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# Case study 1: Model selection for clustering

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# Overview

- What is Model selection?
- Challenges in model selection for clustering
- Clustering algorithms
- Colorectal Tissue Biopsy and Clustering

- Your task and dataset details
- Expected results
- Summary

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# Model selection

- Choosing the best model candidate
  - family of algorithms (e.g. Logistic regression, KNN)
  - different hyperparameters (e.g. regularisation strength, number of neighbours)

- What is ‘the best model’?
  - Define objective (e.g. accuracy, minimise false positives, etc)
  - Complexity
  - Computability
  - Ease of Implementation

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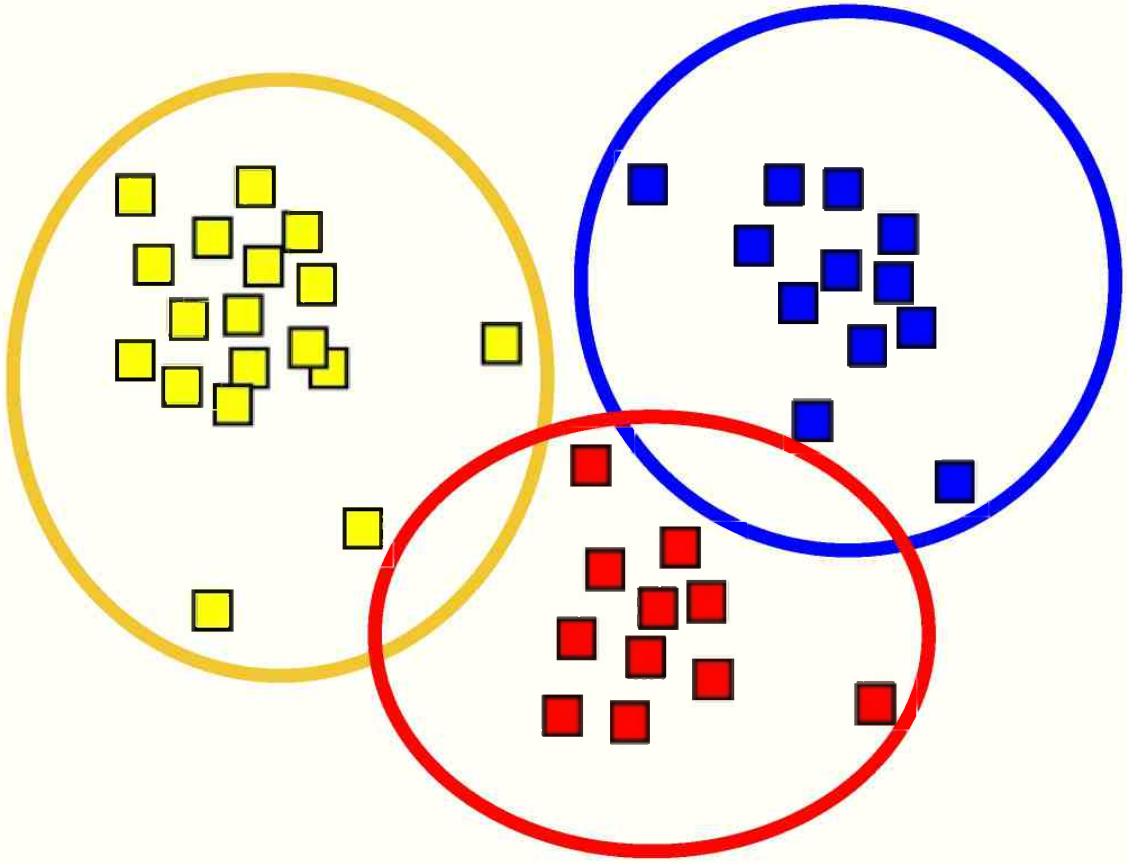
# Why do we need model selection for clustering?



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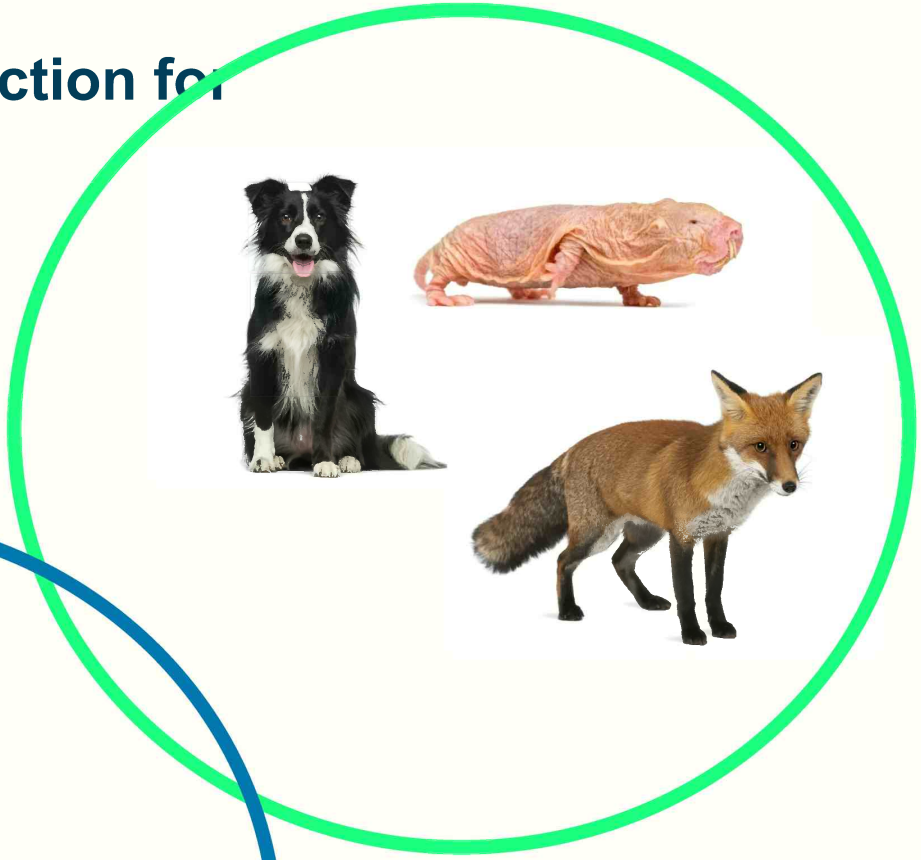

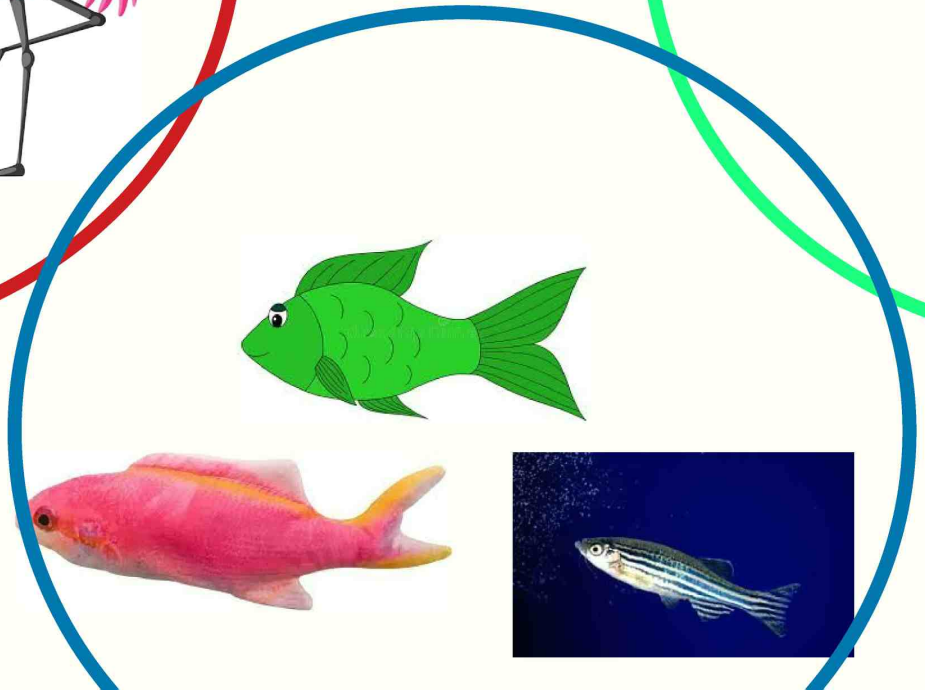

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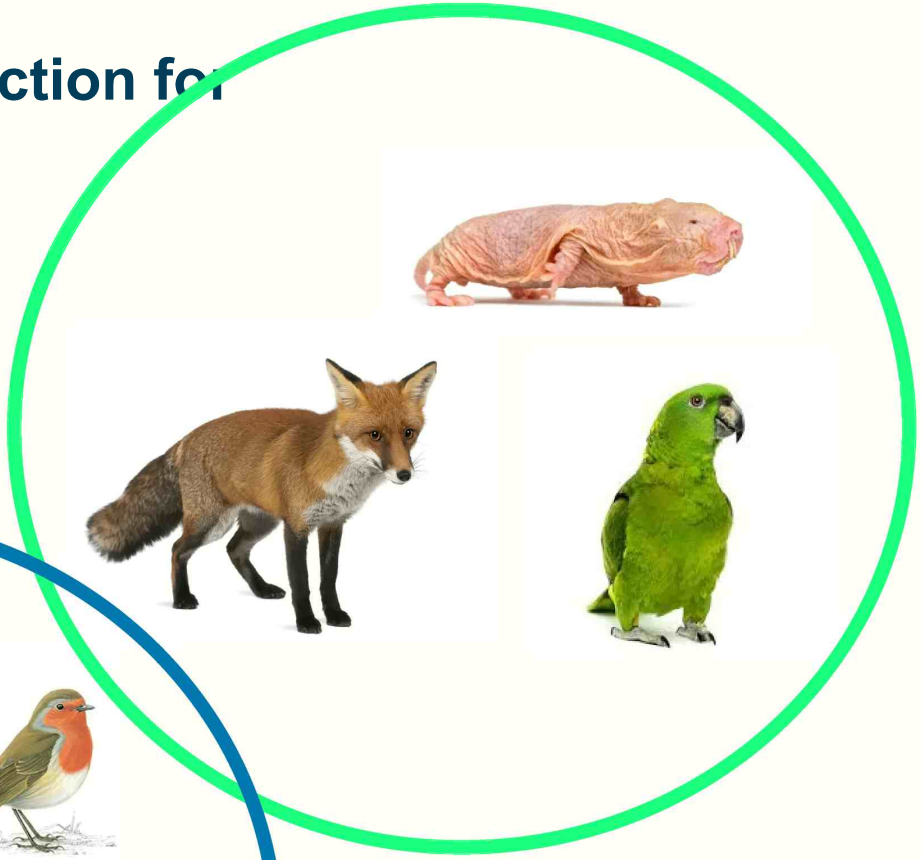

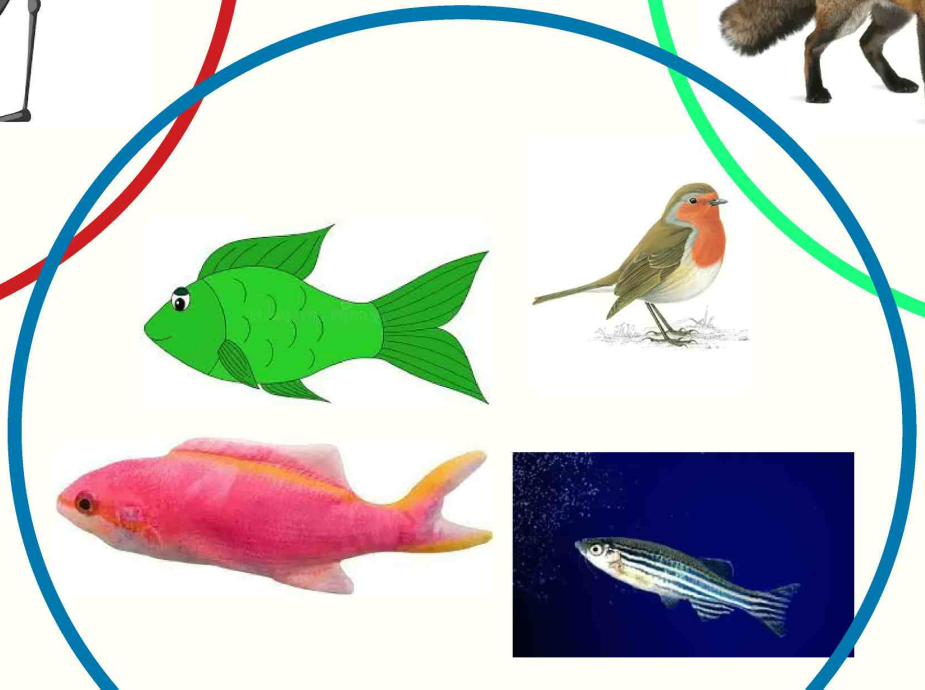

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# Why do we need model selection for clustering?

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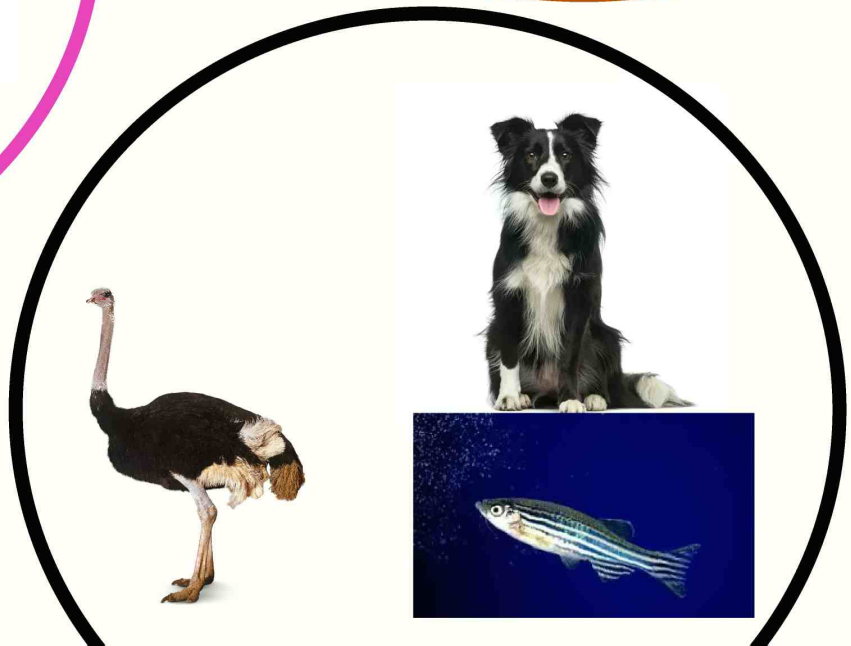

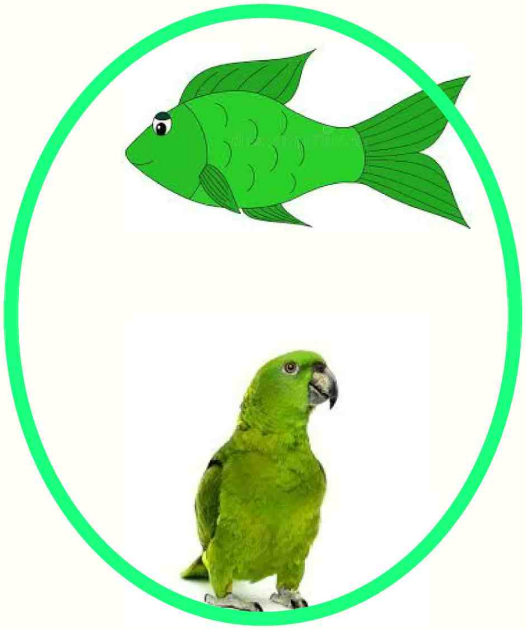

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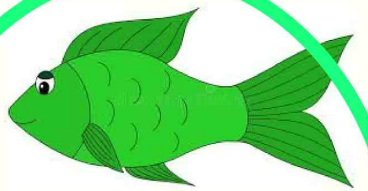

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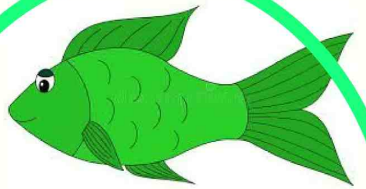

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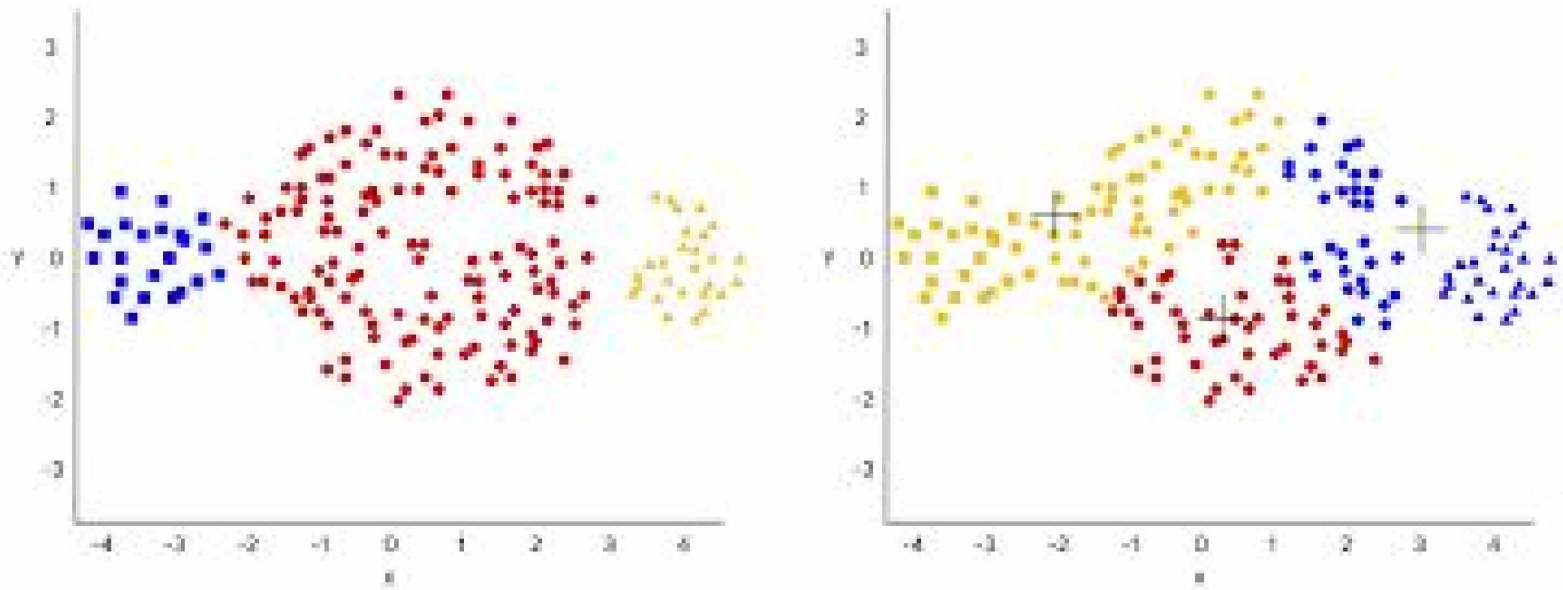
# Why do we need model selection for clustering?

- Group similar objects together
- Constraints on clusters
- Understand the structure of a dataset

The best clustering model will best describe the structure of the data.



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# Examples of clustering algorithms

Cluster numbers can be explicitly specified:

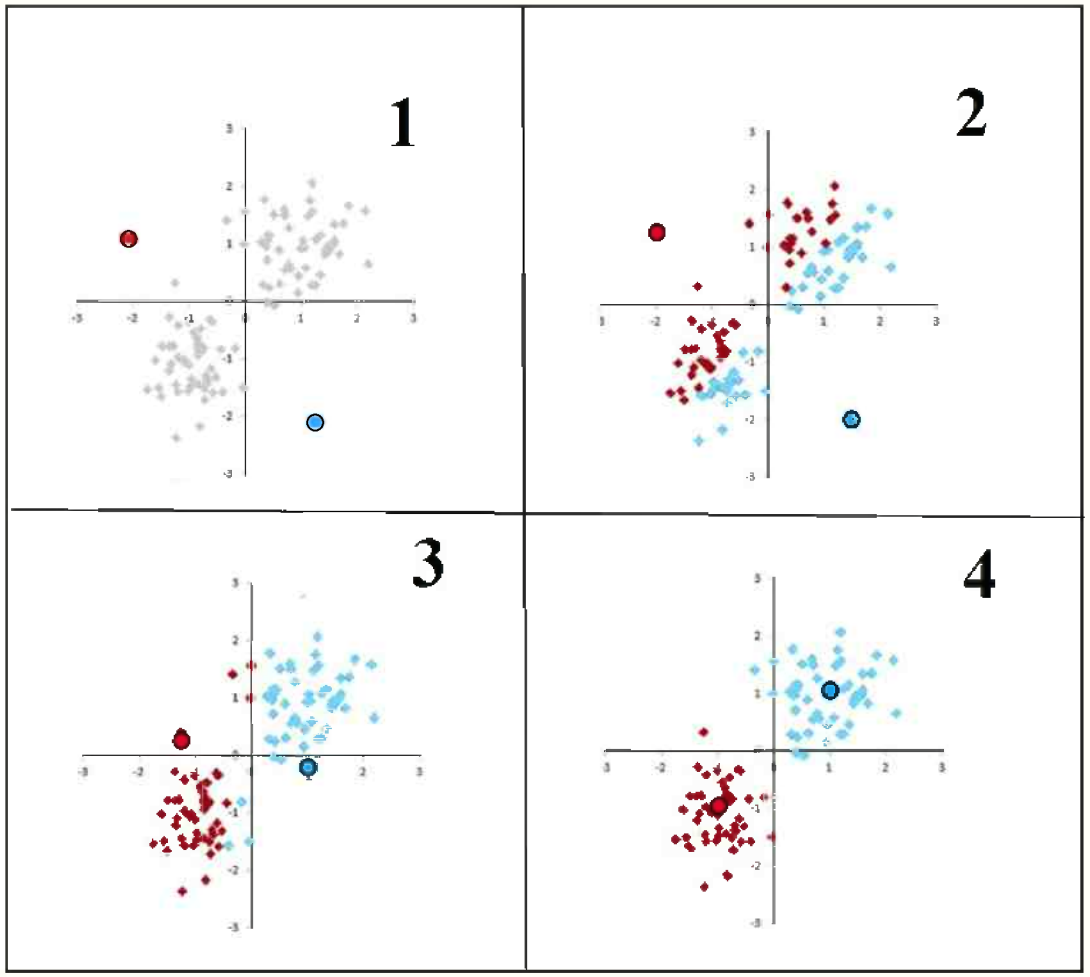
1. K-means
2. Gaussian Mixture Model (GMM)

Or inferred:

1. Hierarchical clustering
2. Louvain Clustering

# K-means

1. Choose *k* random points
2. Partition objects into k subset
3. Compute the new *centroids* (mean points) of the clusters
4. Repeat steps 2+3 until convergence



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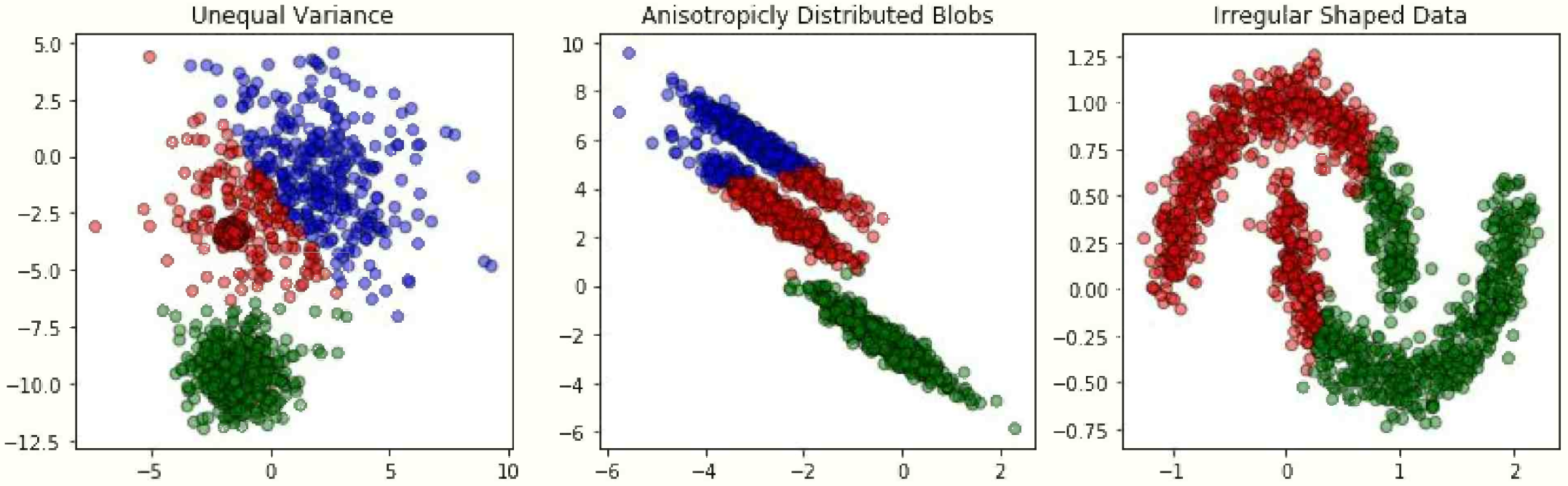
# K-means



# Gaussian Mixture Model (GMM)

- k-means only considers mean points
- GMM considers mean and (co-)variance
- Fit *M* Gaussian components by maximising log-likelihood

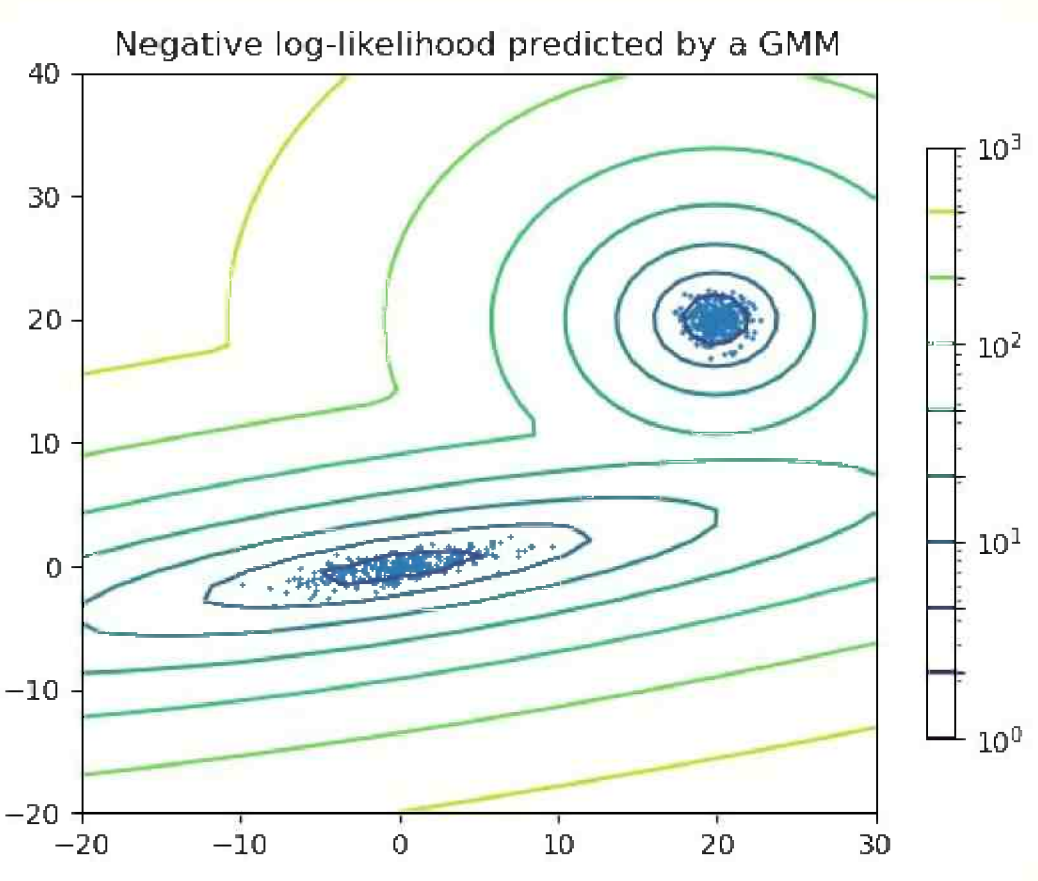
$$\ell(\theta|\mathbf{x}) = \sum_{i=1}^{N} \log\left(\sum_{m=1}^{M} \alpha_m \phi(x_i|\mu_m, \Sigma_m)\right)$$

x – datapoint

$\theta$ - gaussian parameters $\{(\mu_m, \Sigma_m): 0 \leq m \leq M\}$

α - mixing coefficient

Φ – probability density function



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# Initial Random Guess

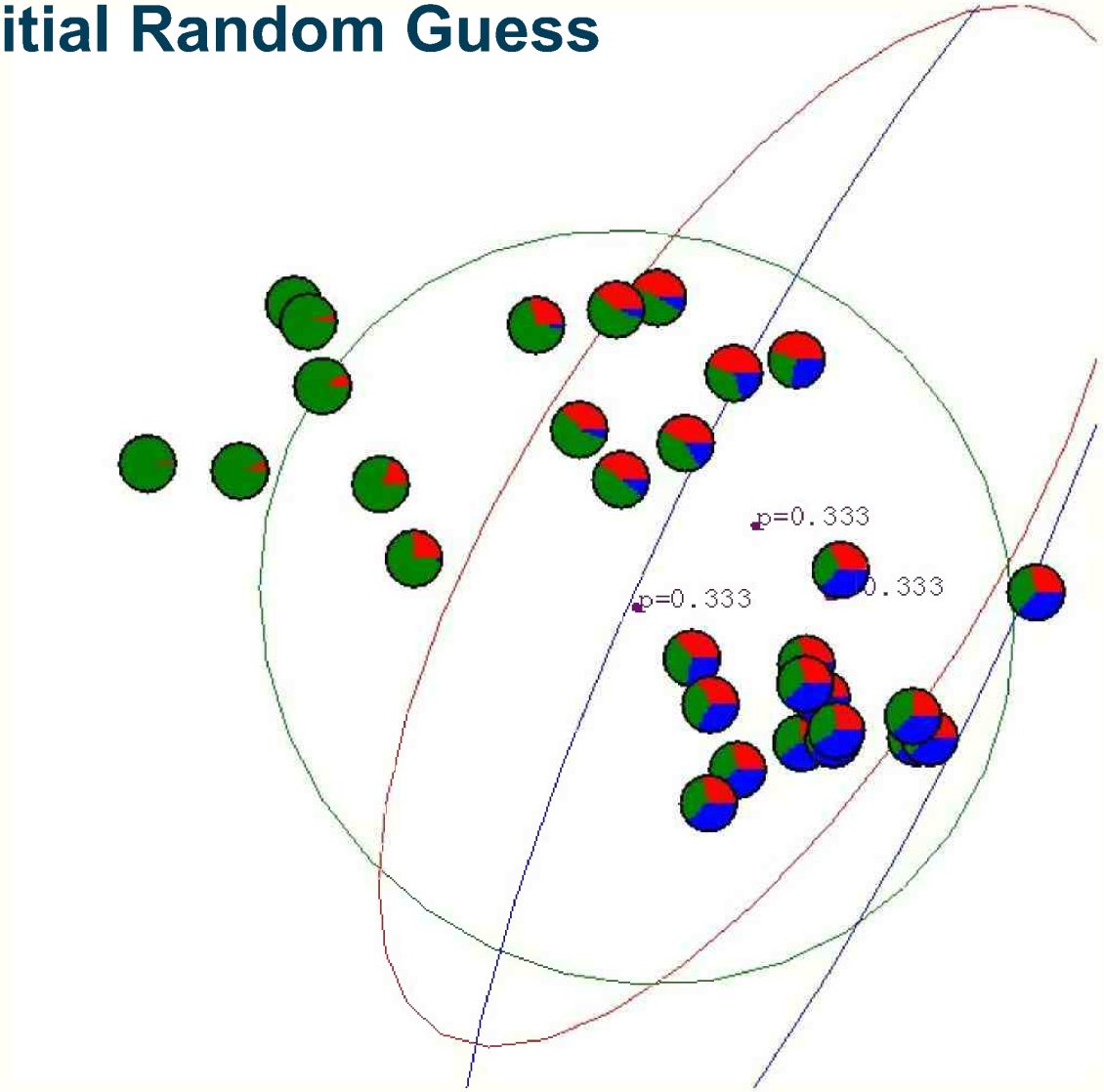
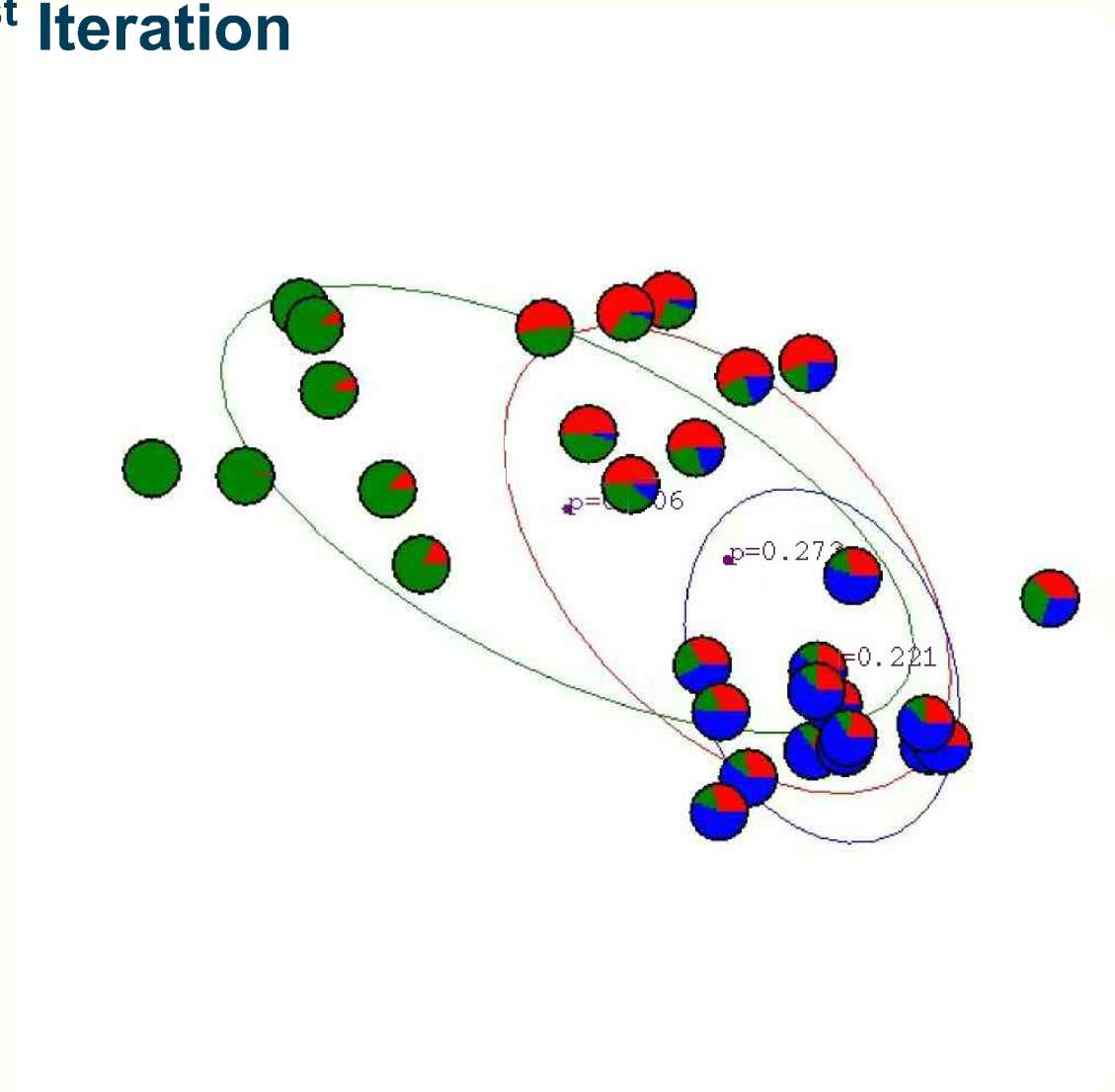



Image credit Prof A Moore, Carnegie Mellon University

# 1st Iteration

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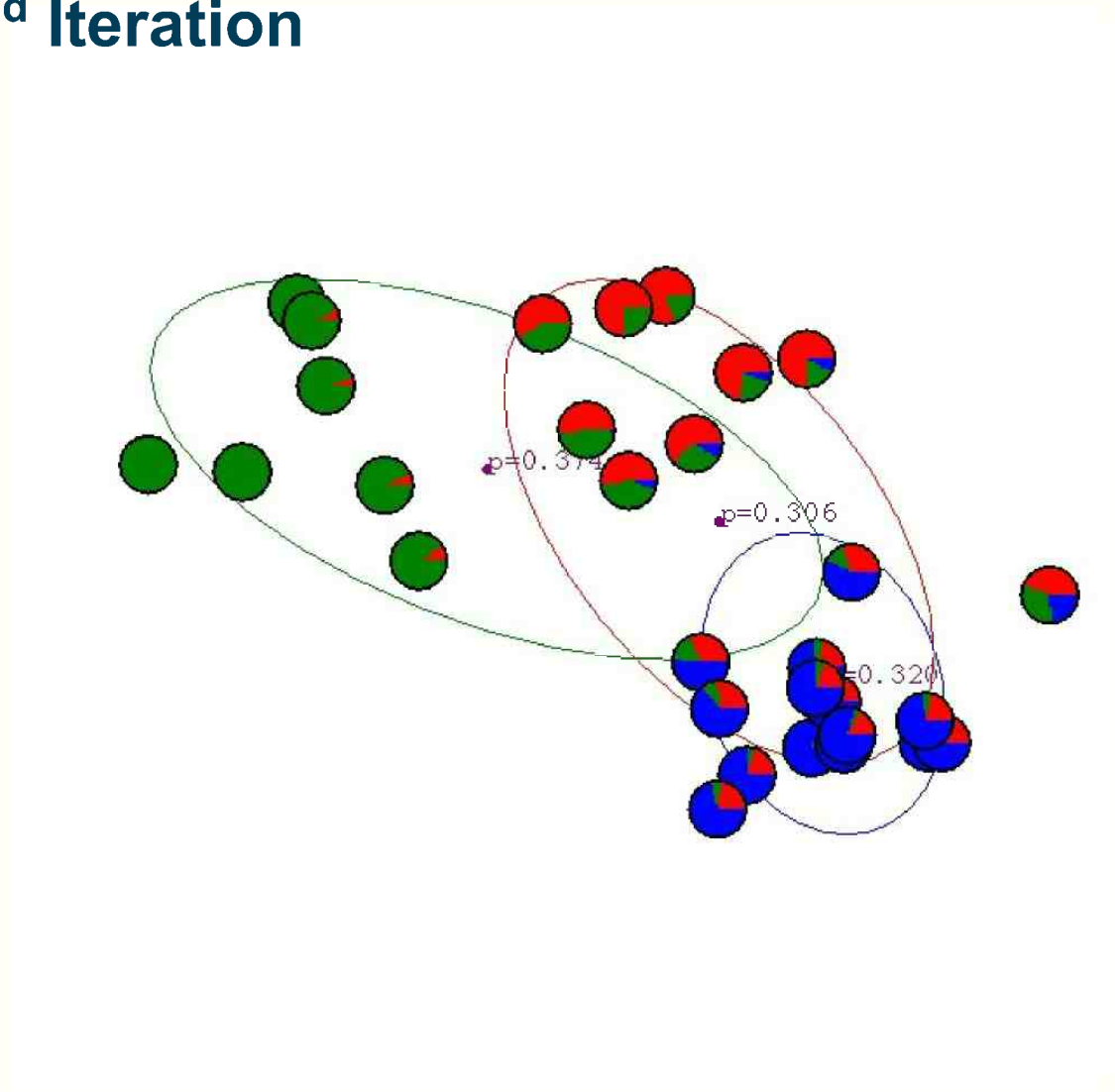
# 2nd Iteration

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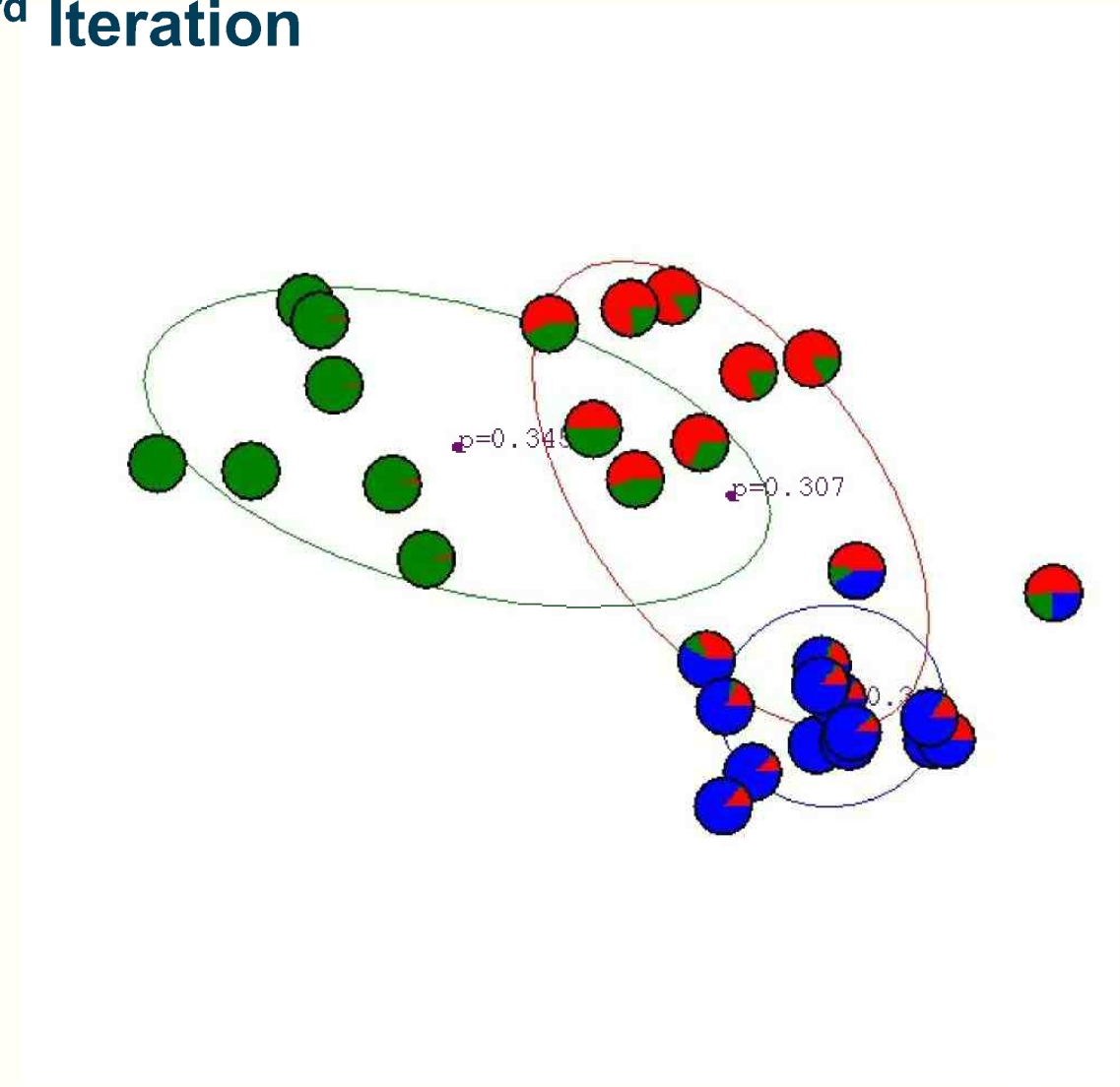
# 3rd Iteration

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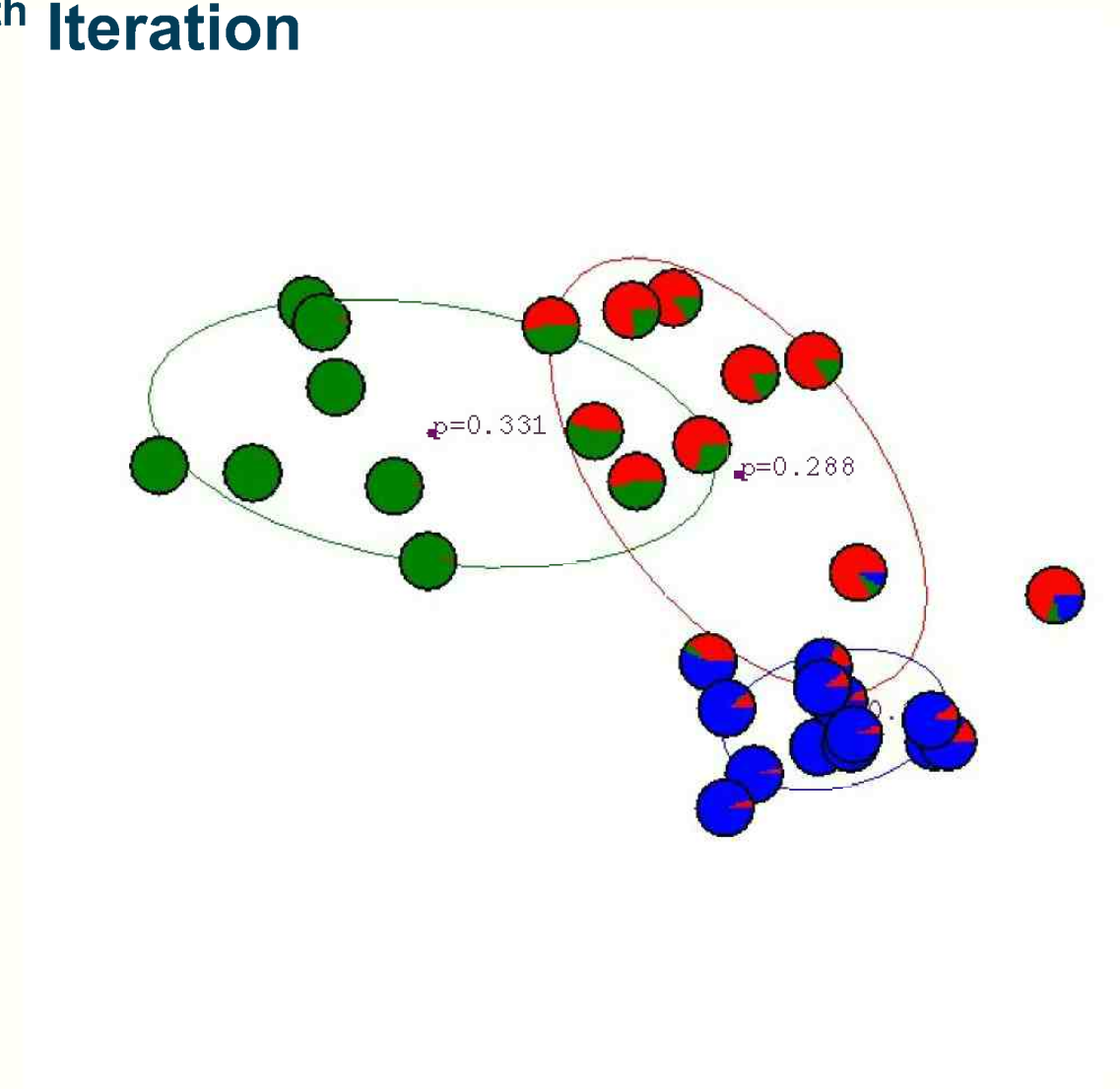
# 4th Iteration

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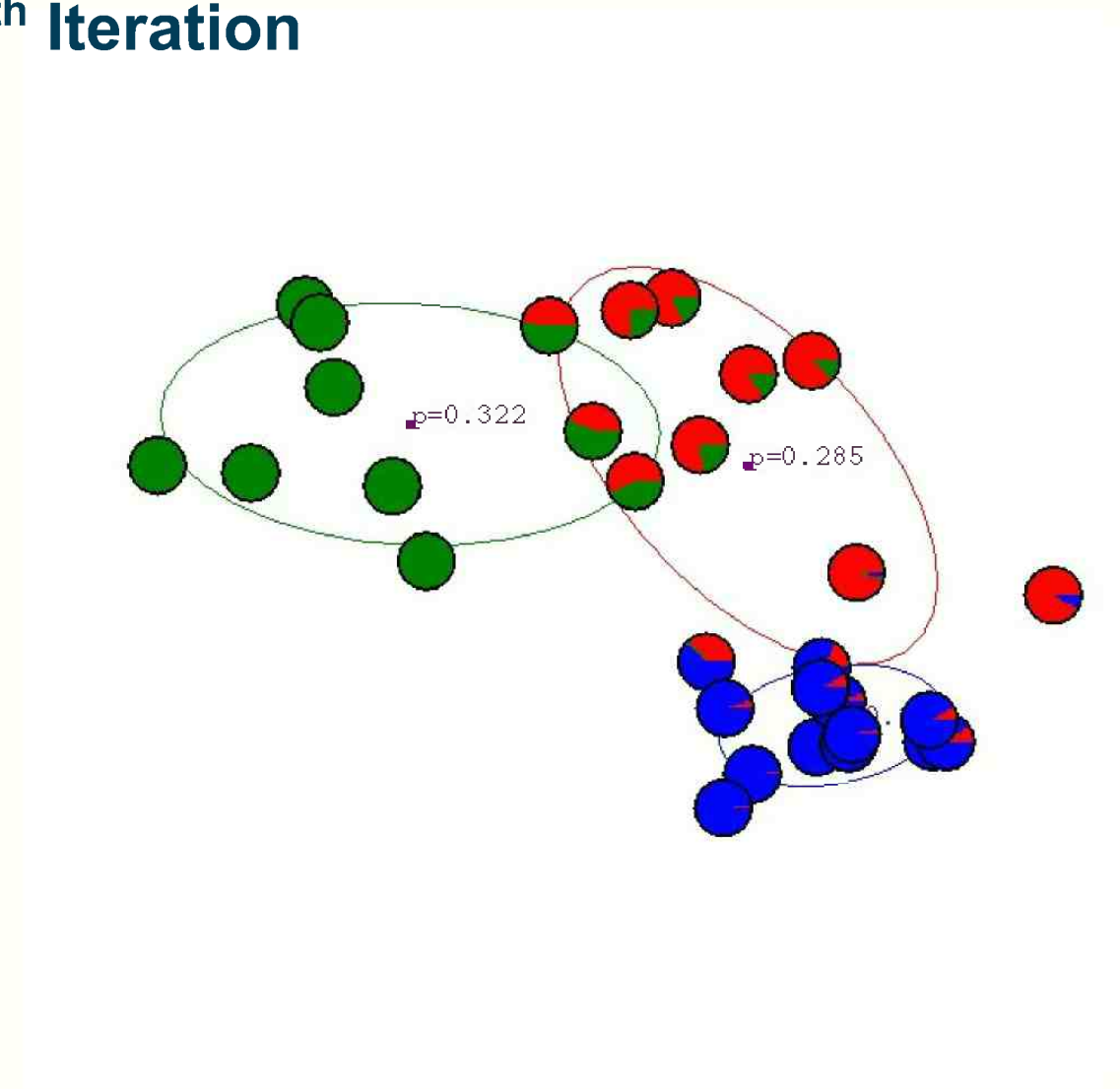
# 5th Iteration

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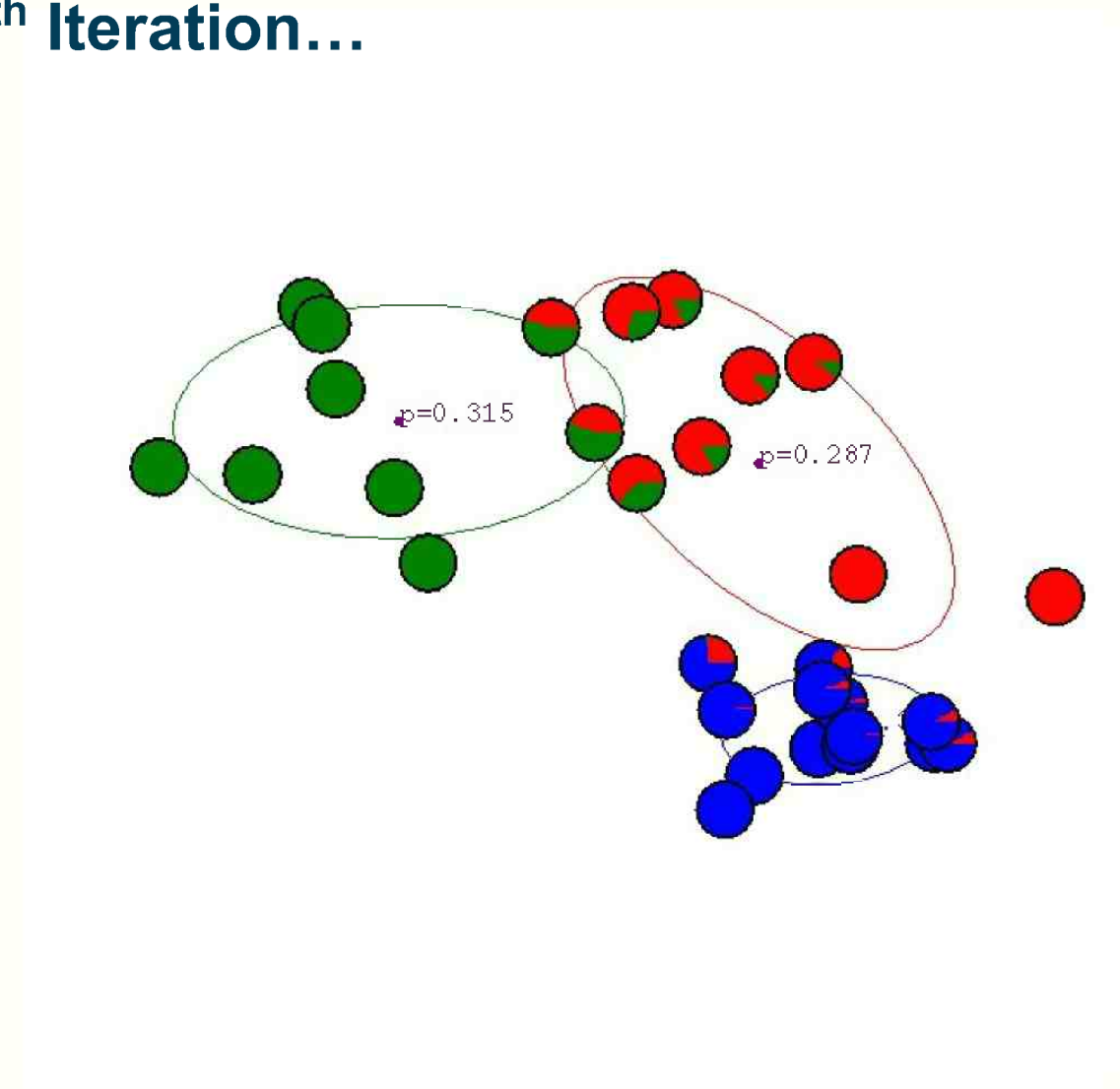
# 6th Iteration…

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# …20th Iteration

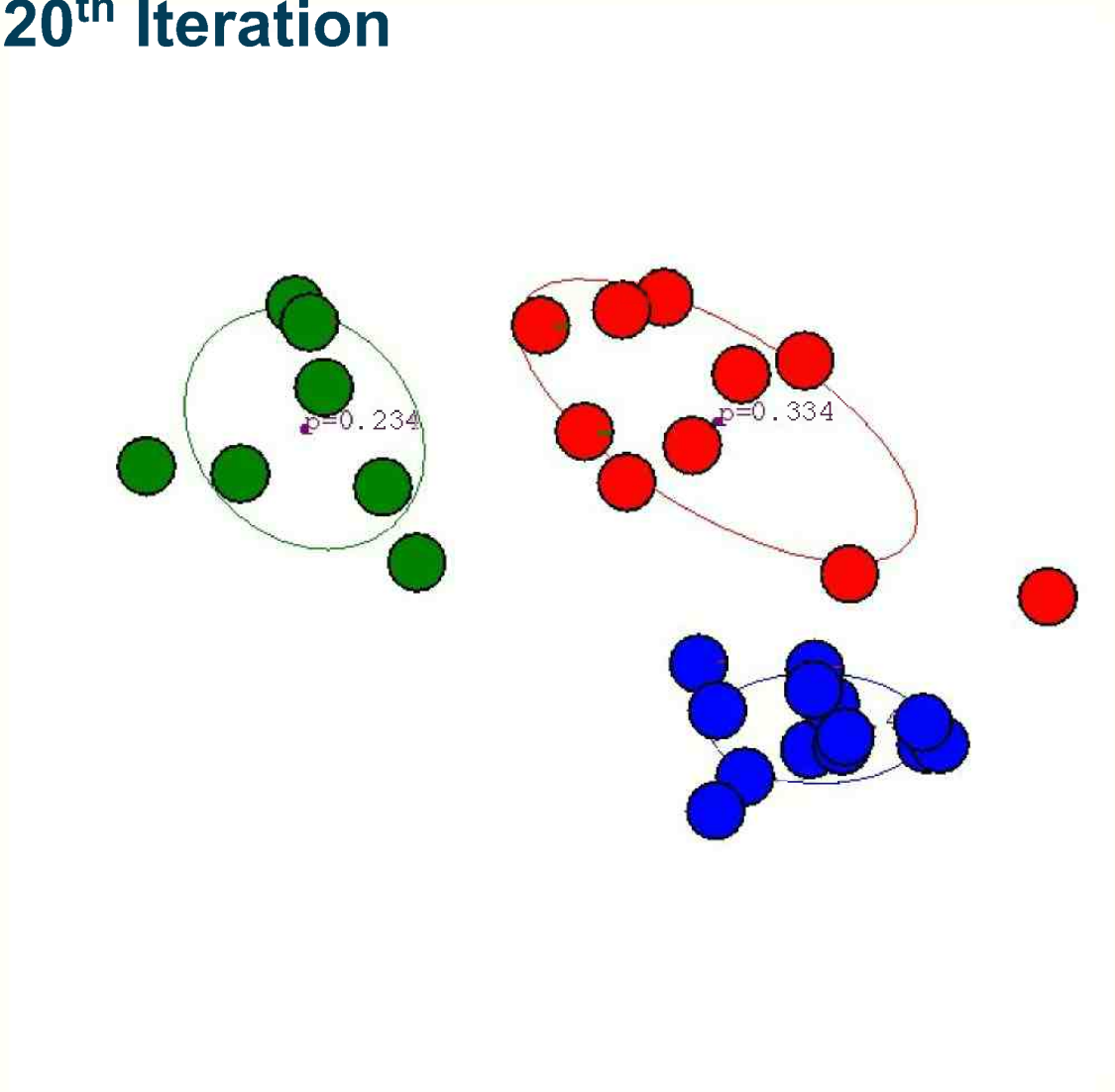


Image credit Prof A Moore, Carnegie Mellon University

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# Gaussian Mixture Model (GMM)

Bio Assay Data

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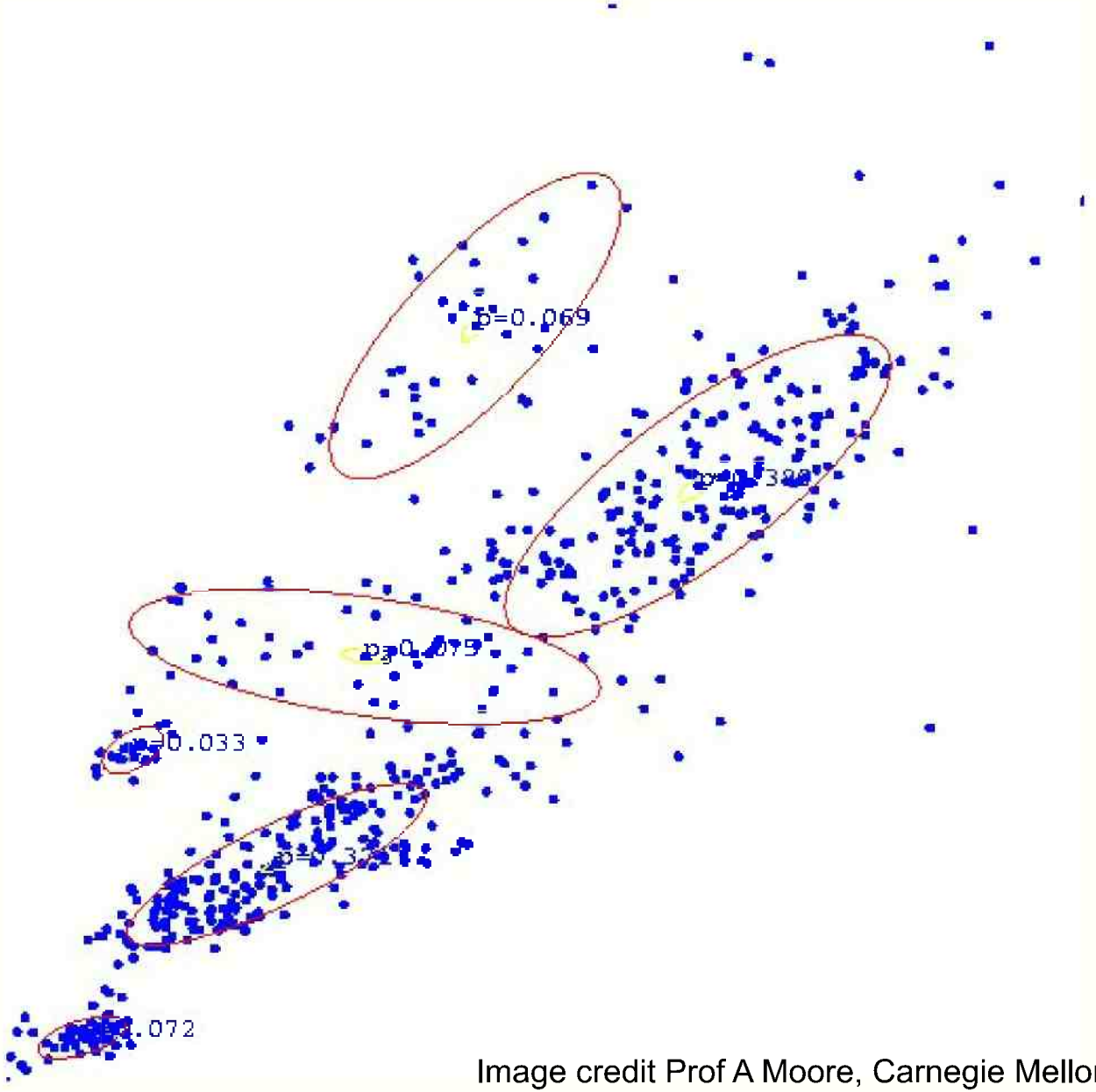


Bio Assay Data

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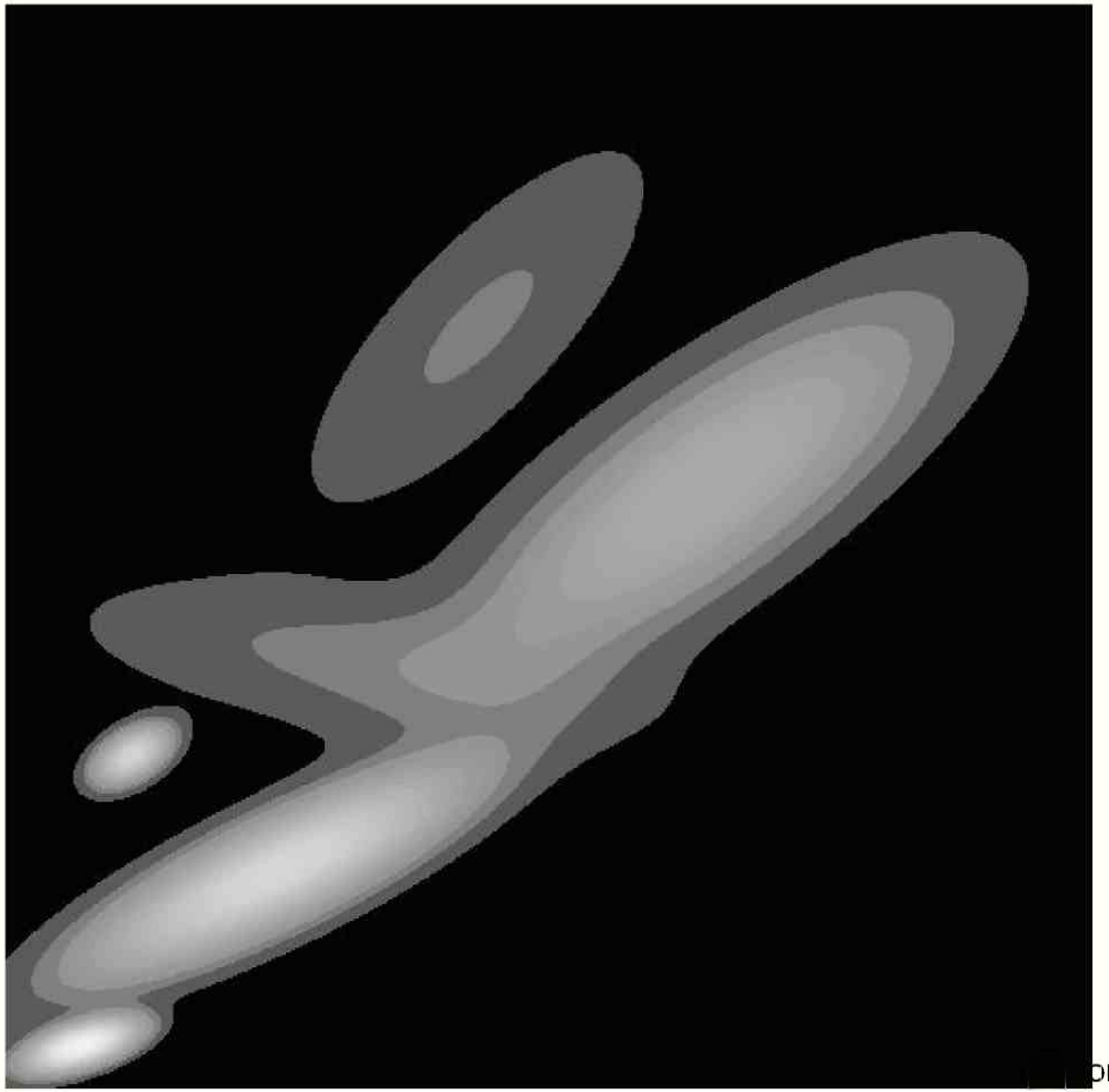
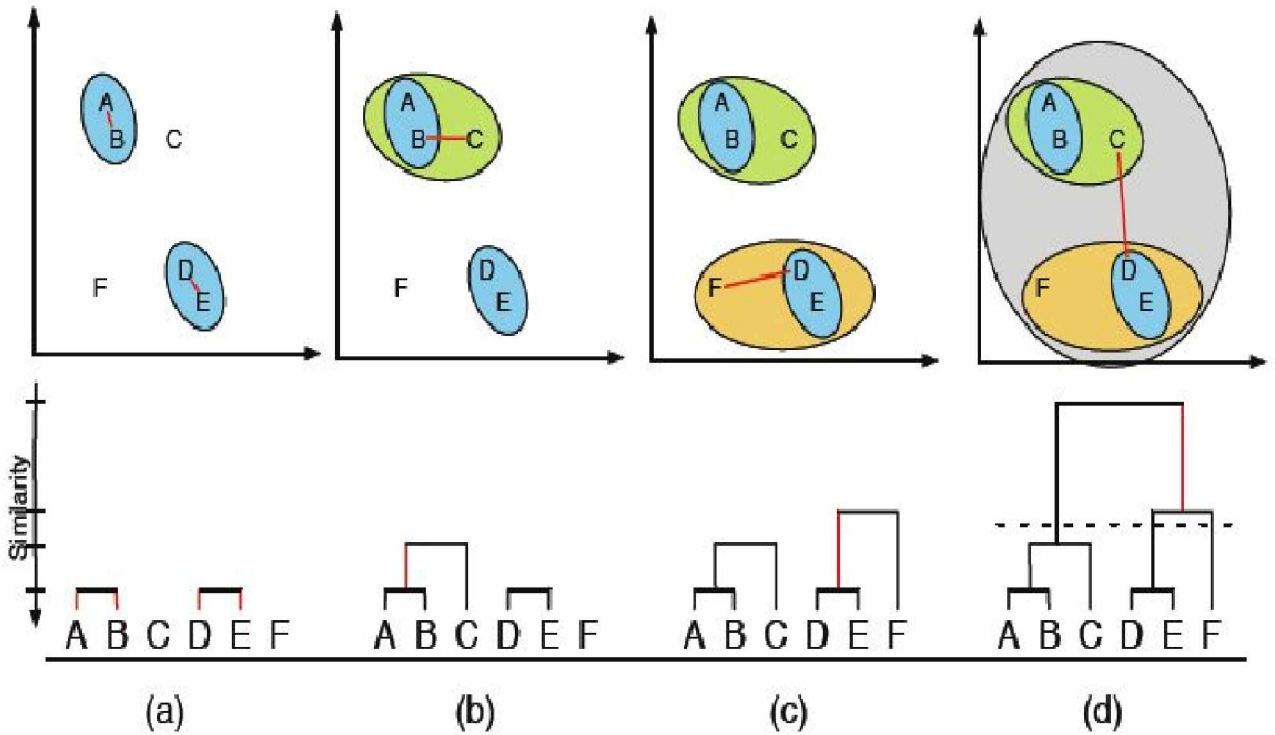


Bio Assay Data

# Hierarchical Clustering (HC)

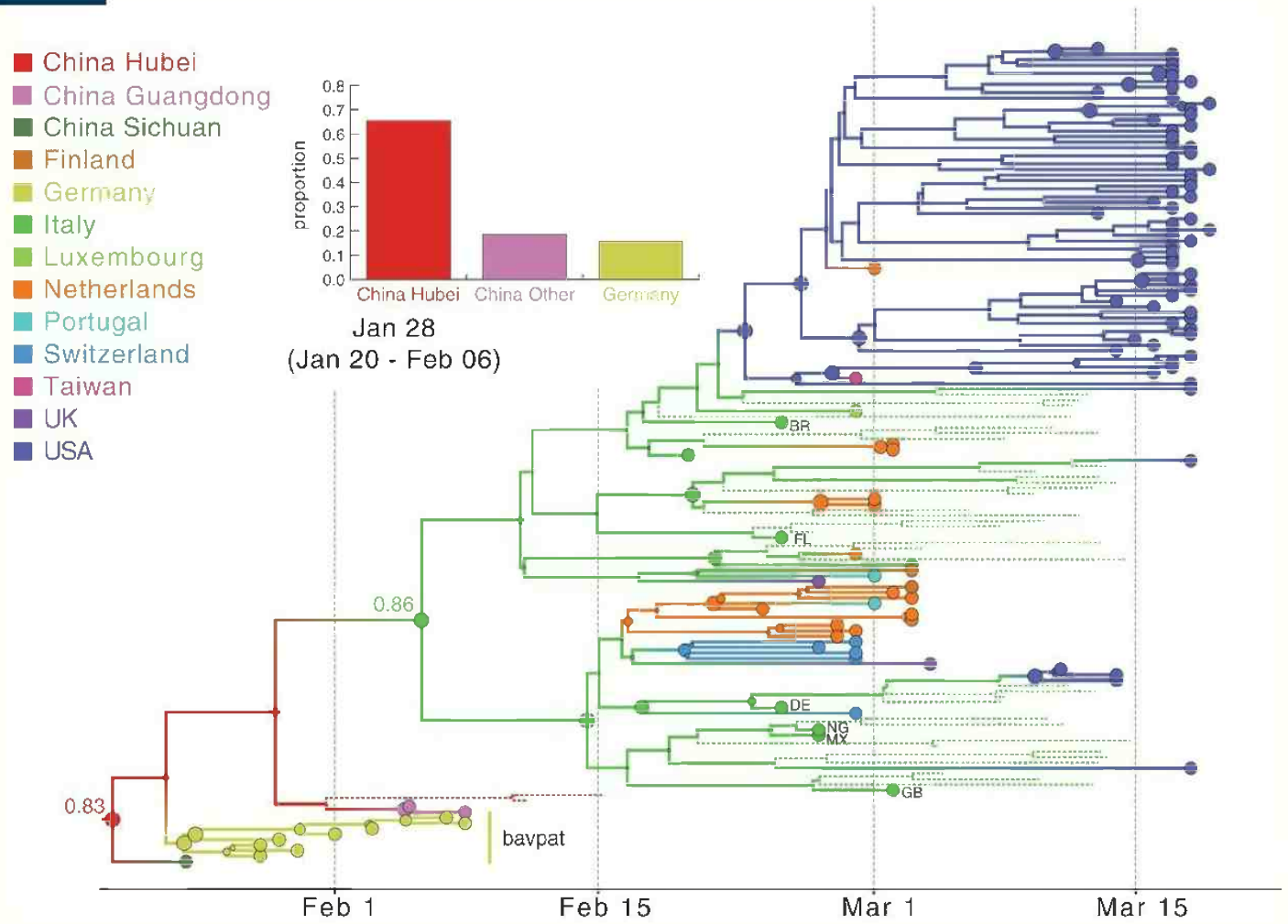



- Consider each data point as separate cluster.
- Consecutively merge clusters until all clusters are connected or specified number of clusters are obtained.

*Dendrograms* illustrate distance between clusters.

No assumption on number of clusters

# Hierarchical Clustering (HC)




DOI: 10.1126/science.abc8169

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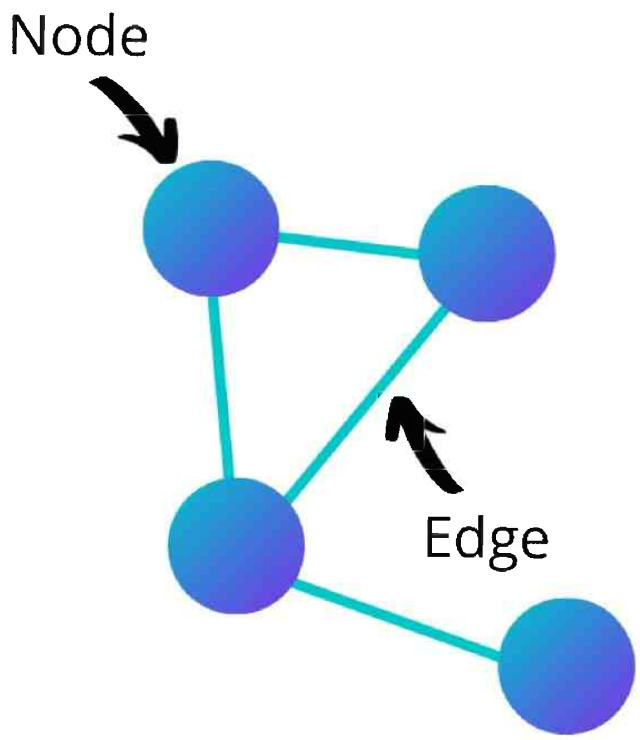
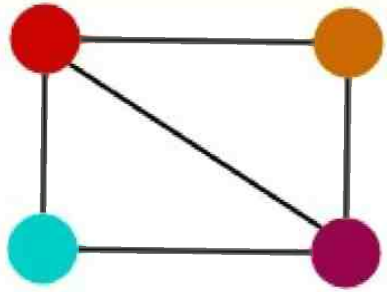
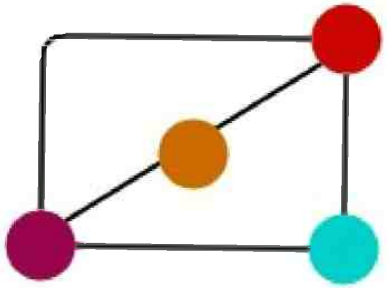
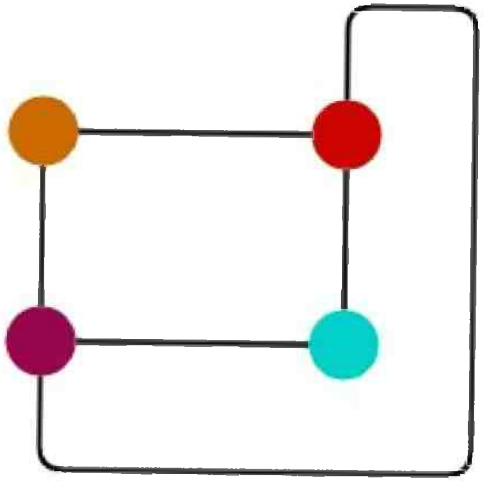
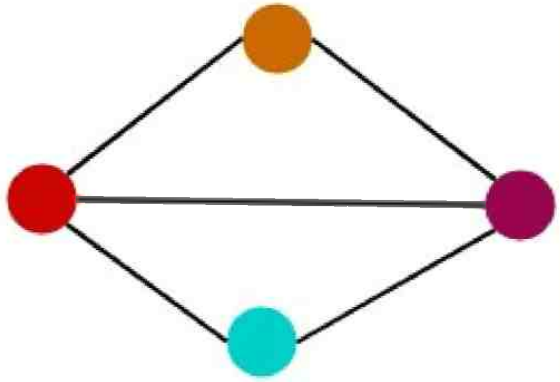
# Graph Theory









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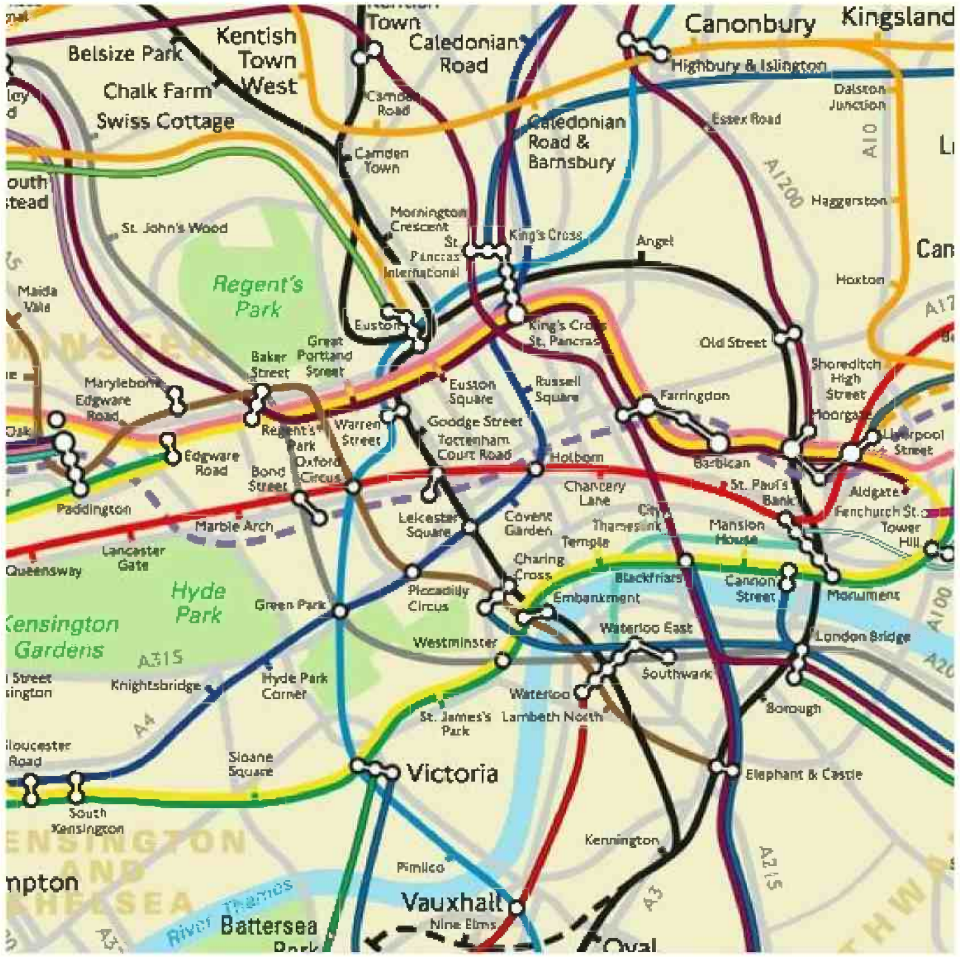
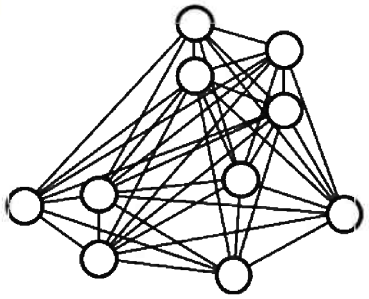
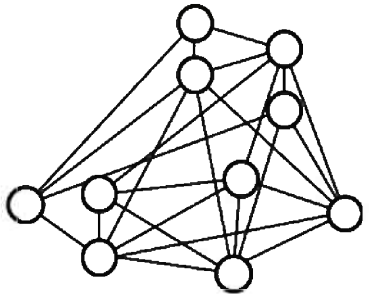
# Making Sense of Arbitrary Shapes



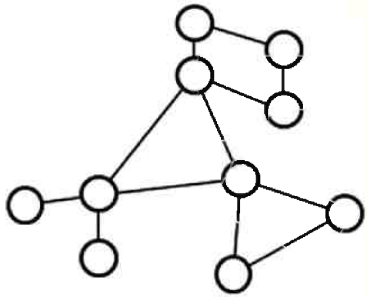
# Graph-based clustering



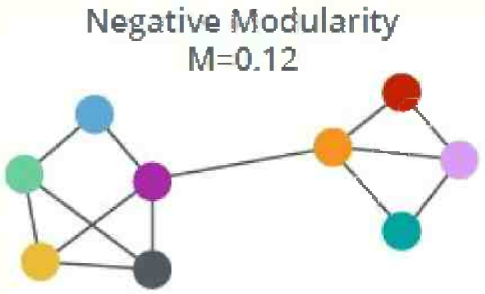
Modularity ≈ -1
(almost complete network)

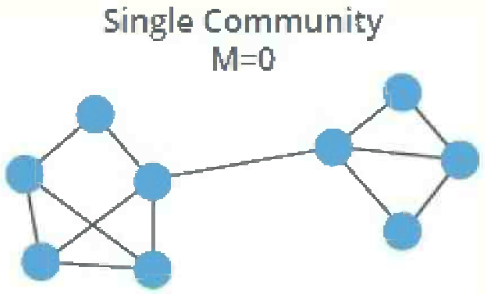


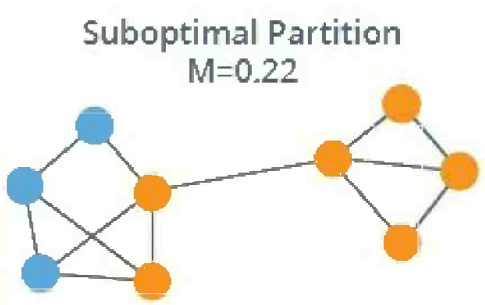
Modularity ≈ 0
(random network)

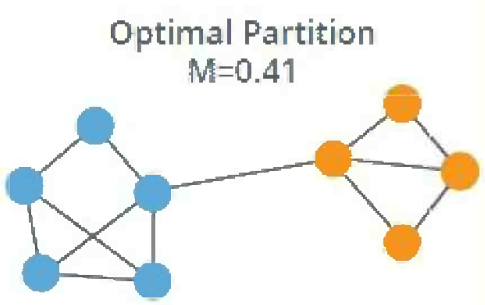


Modularity ≈ 1
(modular network)



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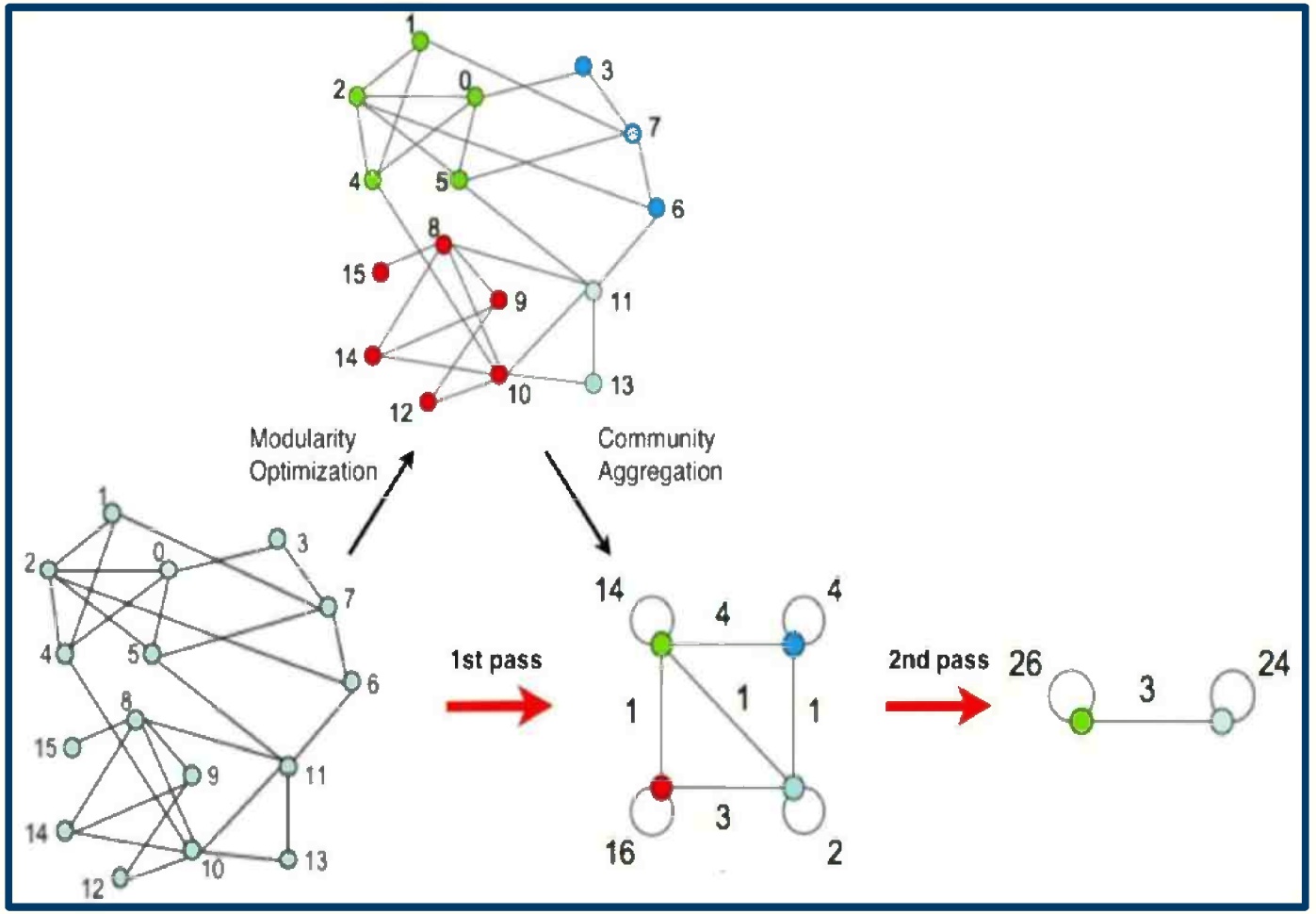
# Louvain Clustering

- Each data point represented as a node
- Similarity between two data points represented by an edge
- Assign nodes to different clusters by Modularity
- Clusters repeatedly combined until no improvement in modularity

*Resolution* parameter in modularity function determines number of clusters.



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# What make model selection for clustering challenging?

- No labels
- Outcomes are subjective
- Hard to define model performance (cluster quality)
- Sensitive to different clustering algorithms and different feature spaces

How do we evaluate then?

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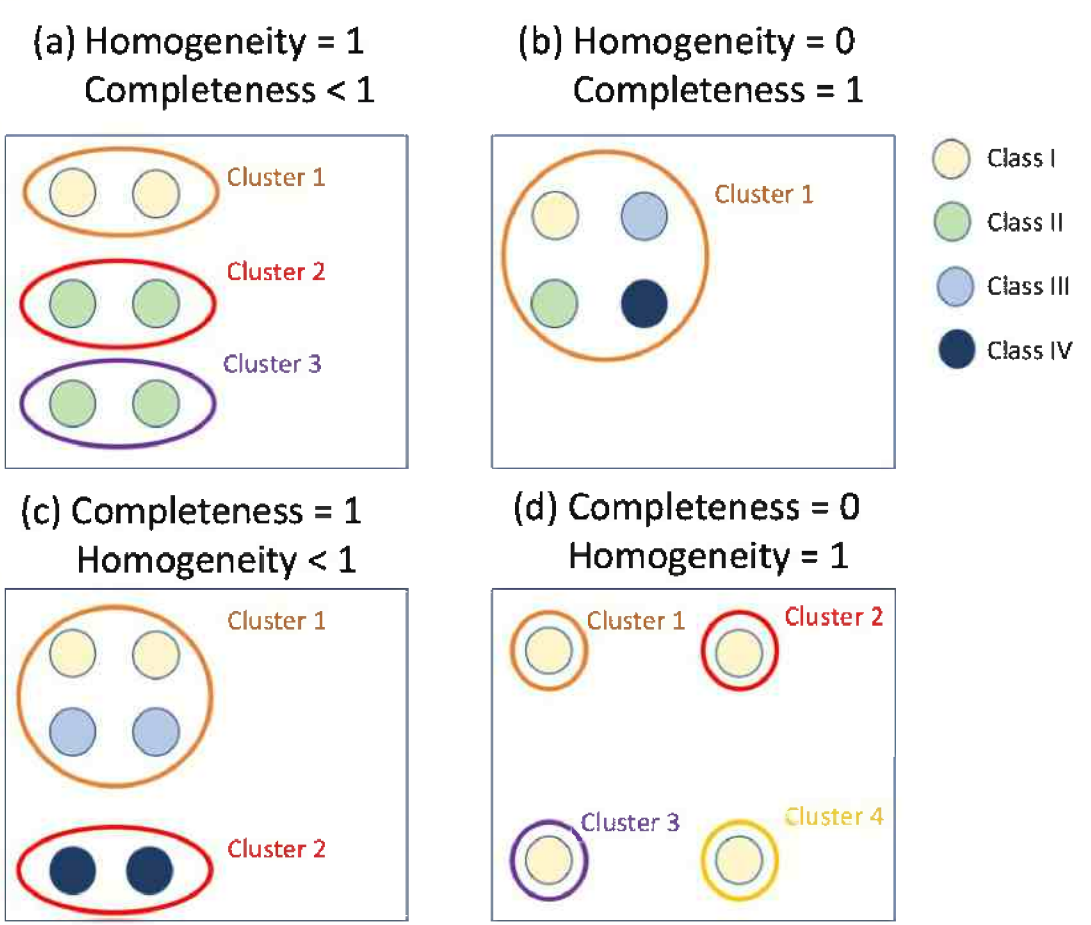
# V-measure

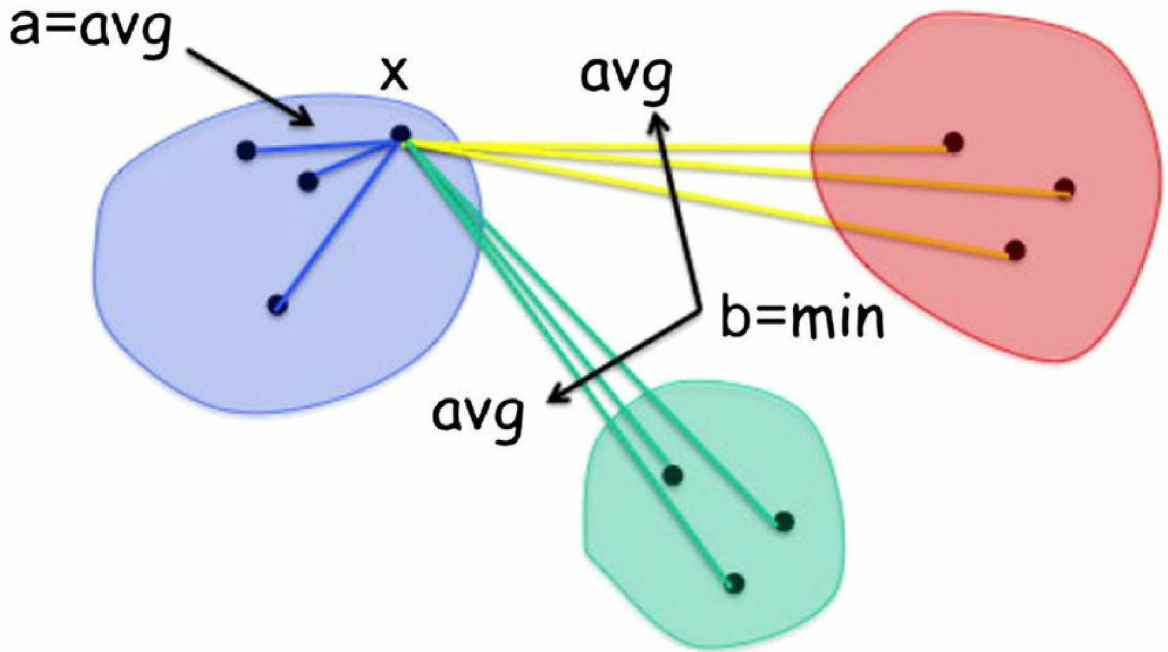
**Given ground truth labels:** Use them!

- homogeneity: each cluster contains only members of a single class
- completeness: members of a given class are assigned to the same cluster

V-measure is the average (harmonic mean) of the two metrics



# Silhouette Score




**If the ground truth labels are not known:**

Evaluate on structure

- -1: incorrect clustering
- ≈0: overlapping clusters.
- +1: highly dense clustering

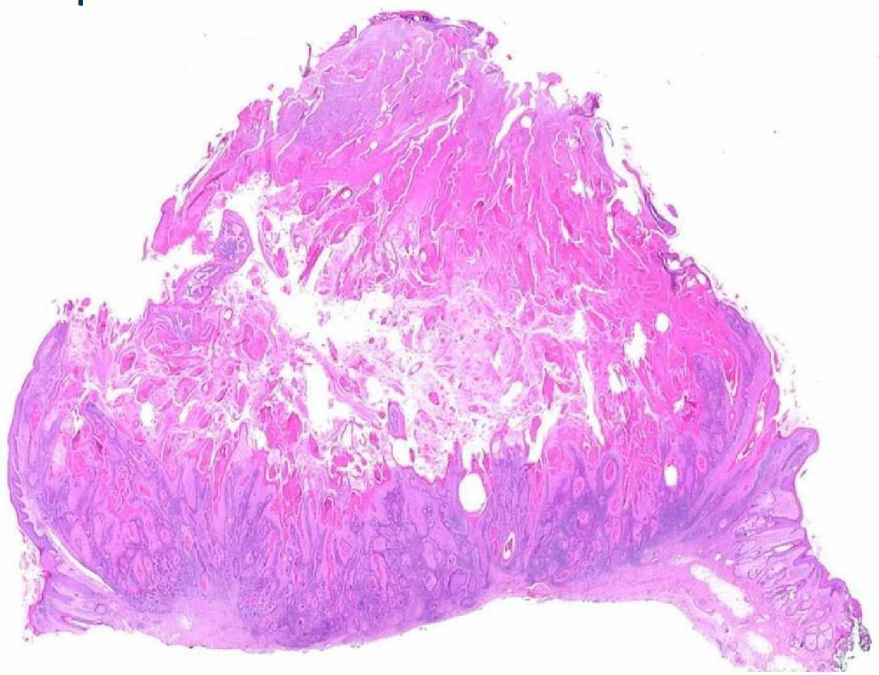
Higher score means clusters are dense and well separated

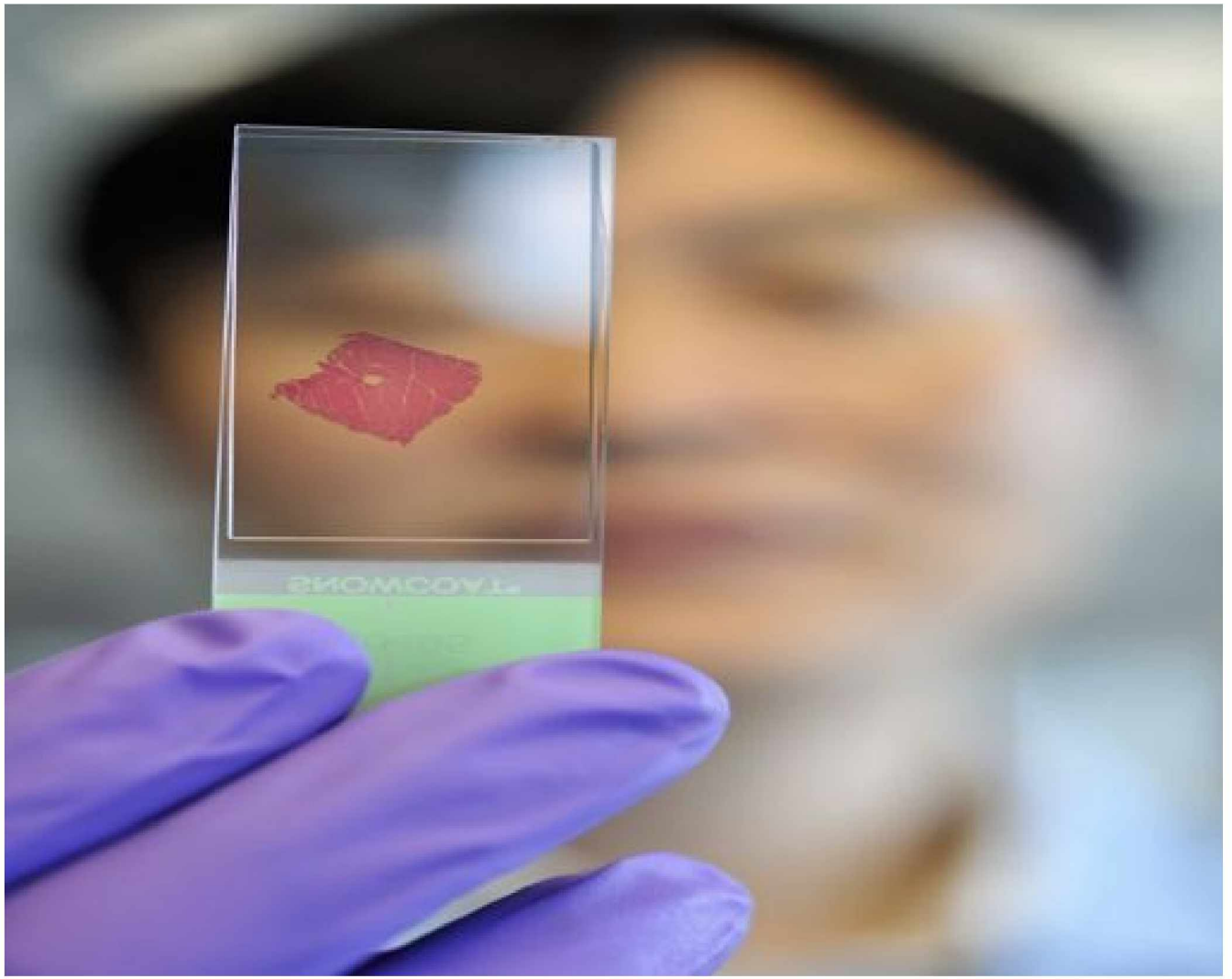
$$s = \frac{b - a}{max(a, b)}$$

a. Mean distance between a sample and all other points in the same class
b. The mean distance between a sample and all other points in the next nearest cluster

# Introduction to digital pathology

- Cancer diagnosed by biopsy
- Removed tissue analysed under digital microscope
- 20Gb on average ~100000x100000 pixels



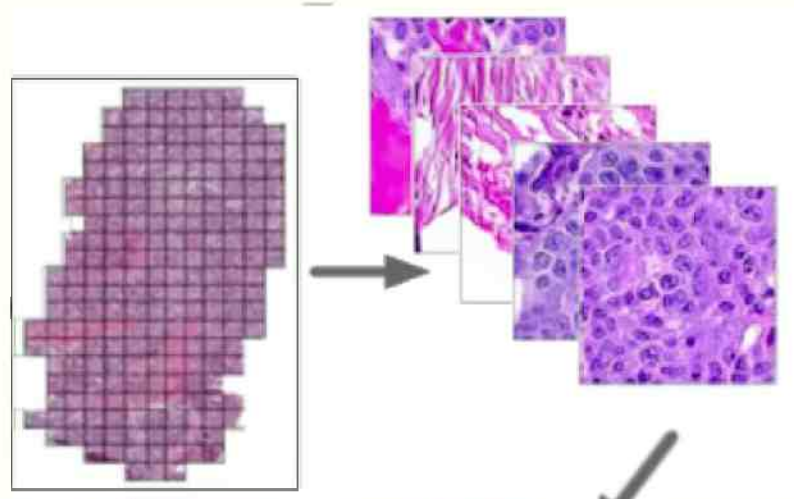


# Image Processing

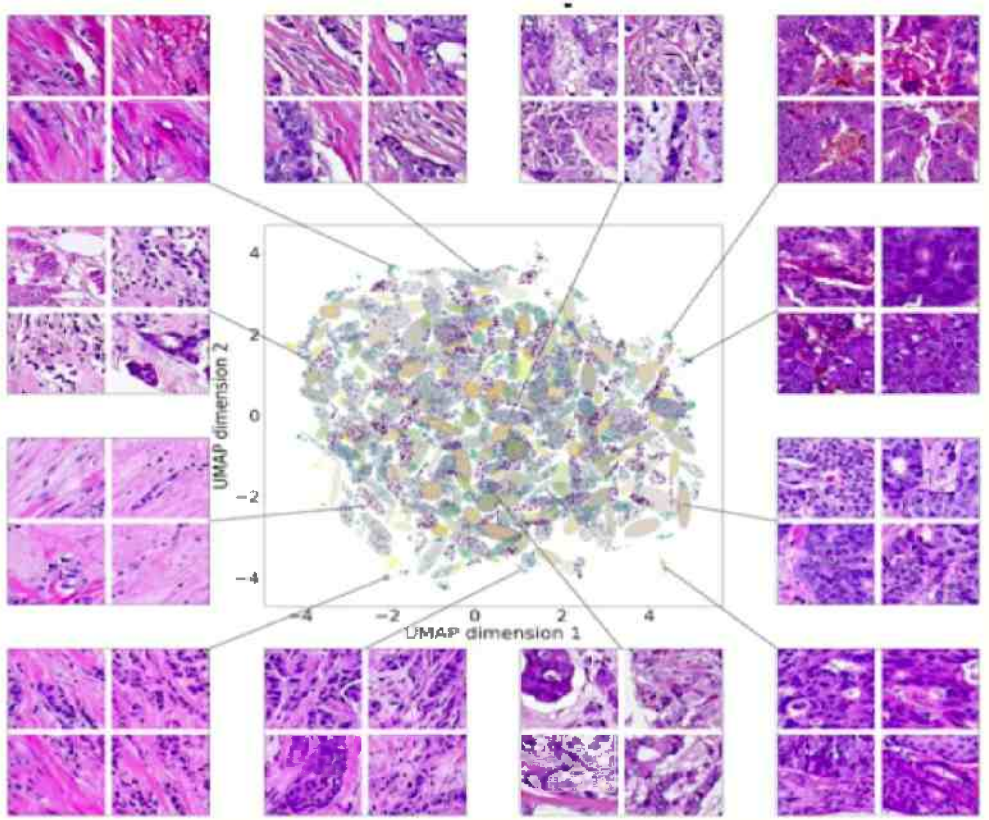
- Break whole slide images (WSIs) into small patches
- (Dimensionality reduction/feature extraction)
- Cluster tissue patches

Clustering gives statistical summary of visual features

**Split whole slide image into patches**



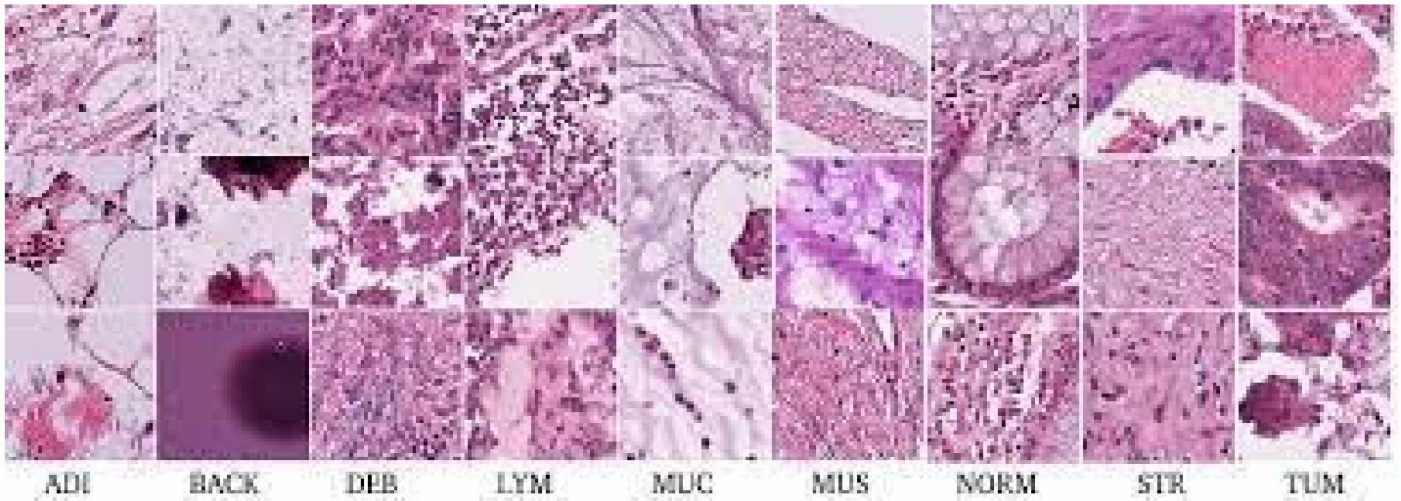
**Group similar patches into the same clusters**



# Your task: model selection for tissue patch clustering

Dataset:

- 5,000 colorectal cancer tissue patches.
- 9 tissue types:
  - Adipose (ADI)
  - background (BACK)
  - debris (DEB)
  - lymphocytes (LYM)
  - mucus (MUC)
  - smooth muscle (MUS)
  - normal colon mucosa (NORM)
  - cancer-associated stroma (STR)
  - colorectal adenocarcinoma epithelium (TUM)




**Your task**

- Select appropriate clustering algorithms (Kmeans, GMM, HC, and Louvain, or HDBScan, Leiden or any other algorithm)
- Apply to a cancer dataset
- Assess model performance (Silhouette score/V measure)

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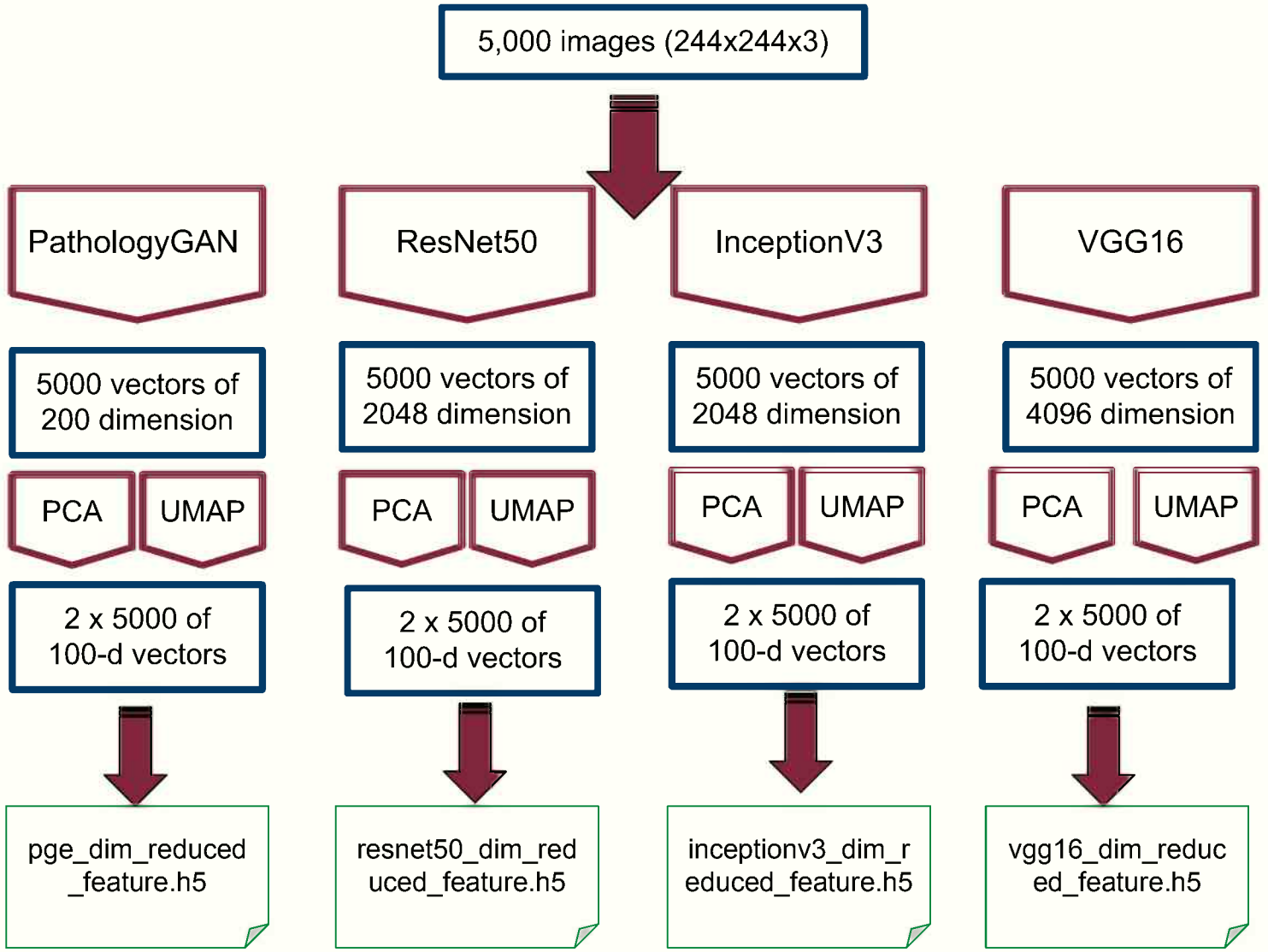
# Feature extraction and preprocessing has been done for you

- **PathologyGAN:**
  - state-of-the-art model for tissue images
  - Trained on unlabelled data
- **ResNet50/InceptionV3/VGG16:**
  - Popular CNN classifiers
  - Trained on ImageNet dataset and achieve 74.9%, 77.9%, 71.3% accuracy

Dimensionality reduction methods reduce each representation size to 100

- **PCA:** the first 100 PCs with highest variance are obtained
- **UMAP:** 100 umap components



# Example of cluster performance report

| Measure A | | | | |
|---|---|---|---|---|
| **Representation** | **Kmeans** | **GMM** | **DBScan** | **Louvain** |
| PathologyGAN | ? | ? | ? | ? |
| ResNet50 | ? | ? | ? | ? |
| InceptionV3 | ? | ? | ? | ? |
| VGG16 | ? | ? | ? | ? |

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# Report summary

**Objective: test clustering algorithms and evaluate performance on real data**

Include in your report:

1. **Introduction**
   Clustering/background/data
2. **Methodology**:
   Theory and intuition behind each algorithm and representation
3. **Experimental framework:**
   Parameter searching and evaluation
4. **Results**
   Report and discuss cluster qualities according to both qualitative and quantitative measures
5. **Conclusion**

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# Summary of Methods

## K-means

- Fast, simple, guaranteed convergence, scales well with dataset size
- Manual number of clusters, sensitive to outliers, scales badly with dimensions

## Hierarchical Clustering

- Simple, guaranteed convergence, scales well, no predetermined number of clusters, gives different resolutions of clustering
- Slow, limited meaningful clustering, can infer artificial relationships

## Gaussian Mixture Model

- Handles outliers, more informative, guaranteed convergence
- Slow, same issues as k-means, computation time scales badly with dataset size

## Louvain Community Detection

- Handles outliers, more informative, scales well with dataset size and dimension, no assumption on shape
- Computationally intensive for small datasets, pre-determined resolution

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# Summary

## Model Selection

- What does *best* mean?
- Consider what outcomes are most important

## Clustering

- Different models give very different results
- Use prior knowledge to select appropriate model
- Evaluate clusters based on structure or labels

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# Summary and extra hints!

1. The objective of this case study is **to test different clustering algorithms on 4 different deep neural network-based representations** extracted from colorectal tissue patches by reporting the cluster qualities according to both intrinsic and extrinsic measures
2. In your report, you are expected to present…
   - Introduction  to tasks/backgrounds/data
   - Methodology:

     Theory and Intuition behinds each algorithm and representation
   - Experimental framework:

     Parameter searching and evaluation
   - Result discussion
   - Conclusion


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THANK YOU