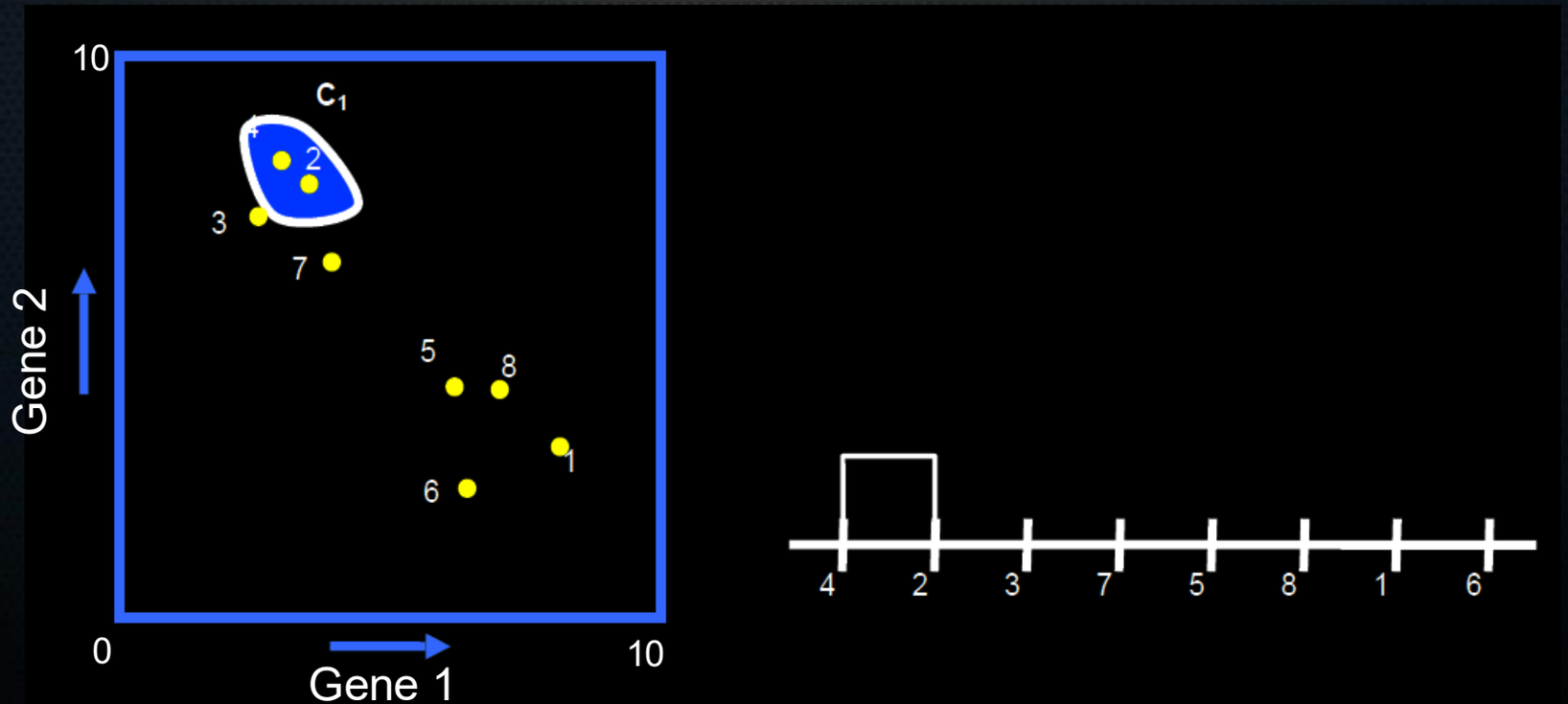




How do we define cluster similarity?

Cluster	Gene 1	Gene 2
1	8	3.5
2+4	?	?
3	2.5	7

Distance	1	2+4	3
1	0	-	-
2+4	?	0	-
3	6.52	?	0



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- Three main methods (but there are *MANY*):

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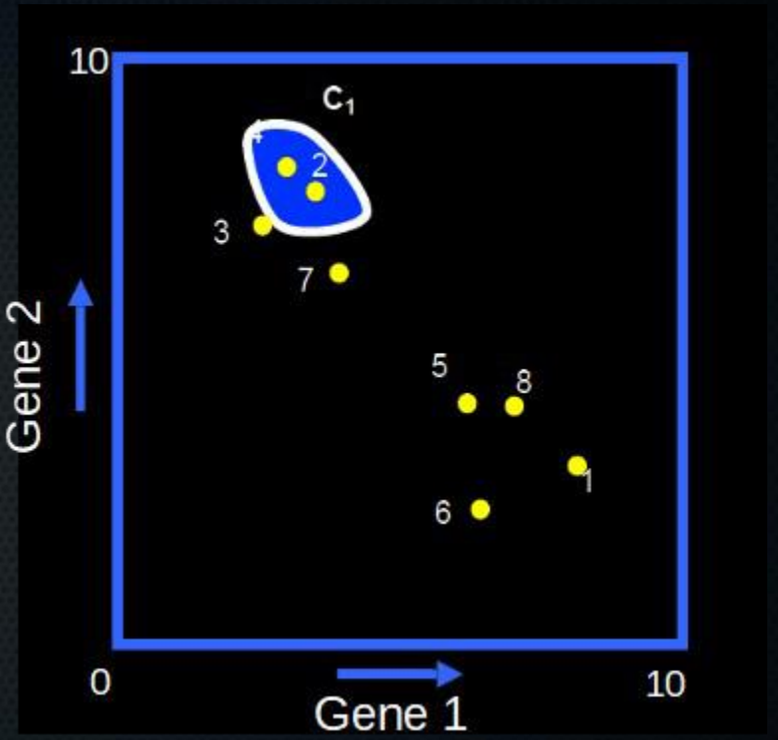
  - **Average linkage (UPGMA)**
    Make centroids: distance to a cluster is distance to its mean features



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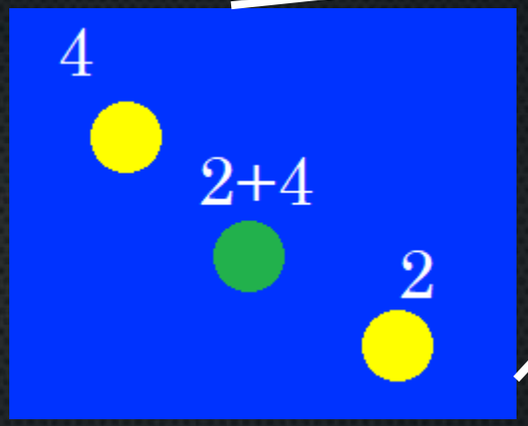

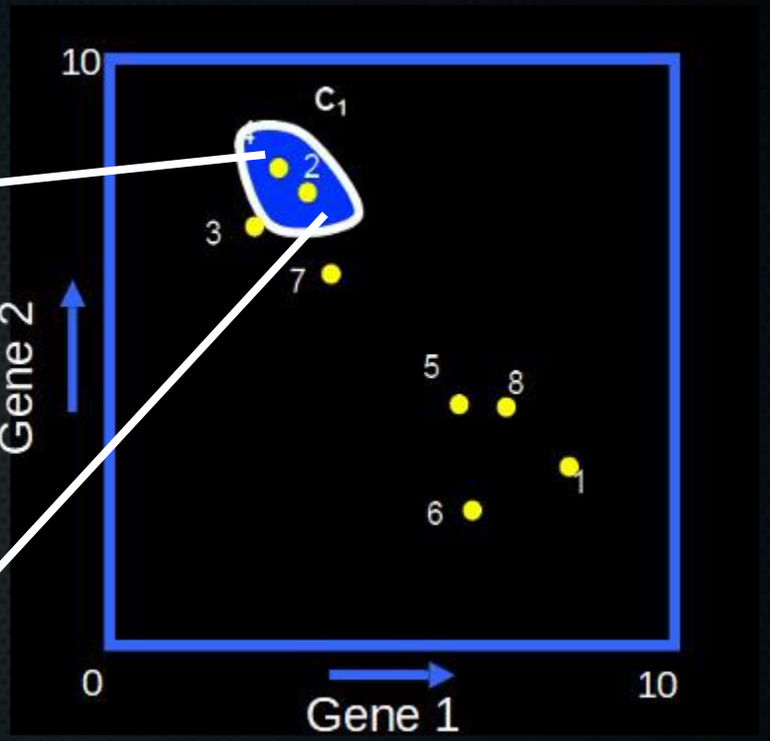

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→

Cluster	Gene 1	Gene 2
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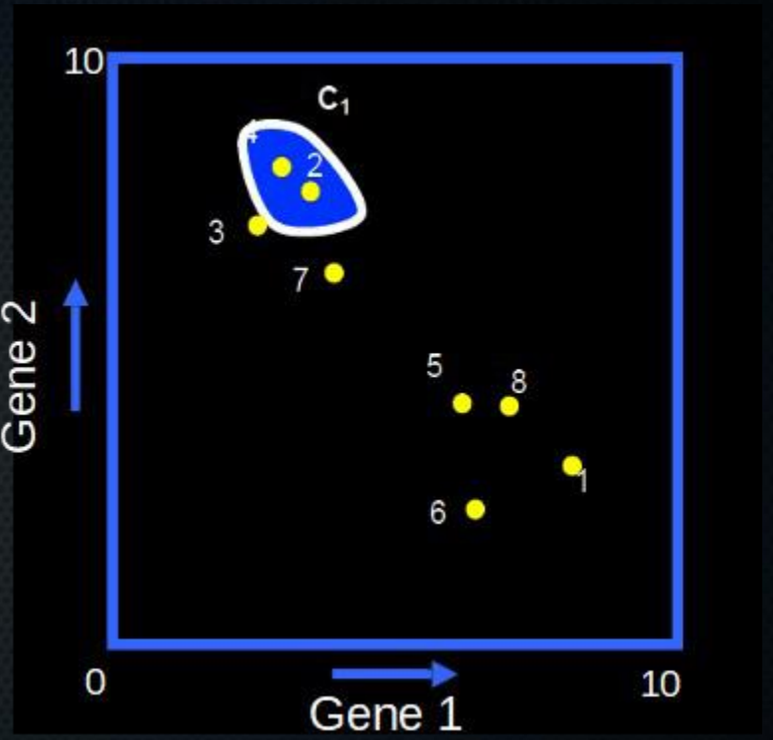
2+4	3.05	7.7
3	2.5	7

How do we define cluster similarity?

- Three main methods:
  - Average linkage (UPGMA)
  - **Single linkage**
    Distance between two clusters = distance between their closest component points



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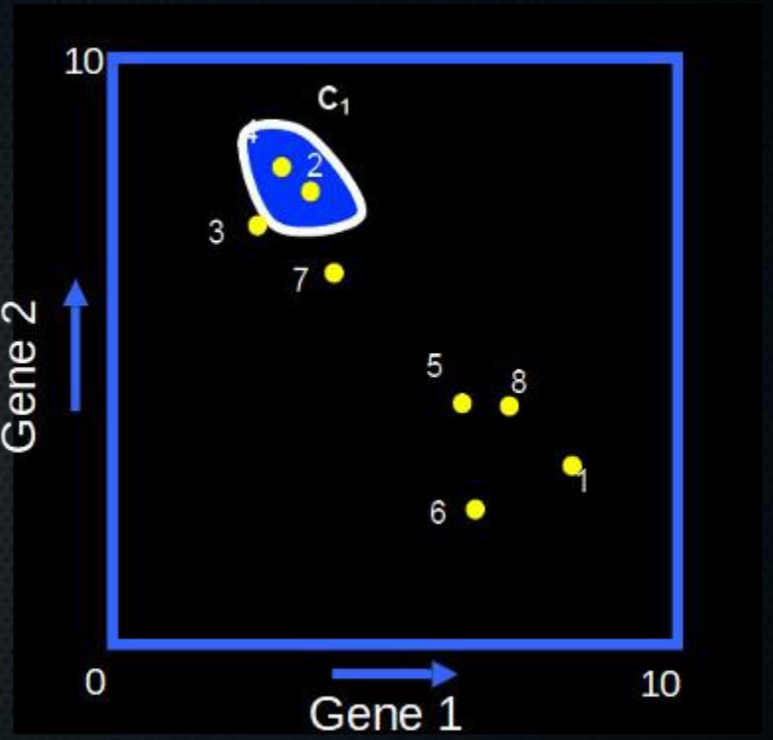

Distance between 3 and 2+4?

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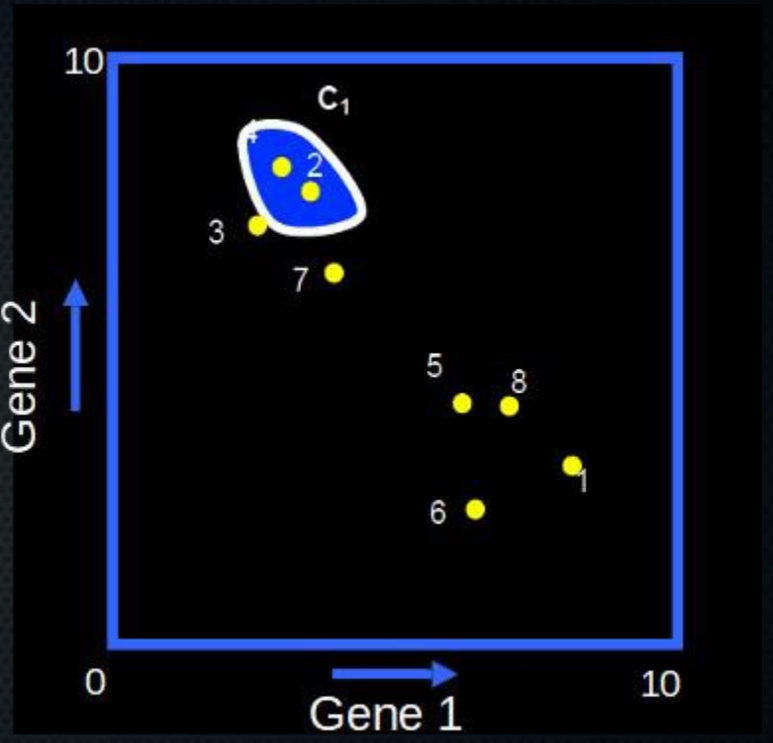

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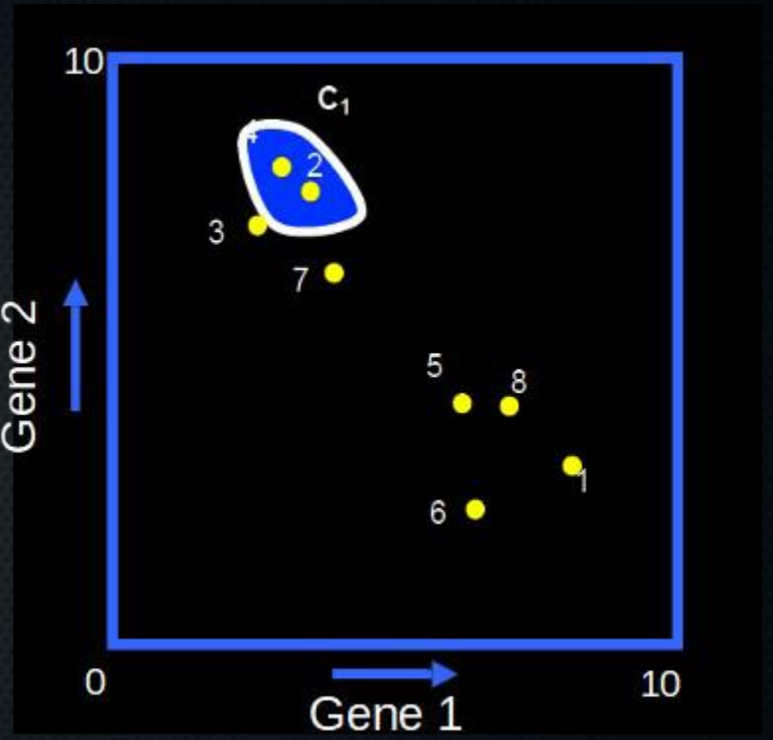
How do we define cluster similarity?

- Three main methods:
  - Average linkage (UPGMA)
  - Single linkage
  - **Complete linkage**
    Distance between two clusters = distance between their furthest component points



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How do we define cluster similarity?

- Three main methods:
  - Average linkage (UPGM
  - Single linkage
  - Complete linkage
- Quite different results:

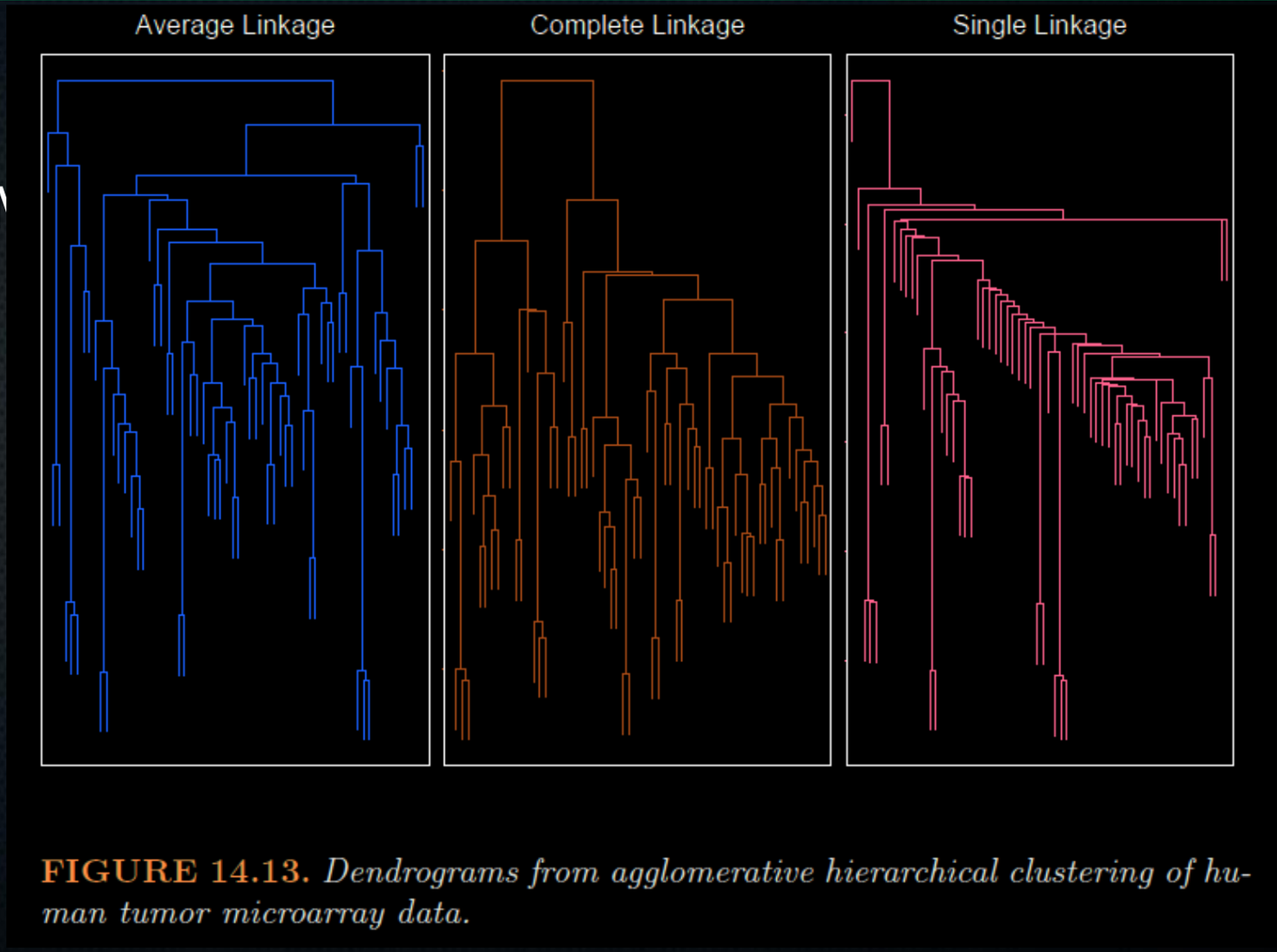

FIGURE 14.13. *Dendrograms from agglomerative hierarchical clustering of human tumor microarray data.*

Source: Hastie, T., Tibshirani, R., & Friedman, J. (2009). The elements of statistical learning: data mining, inference, and prediction. Springer Science & Business Media.

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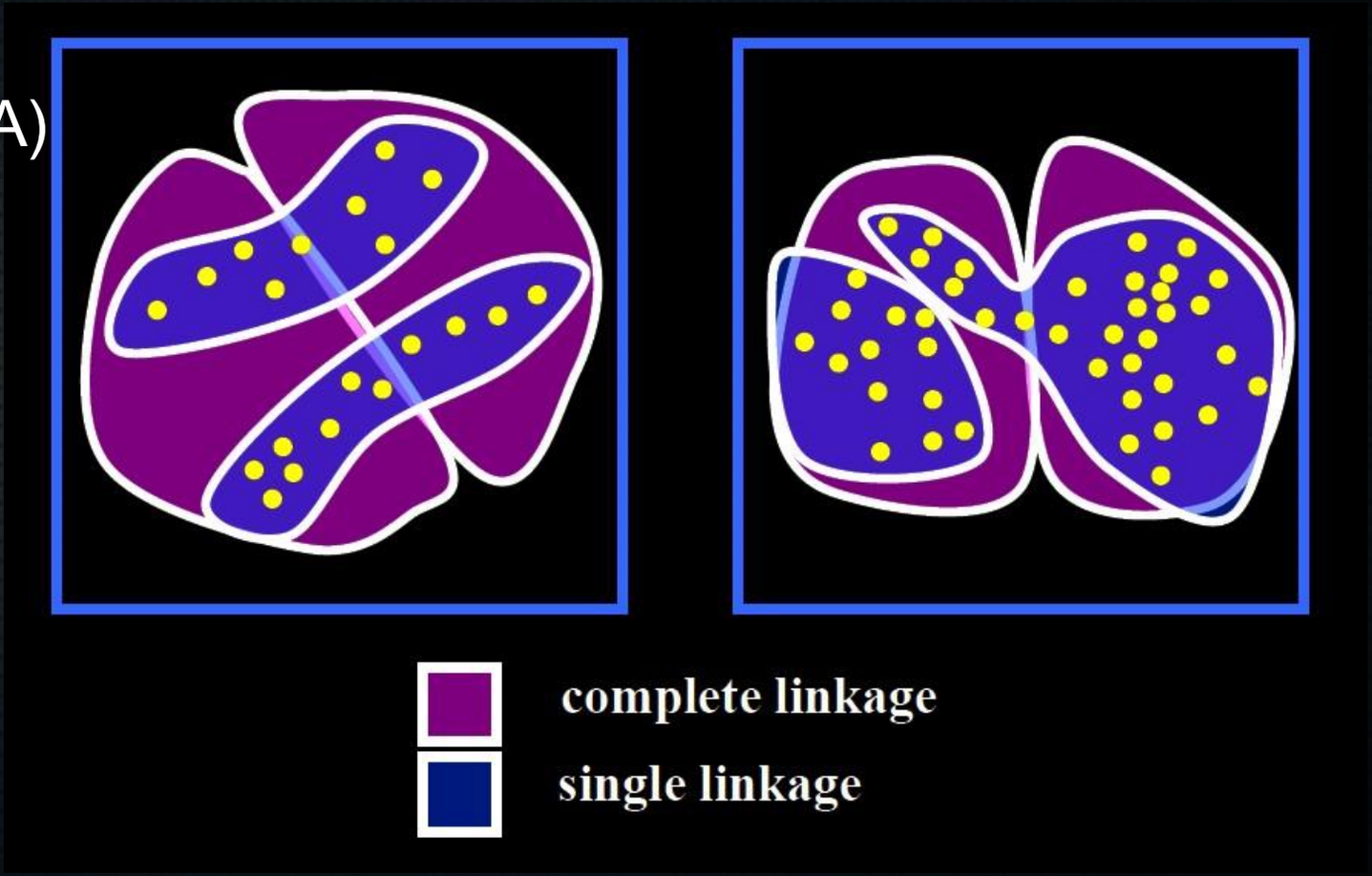
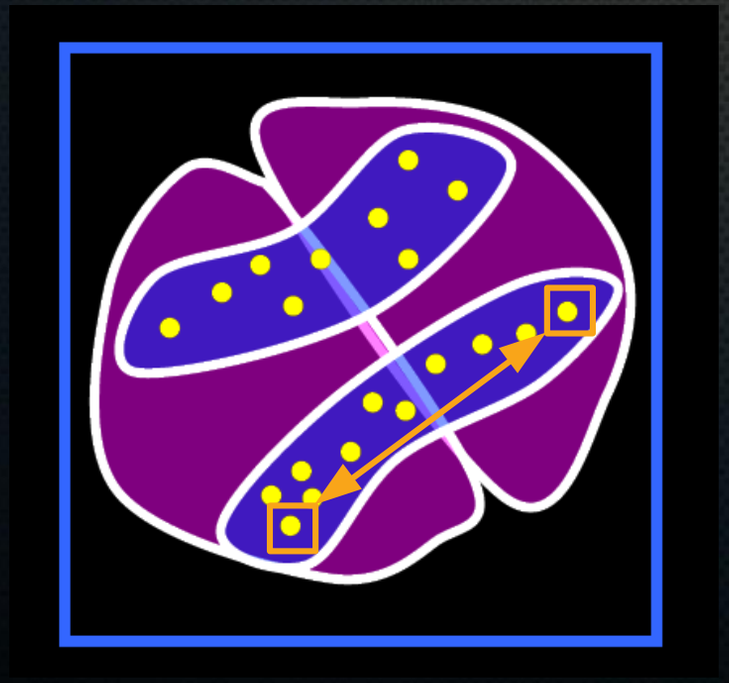
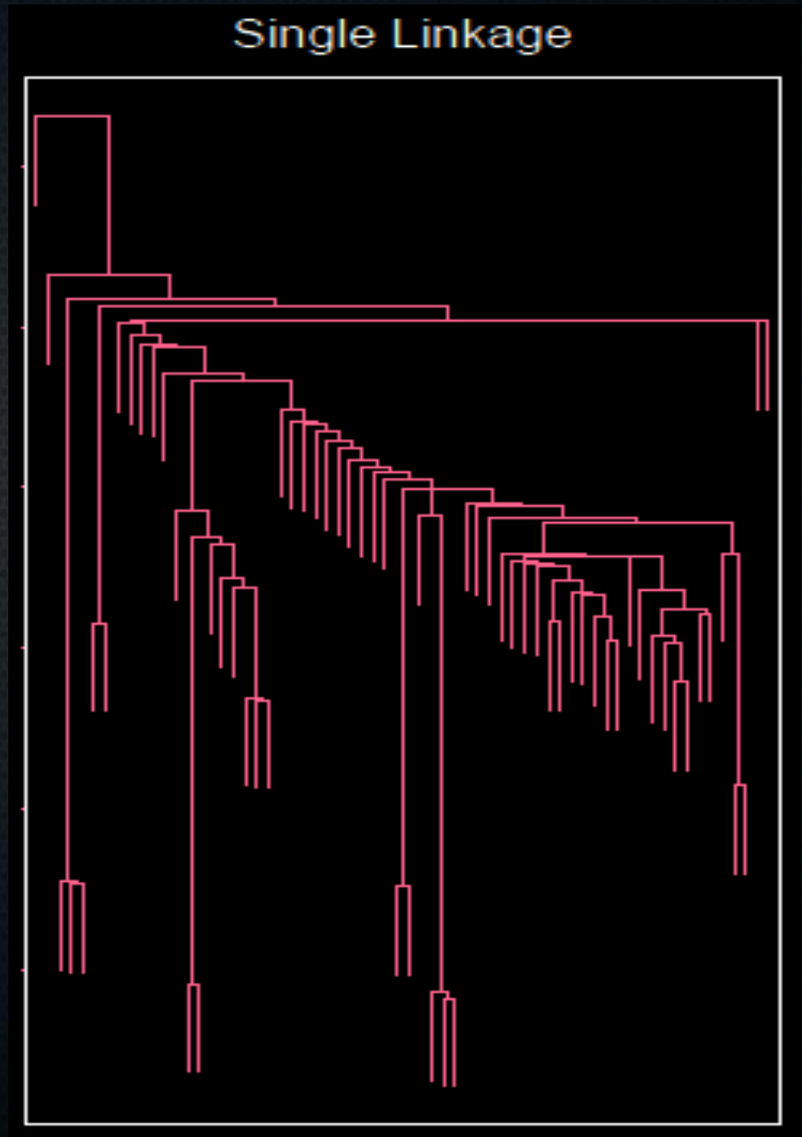


Source: Jeroen de Ridder

Which linkage method to pick?

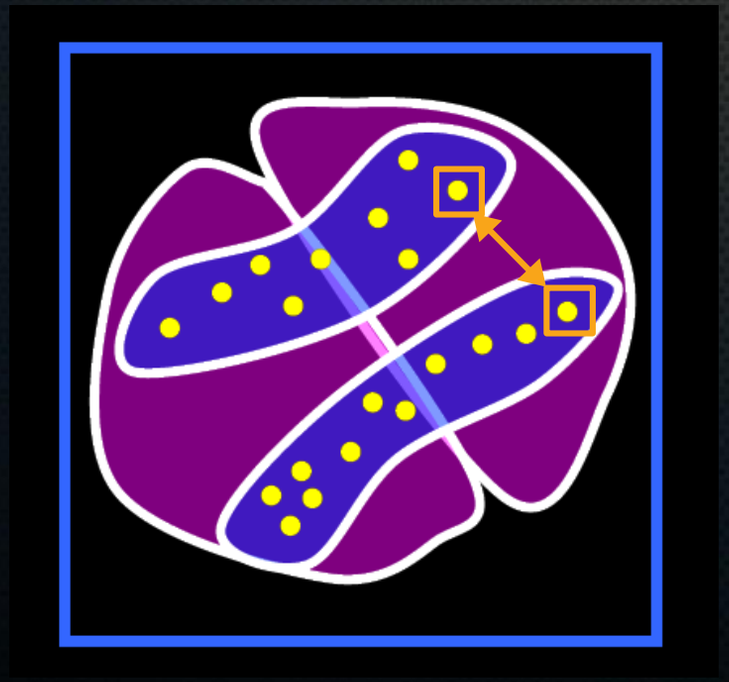
- Single linkage drawback:
  - Chaining → combines observations that are very far away by many small intermediate steps

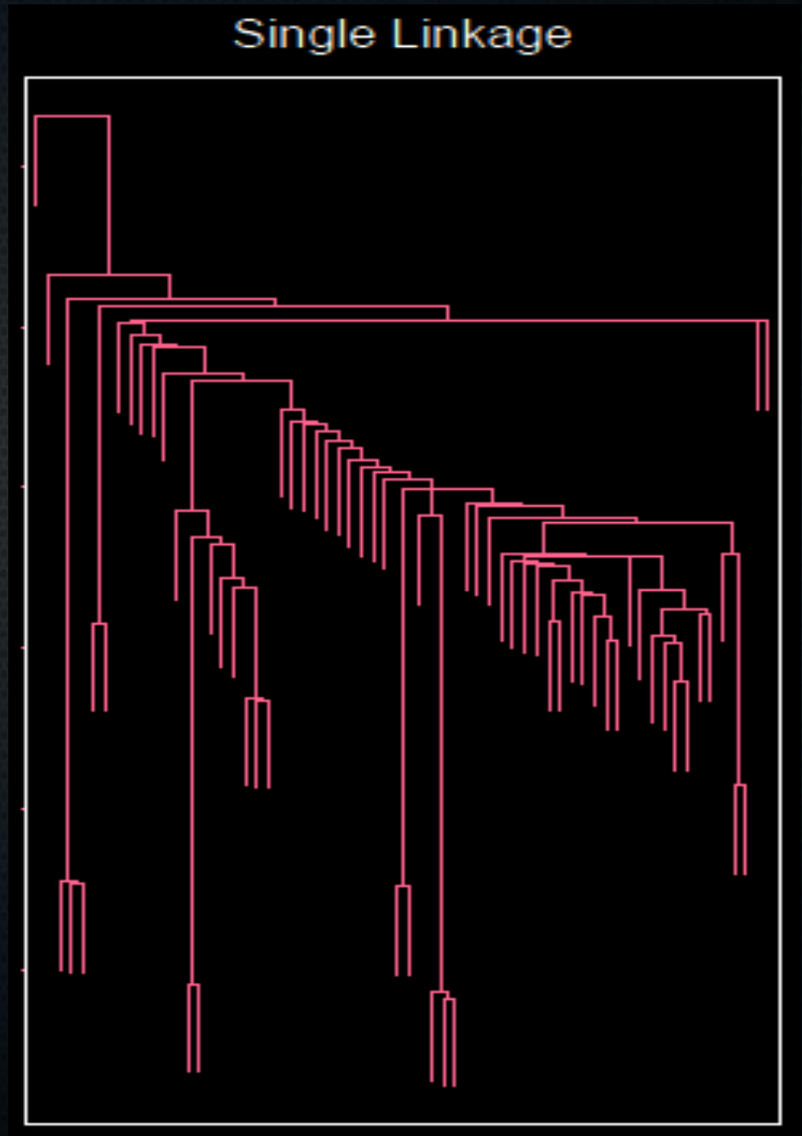




Which linkage method to pick?

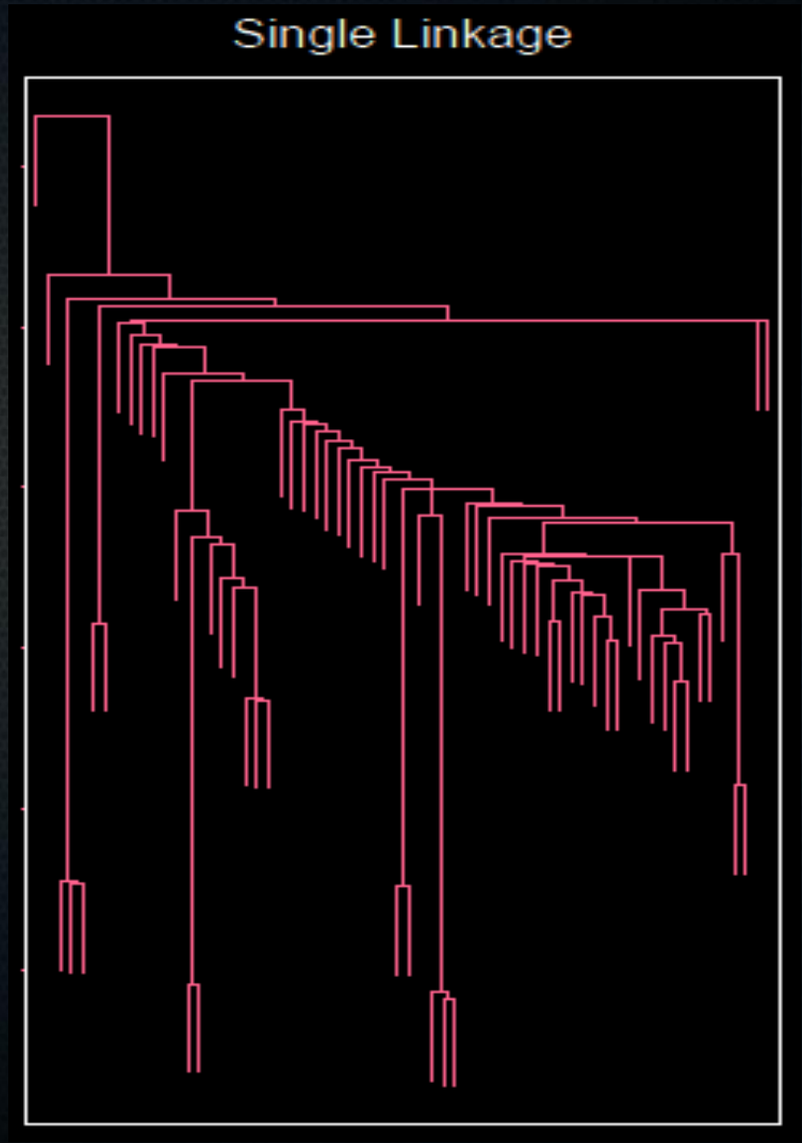
- Single linkage drawback:
  - Chaining → combines observations that are very far away by many small intermediate steps





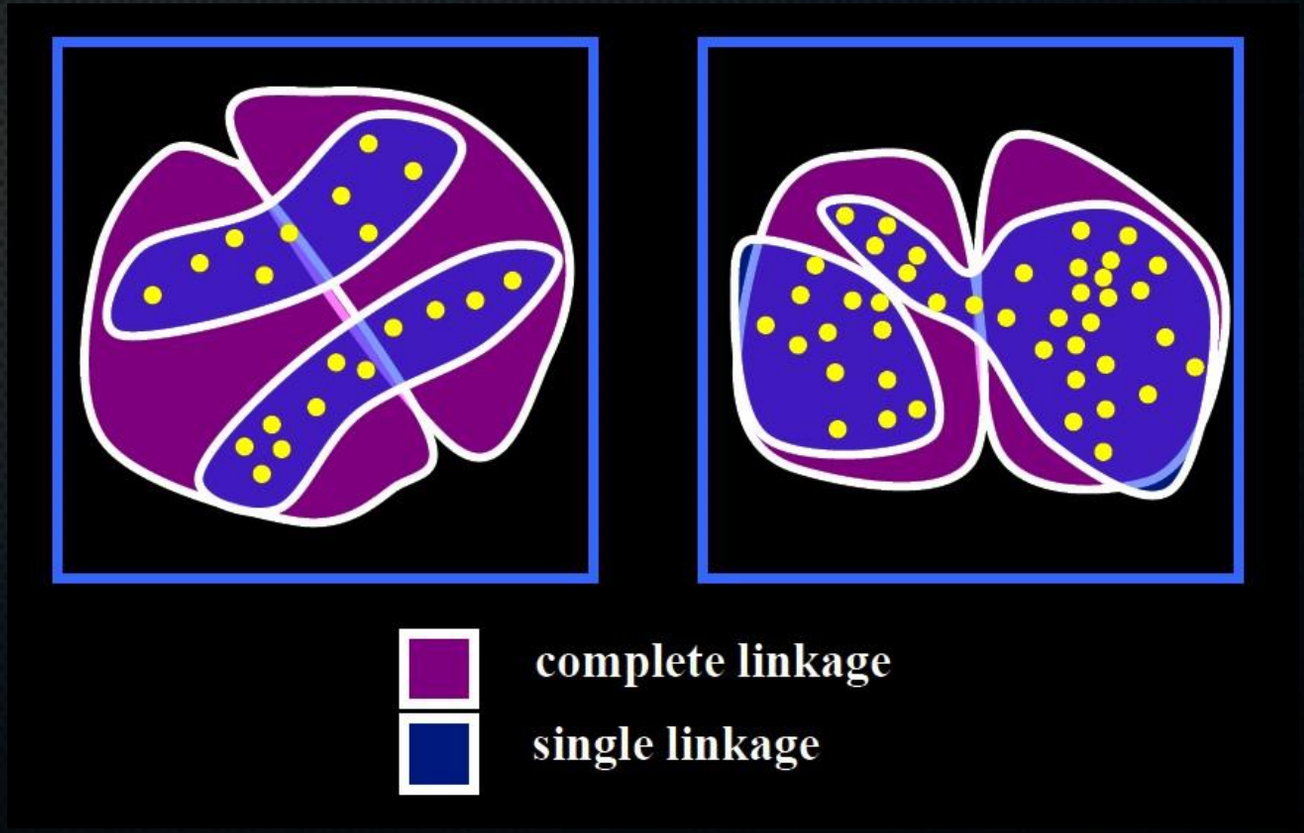
Which linkage method to pick?

- Single linkage drawback:
  - Chaining → combines observations that are very far away by many small intermediate steps
  - Doesn‘t lead to compact clusters



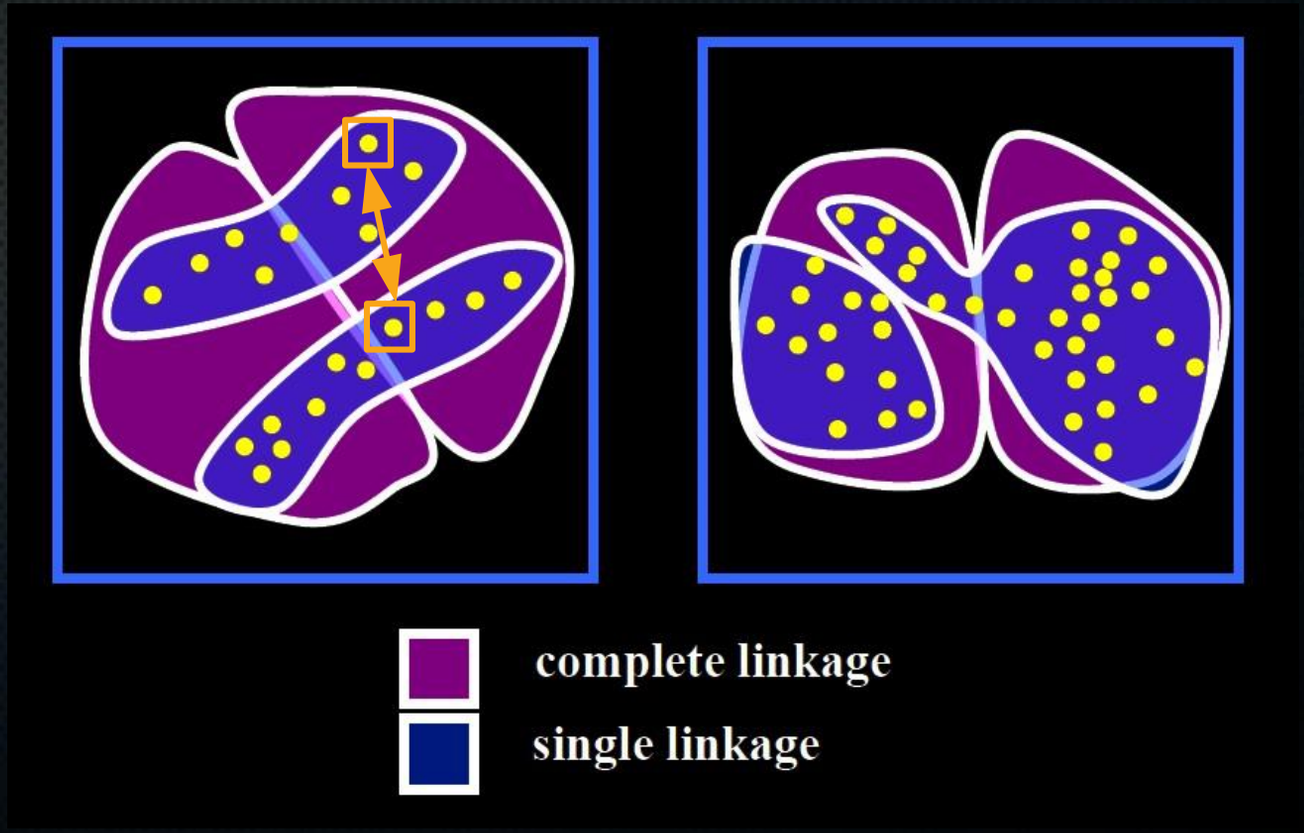
Which linkage method to pick?

- Complete linkage drawback:
  - Opposite problem: close only if close to all members of a group.



Which linkage method to pick?

- Complete linkage drawback:
  - Opposite problem: close only if close to all members of a group, so *samples* that are close can get assigned to very different clusters



Which linkage method to pick?

- Complete linkage drawback:
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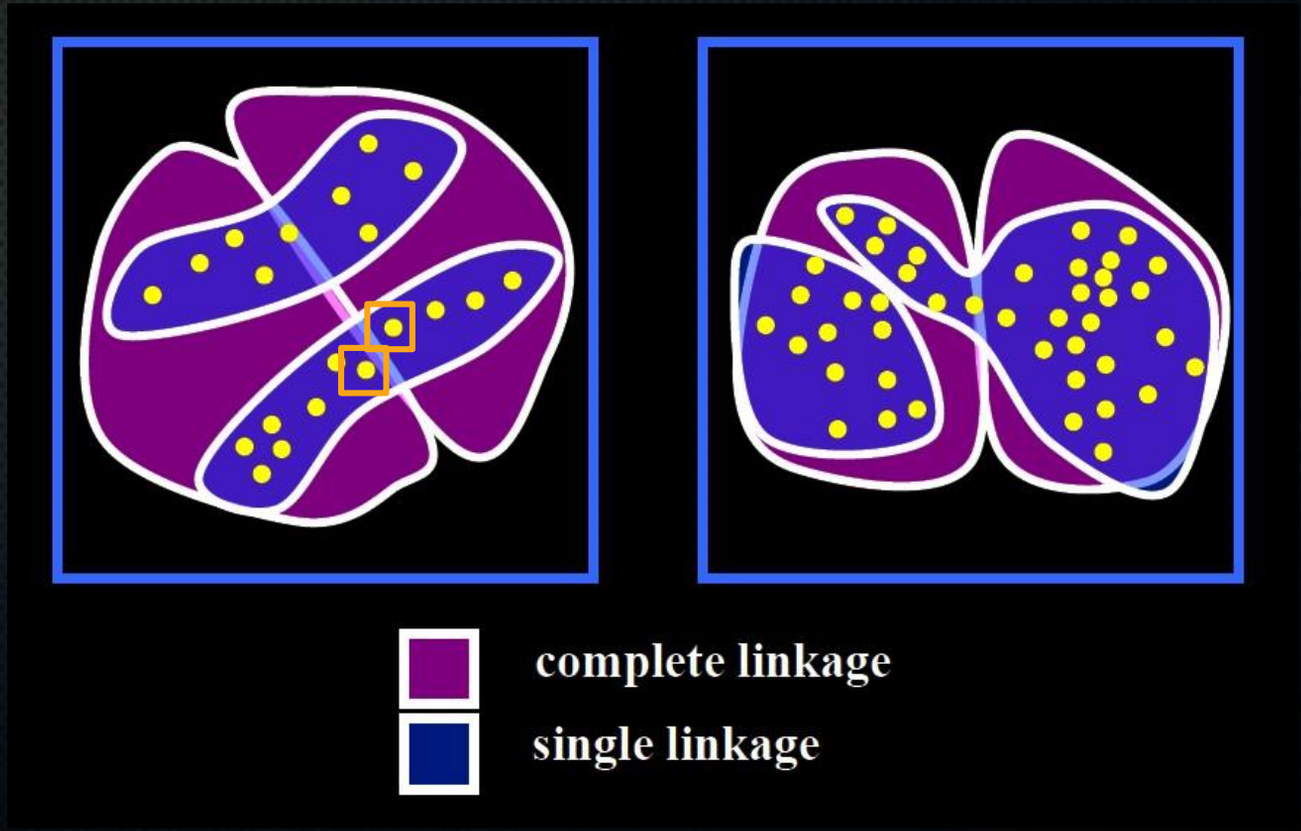
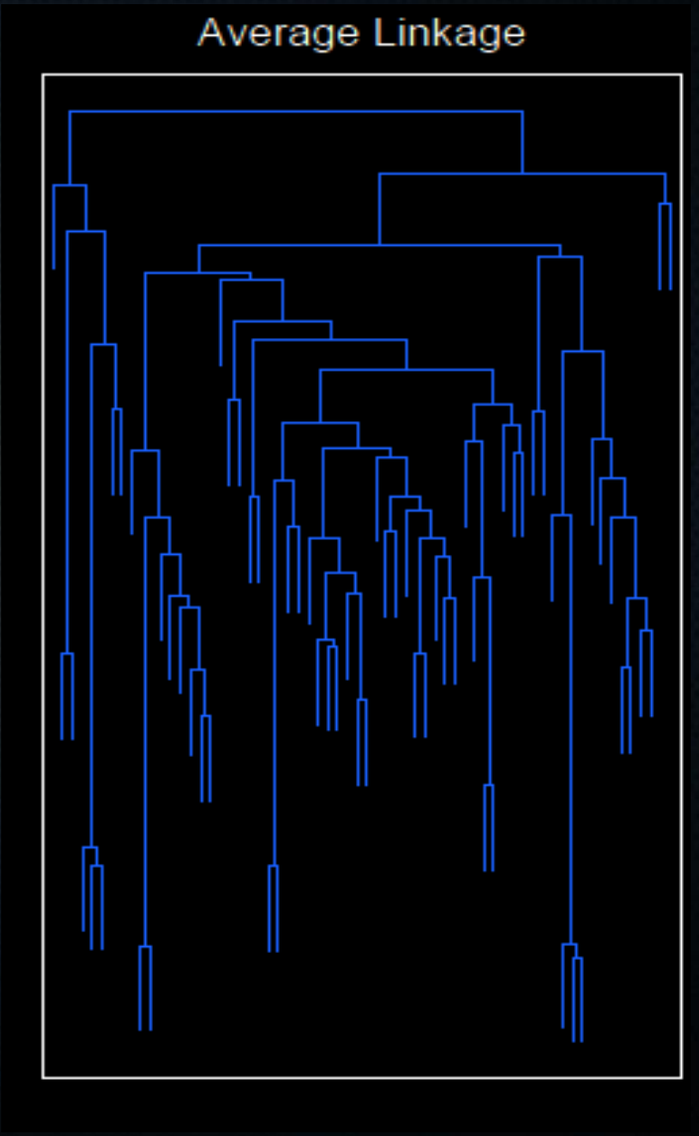


Which linkage method to pick?

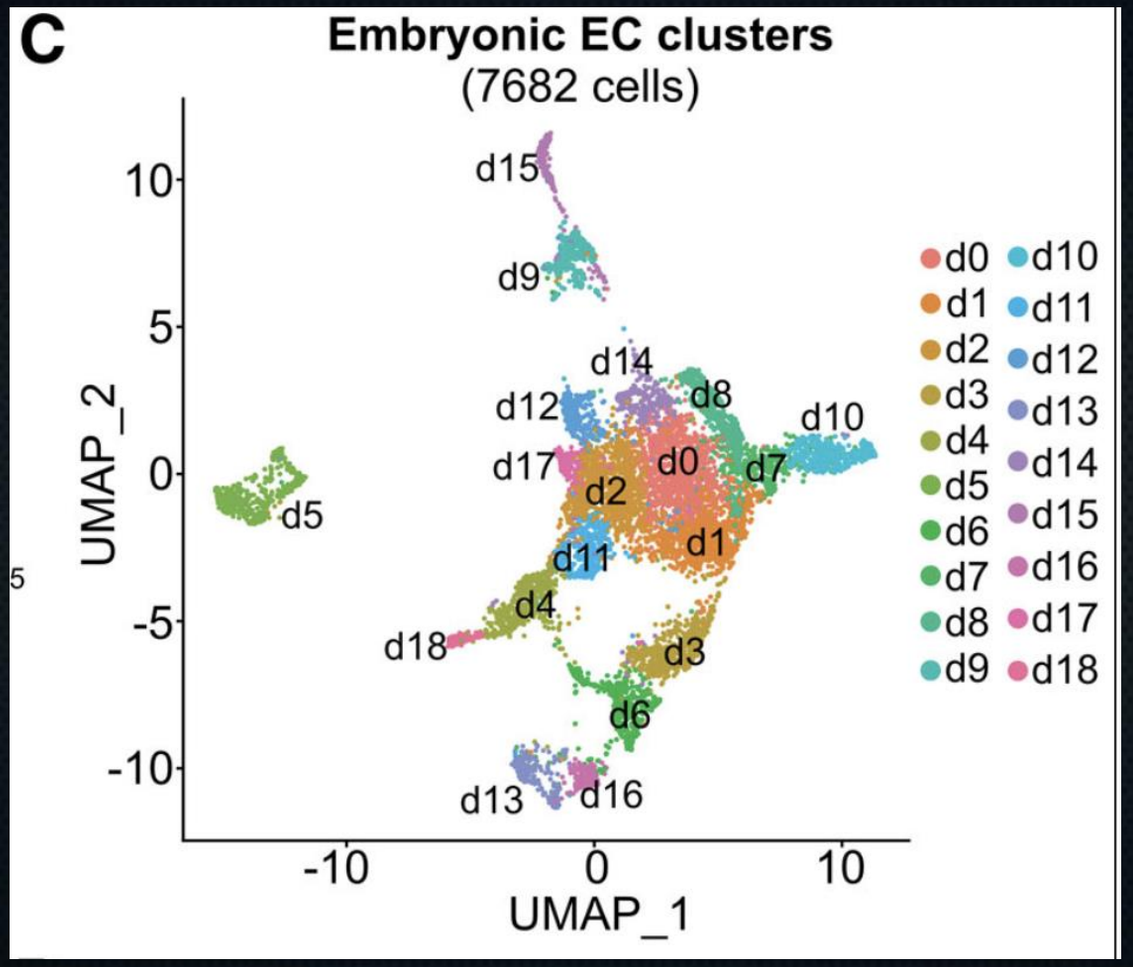
- Average linkage (UPGMA):
  - Compromise between the two.
  - Does depend on the numerical scale



Summary agglomerative/hierarchical clustering

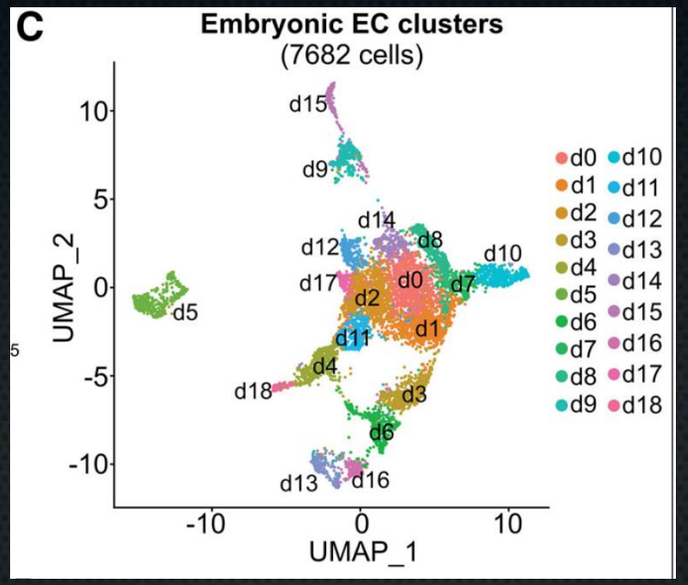
- Start with each data point in a cluster by itself
- Calculate distances between all clusters
- Join closest clusters together
- Recalculate distances (depending on linkage method!)
- Iterate until all clusters are connected
- Make clusters by ‚cutting through‘ the tree at any level of clustering.

Real life



https://www.ahajournals.org/doi/full/10.1161/CIRCRESAHA.123.323956

Real life



Find out with your neighbors:
- what did they do to get these clusters (see supplement page 3)
- Go as deep as you can. What are they doing with these neighbours? What data preprocessing do they do?

Break for short practical