Machine Learning for Bioinformatics & Systems Biology

3. Feature selection and extraction

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Some material courtesy of Robert Duin and David Tax

Overview

- Feature extraction:
  - Linear:
    - PCA,
    - Fisher
  - Non-linear
    - MDS
- Feature selection:
  - Criteria
  - search algorithms
    - forward,
    - backward,
    - branch & bound.
- Regularized classifiers:
  - PAM (shrunken centroids)
  - Ridge,
  - LASSO

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Dimensionality reduction

Use of dimensionality reduction:

1. **Fewer parameters**: faster, easier to estimate – possibly better performance
2. **Explain** which measurements (genes) are useful and which are not (reduce redundancy)
3. **Visualisation**

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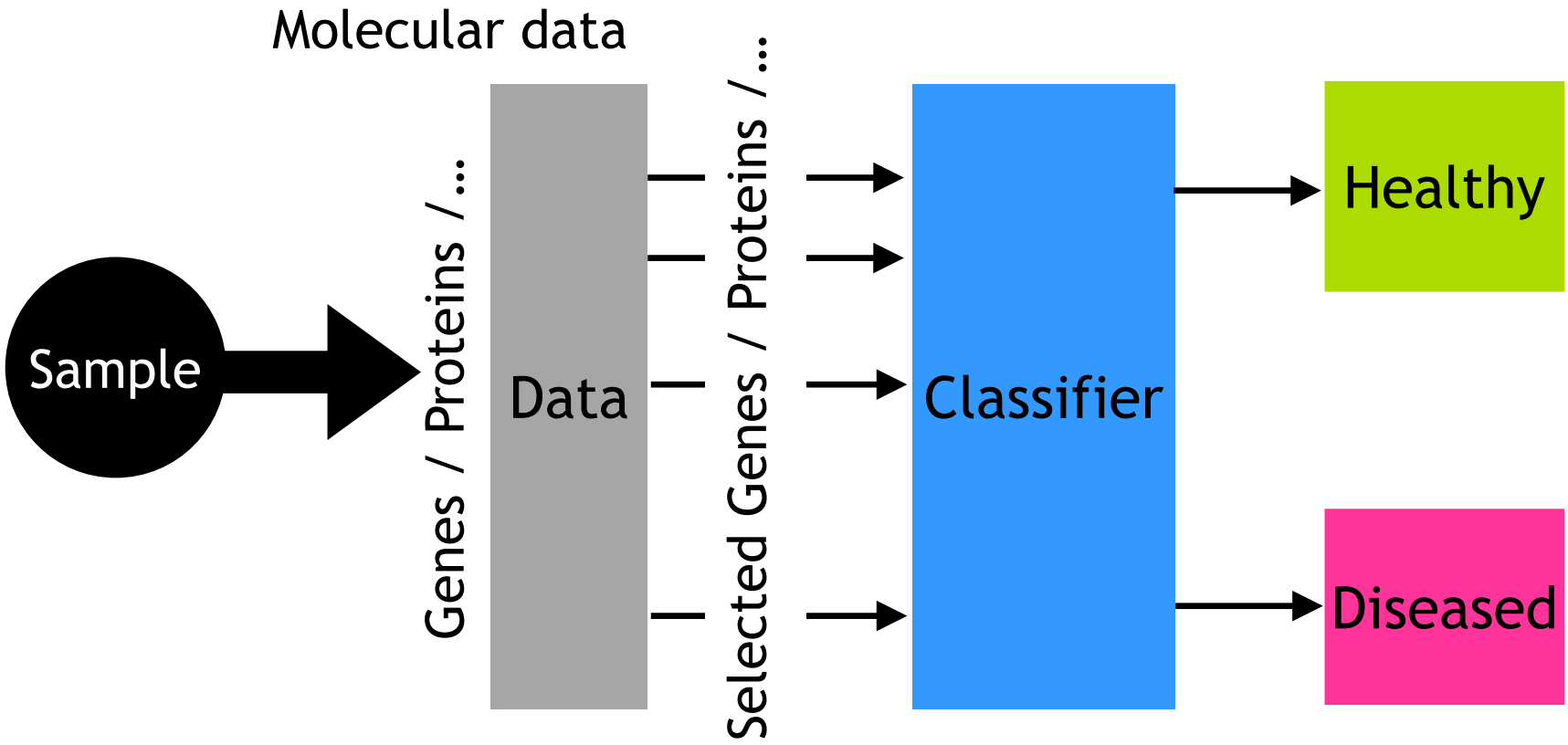
Example: molecular diagnostic classifiers



Molecular data (e.g. RNAseq data)

- Curse of dimensionality:
  - as number of features *increases*, number of parameters increases;
  - for fixed sample size, performance *decreases*.

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  - need 5-10 times as many samples as there are parameters;
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- But genomic data (e.g. RNAseq) is extreme:
  - 100-1000 times *fewer* samples than parameters!

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- But genomic data (e.g. RNAseq) is extreme:
  - 100-1000 times *fewer* samples than parameters!
- For example: nearest mean classifier on Golub data
  - $p = 3051$, $k = 2 \rightarrow$ number of parameters = 6102
  - Number of samples, $n = 38$

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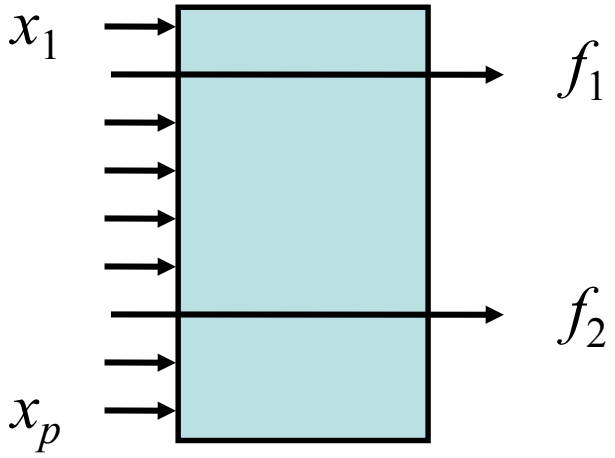
Feature selection vs. extraction

- **Feature selection:**
  select d out of p measurements



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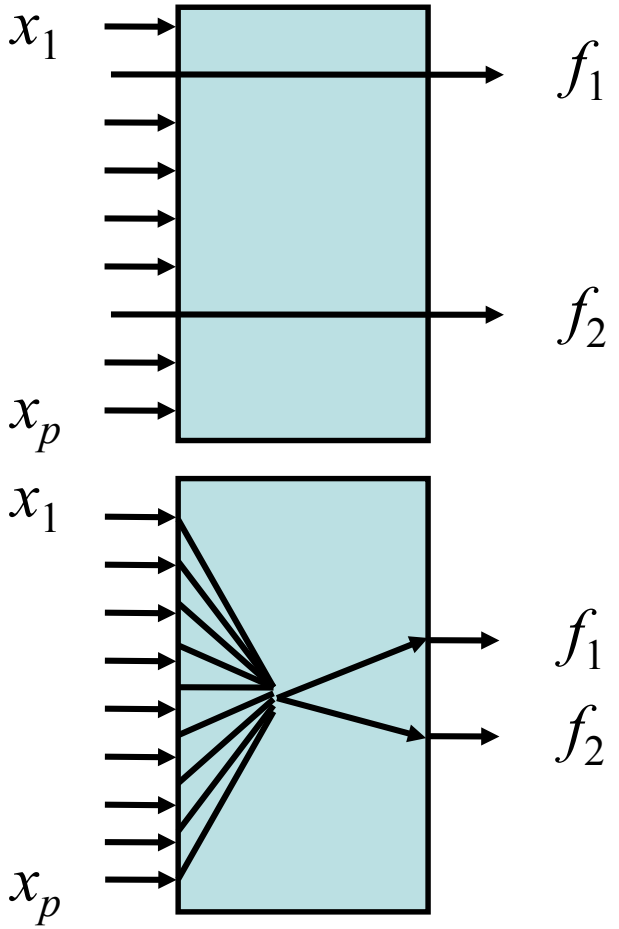
Feature selection vs. extraction

- **Feature selection:**
  select d out of p measurements

- **Feature extraction:**
  map p measurements
  to d measurements
  (e.g. PCA, CCA, LDA, MDS)



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Feature selection v extraction (2)

	Advantage	Disadvantage
Selection	cut in measurements	expensive
	easy interpretation	often approximate
Extraction	cheap	need all measurements
	can be nonlinear	criterion sub-optimal
	not axis aligned	

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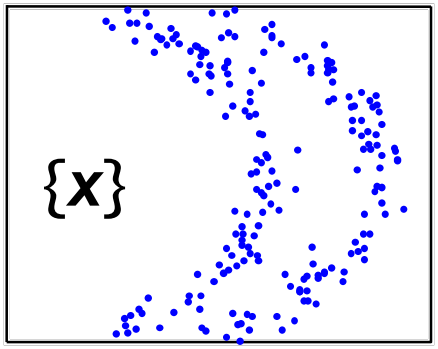
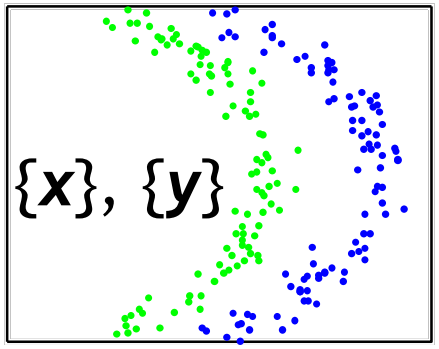
Feature extraction (1)

Main types: supervised/unsupervised



Unsupervised



Supervised

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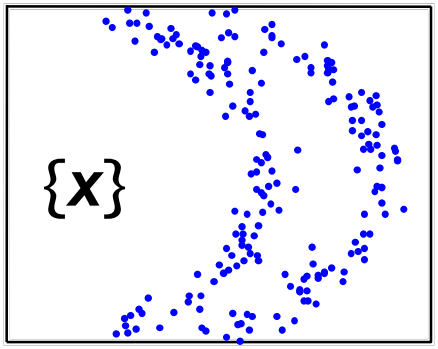
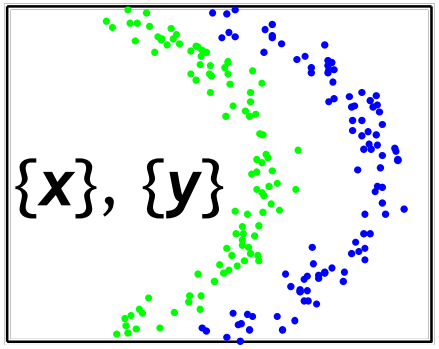
Feature extraction (1)

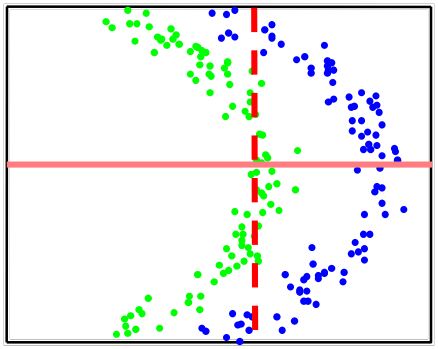
Main types: Linear / Nonlinear



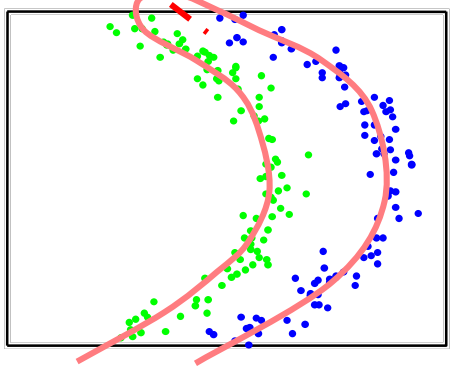
Unsupervised



Supervised



Linear



Nonlinear

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Feature extraction (2)

- Subjects:
  - Linear, unsupervised:
    - Principal Component Analysis (PCA)
  - Linear, supervised:
    - Linear Discriminant Analysis (LDA)

- PCA is perhaps *the* most important mapping technique

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Principal component analysis (Unsupervised feature extraction)

- Principal component analysis (PCA, 1901):
  find directions in data...
  - which retain as much *variation* as possible
  -

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  find directions in data...
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  - which make projected data *uncorrelated*
  -

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Principal component analysis (Unsuperrvised feature extraction)

- Principal component analysis (PCA, 1901):
  find directions in data...
  - which retain as much *variation* as possible
  - which make projected data *uncorrelated*
  - which minimise squared *reconstruction error*

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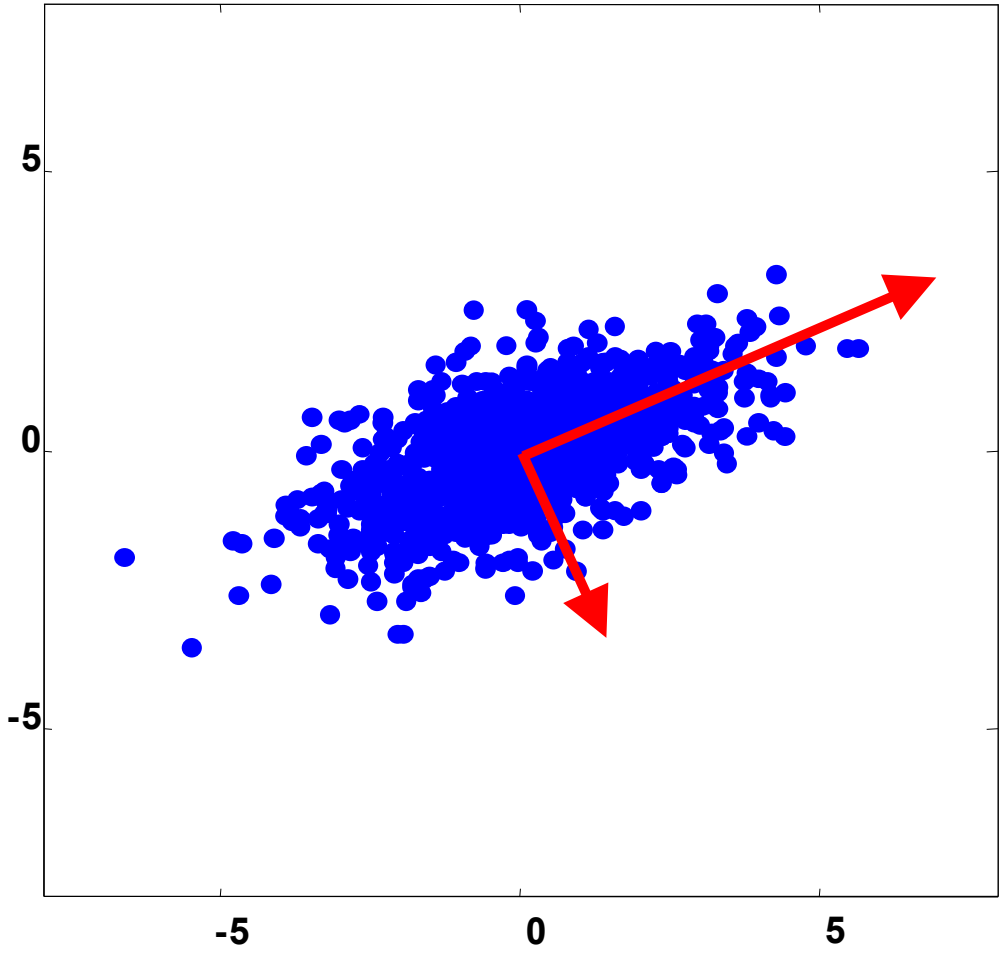
Principal component analysis (Unsuperrvised feature extraction)



Steps:

1. Center data
2. Compute covariance, C
3. Perform PCA on C

Output:

1. Eigenvectors: $\boldsymbol{e}_1$, $\boldsymbol{e}_2$
2. Eigenvalues: λ_1, λ_2

Reducing dimensions:

Choosing '*d*'

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Choosing reduced dimensionality

- To choose d inspect the retained variance,

$$\sum_{i=1}^{d} \lambda_i$$

- or the ratio of retained variance,

$$\sum_{i=1}^{d} \lambda_i \Big/ \sum_{j=1}^{p} \lambda_j$$

- 'Intrinsic dimensionality':
  d for which 90%-95% variance is retained (rule-of-thumb)

- Reduced dimensionality data set
  - $[\boldsymbol{x}_1^T; \boldsymbol{x}_2^T ; \dots ; \boldsymbol{x}_2^T][\boldsymbol{e}_1, \boldsymbol{e}_2 , \dots , \boldsymbol{e}_d]$

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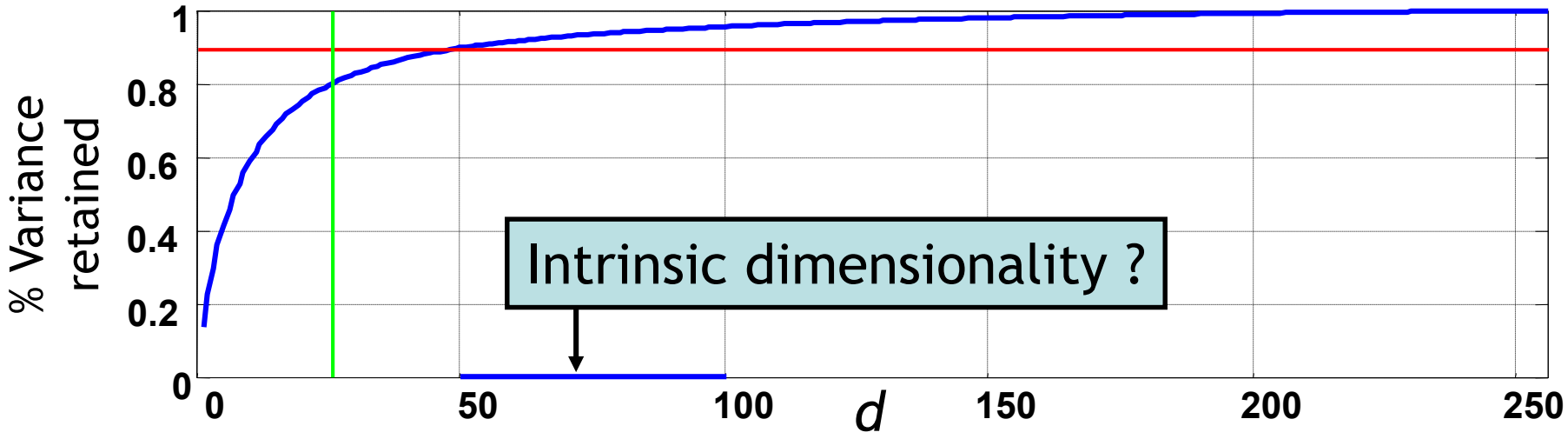
PCA example

- *e.g.* NIST digits: 2000 samples, $p = 256$



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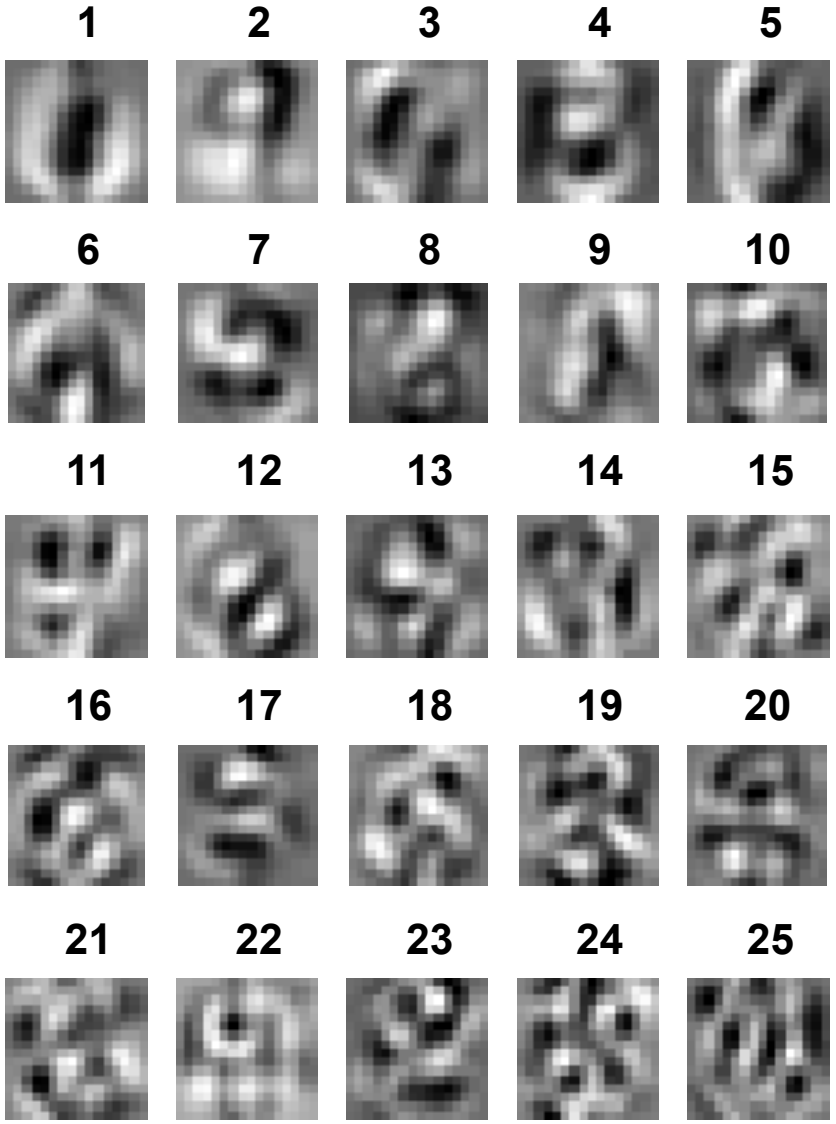
PCA example (2)

- For image data, principal components can also be interpreted...

  most often occuring variations between digits



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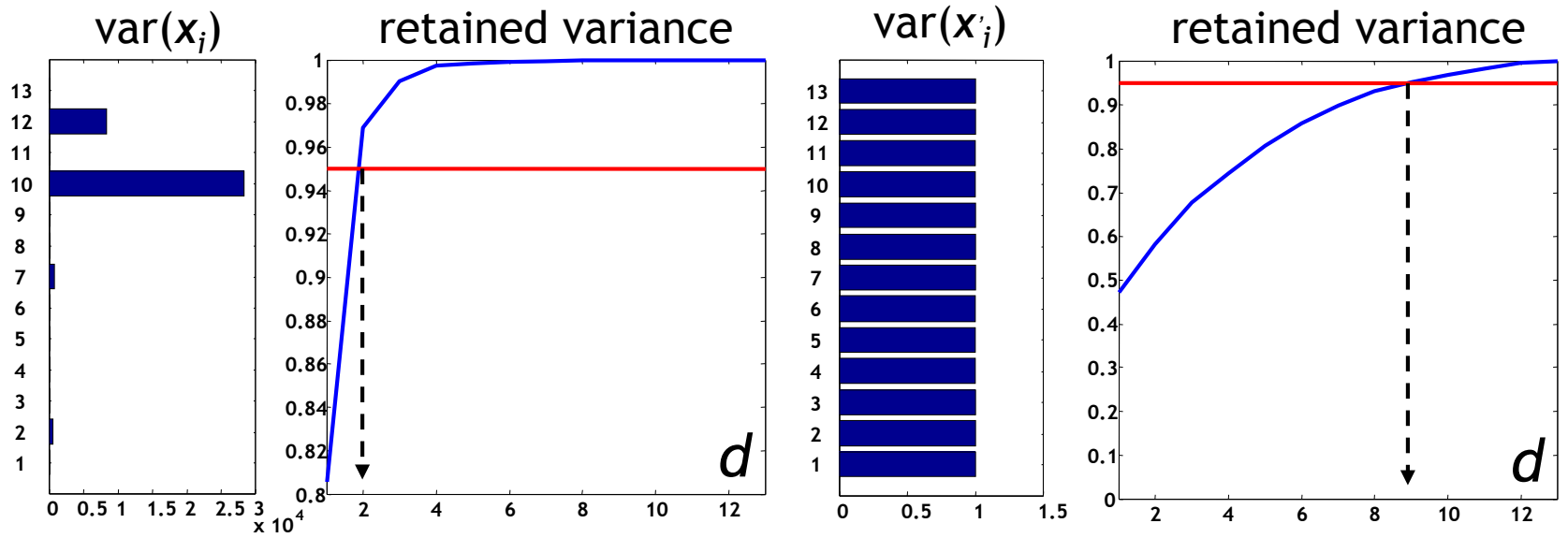
PCA tips

- Derivation supposes mean of data is zero, so it should be removed: $x' \leftarrow (x - \mu)$
- PCA is sensitive to scaling (*e.g.* length in cm has a much larger variance than length in m), so it's best to standardise: $x' \leftarrow (x - \mu) / \sigma$



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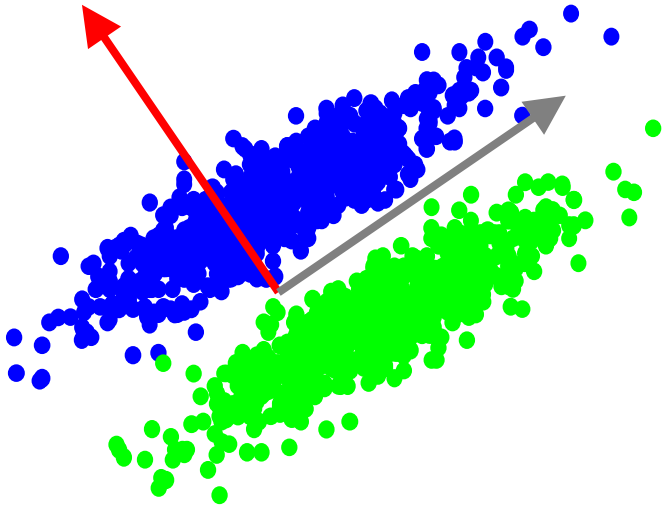
PCA conclusions

- PCA:
  - Is **global** and **linear** (but mixtures can be used)
  - Is **unsupervised** (but we can do PCA on each class)
  - Needs a **lot of data** to estimate Σ well.

- Danger:
  criterion is not necessarily related to the goal; might discard important directions



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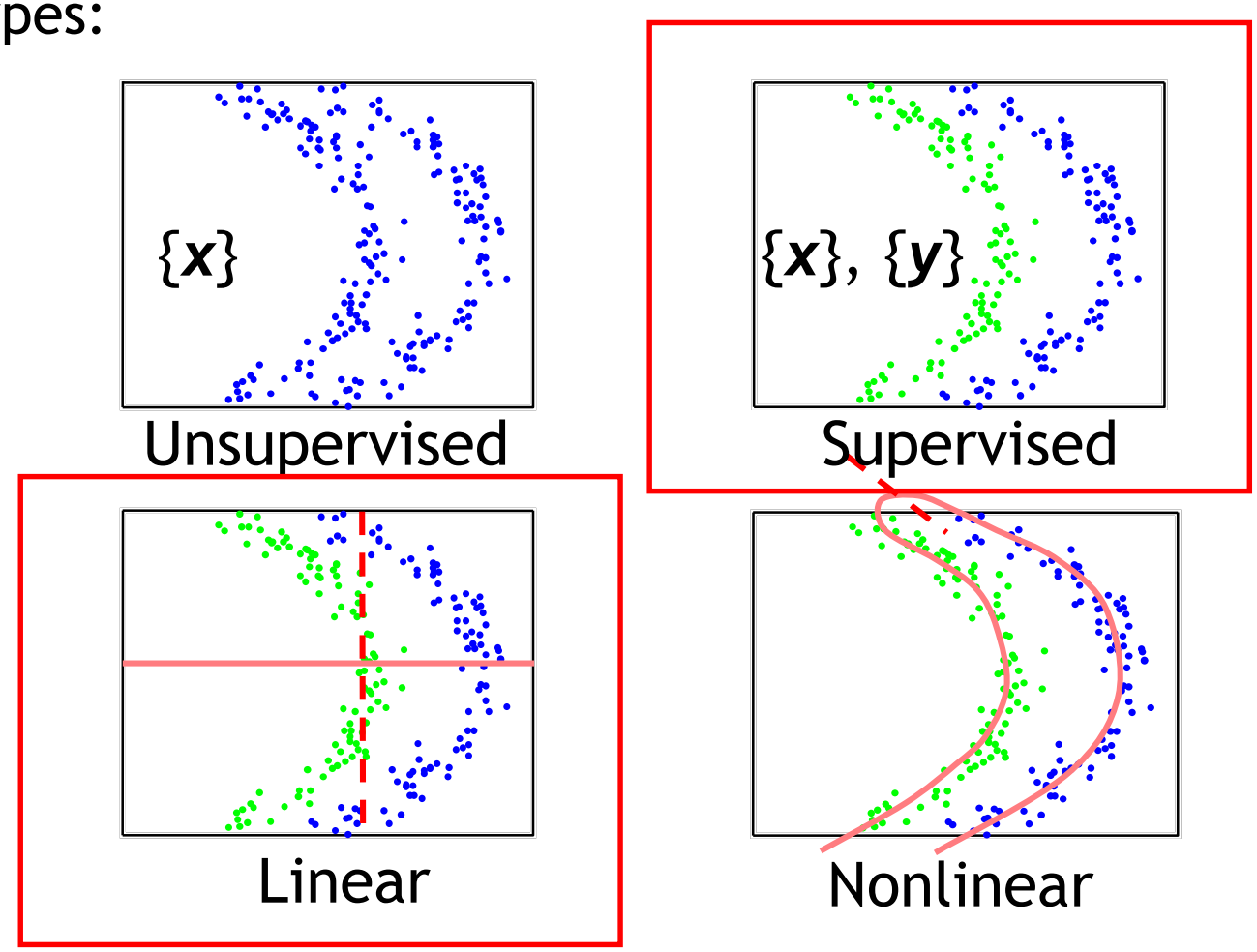
Feature extraction overview

Main types:



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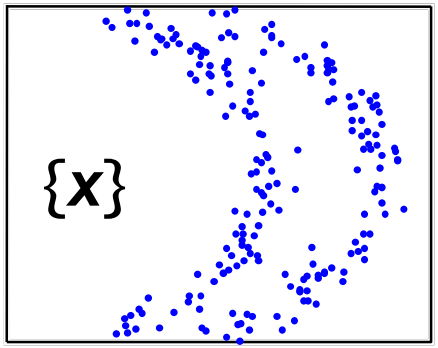
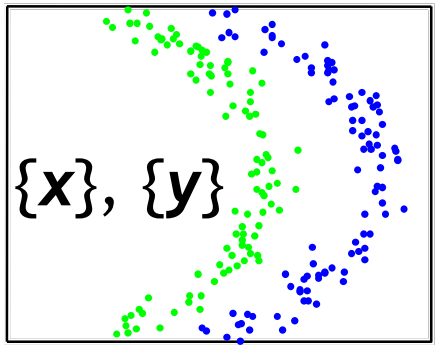
Supervised feature extraction

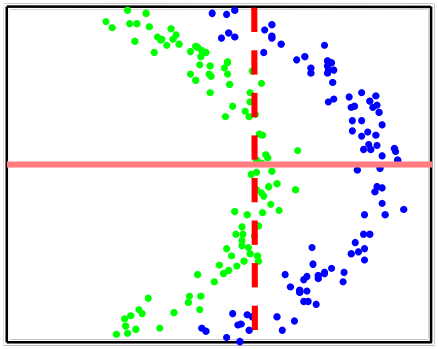
- If class label ω (or y) is given, supervised extraction
- Examples: Fisher mapping; Linear Discriminant Analysis (Day 2)



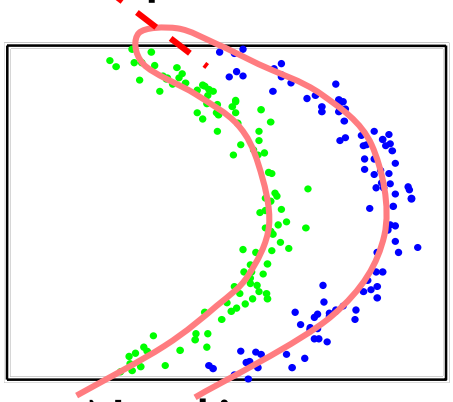
Unsupervised



Supervised



Linear



Nonlinear

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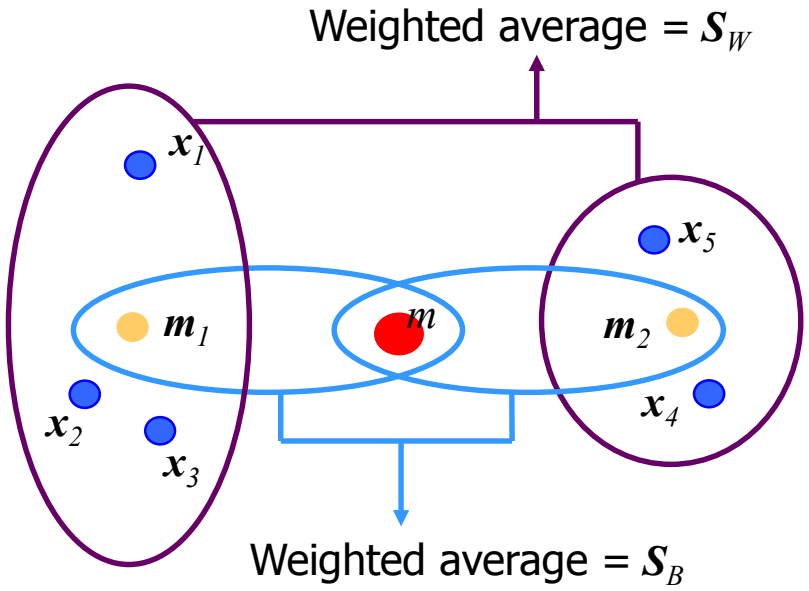
Supervised feature extraction (2)

Within-class and between-class scatter matrices:

- With-class: $\boldsymbol{S}_w = \sum_{i=1}^{C} \frac{n_i}{n} \boldsymbol{\Sigma}_i$
- Between-class: $\boldsymbol{S}_B = \sum_{i=1}^{C} \frac{n_i}{n} (\boldsymbol{m}_i - \boldsymbol{m})(\boldsymbol{m}_i - \boldsymbol{m})^T$



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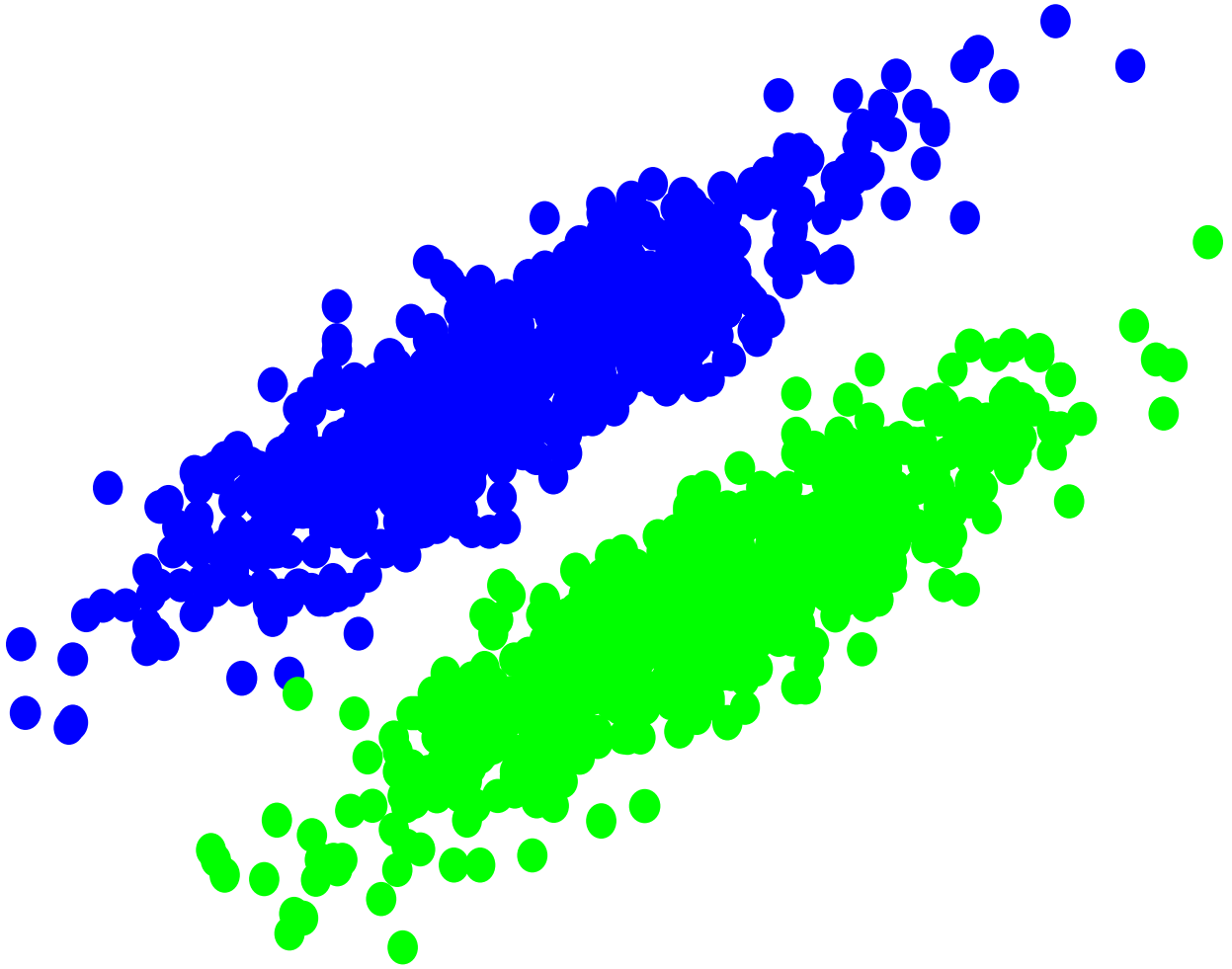
Fisher mapping



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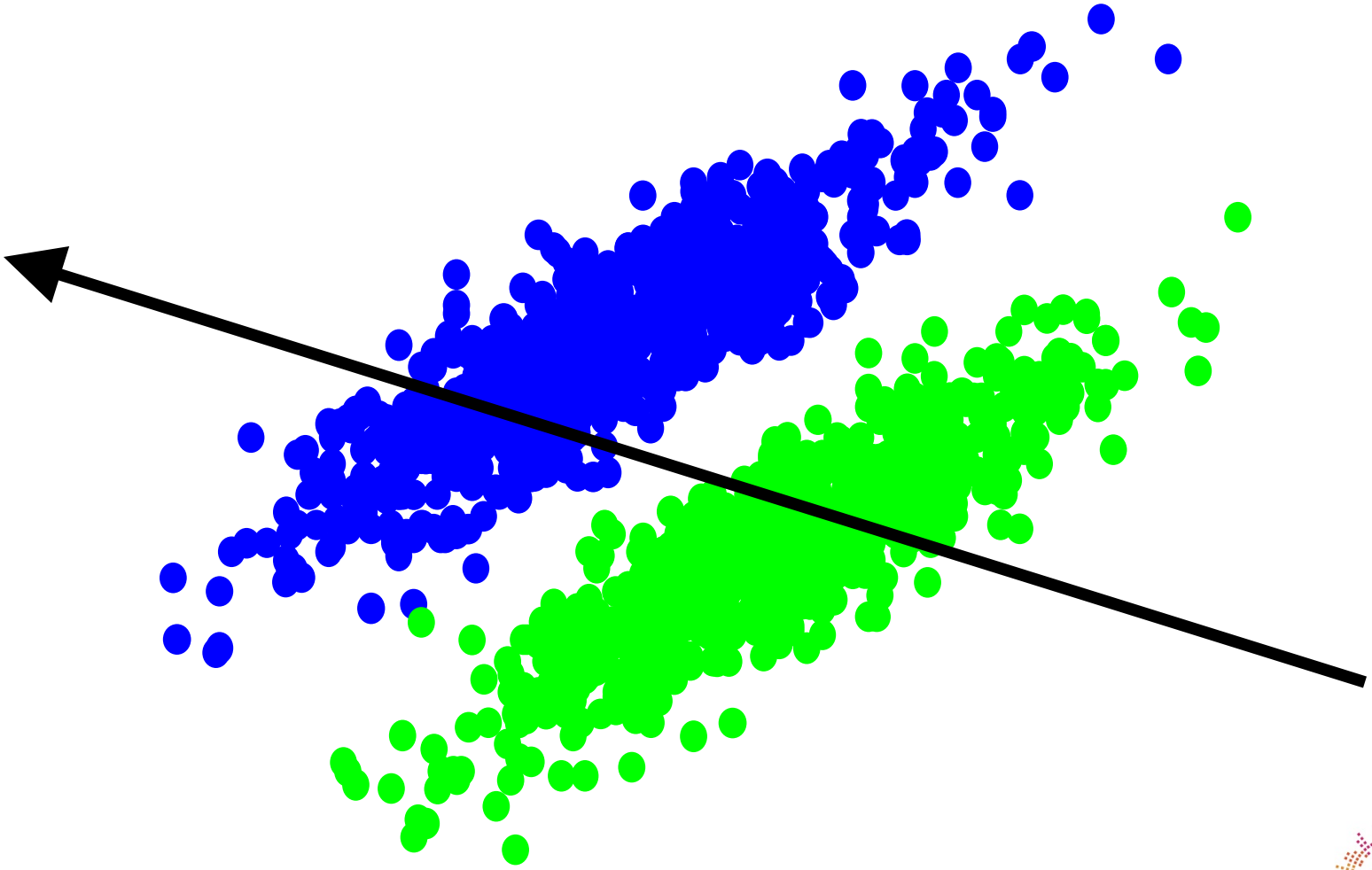

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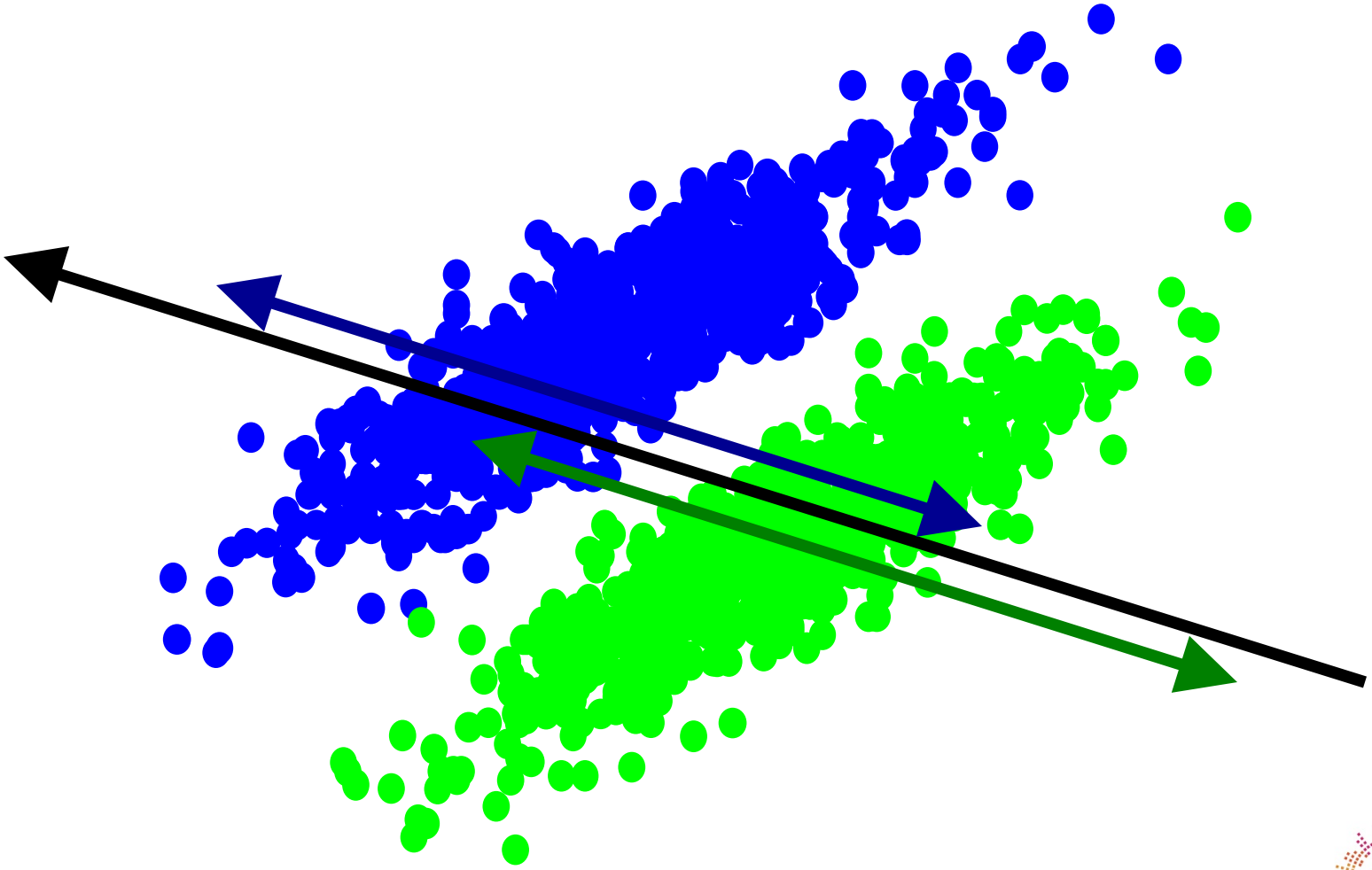

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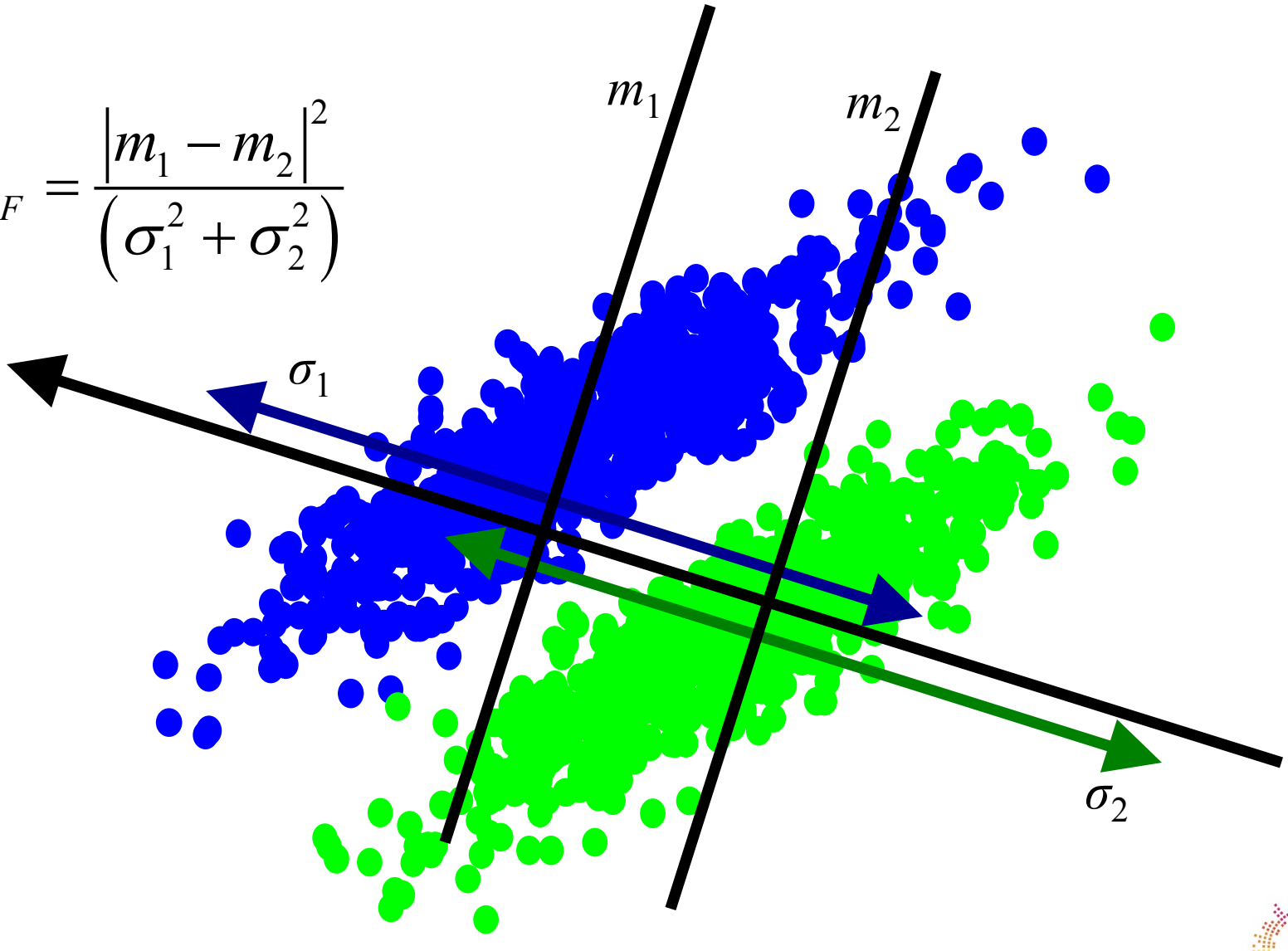
Fisher mapping

$$J_F = \frac{\left|m_1 - m_2\right|^2}{\left(\sigma_1^2 + \sigma_2^2\right)}$$



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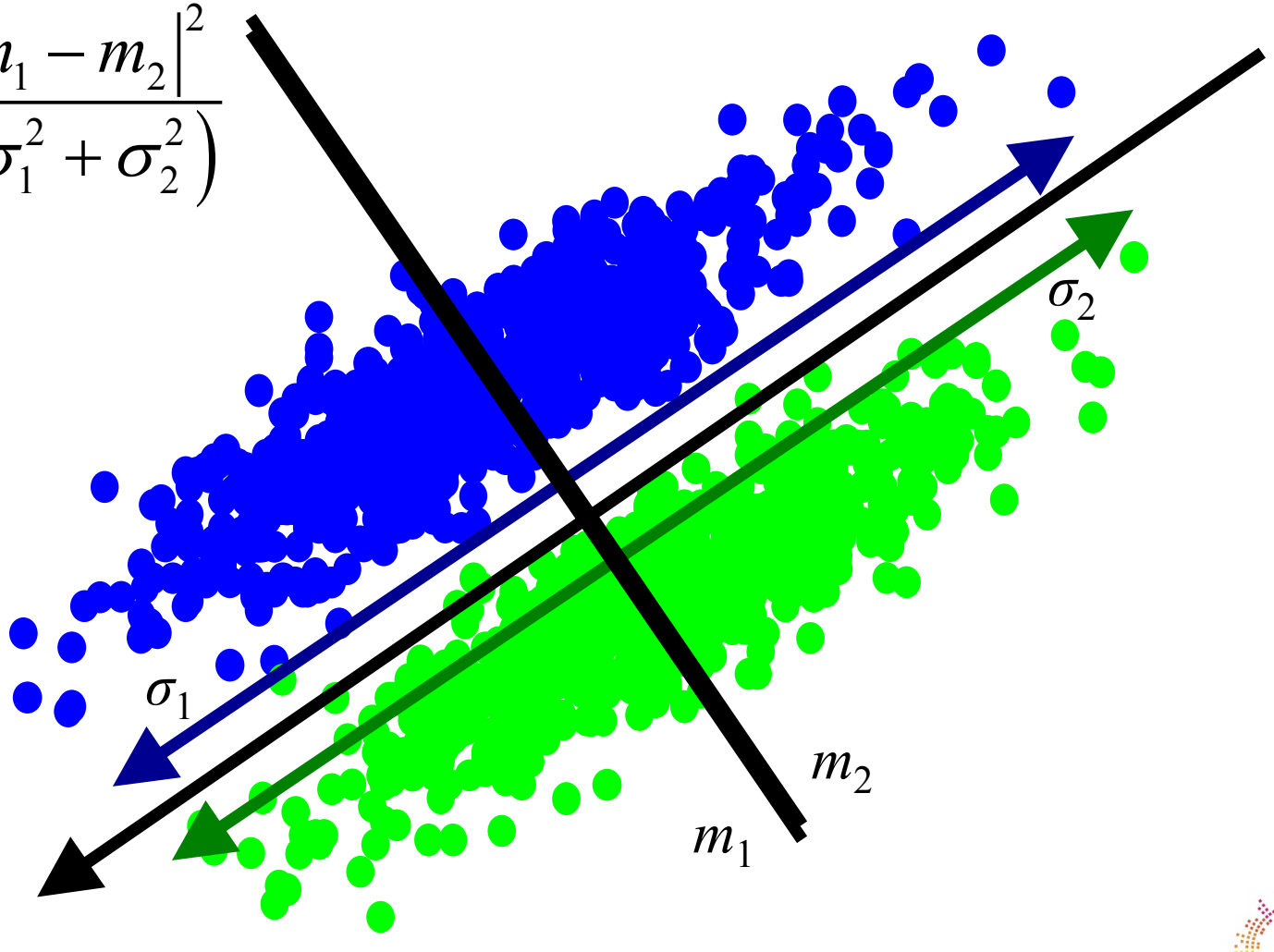

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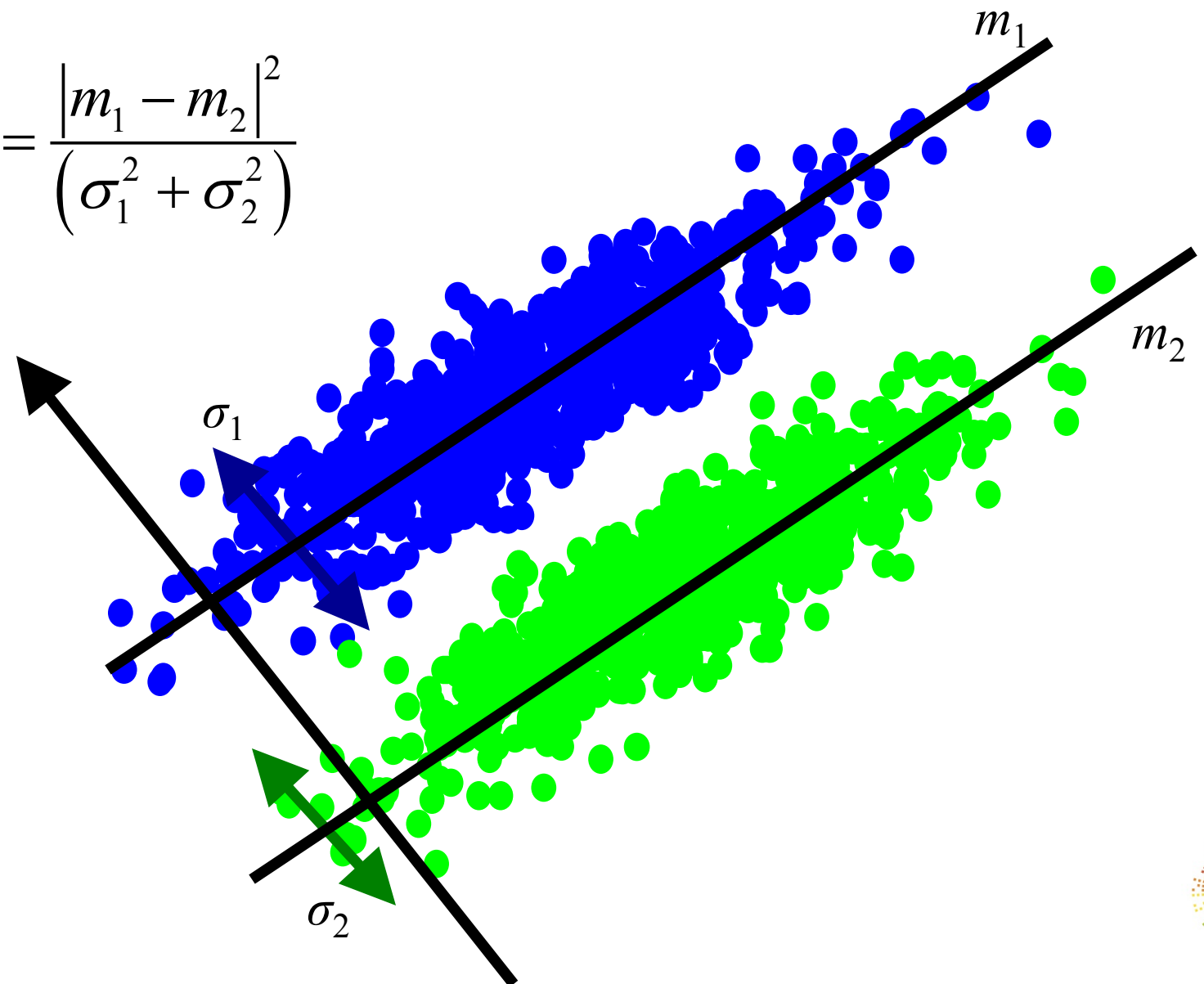

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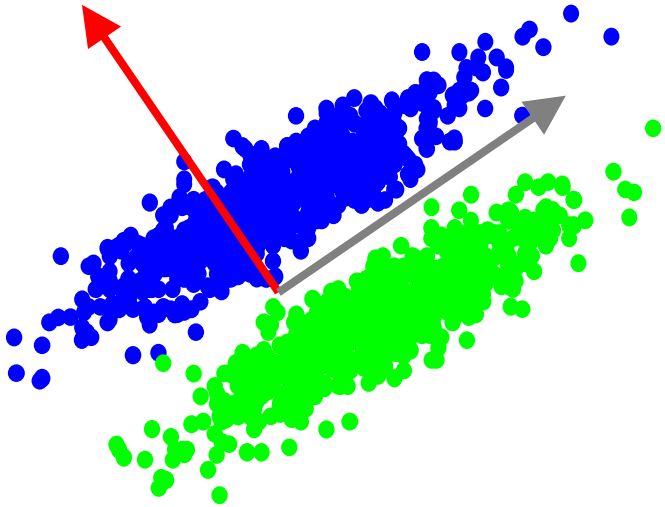
Fisher mapping

- Find basis vector $\boldsymbol{a}_1$ for $\{\boldsymbol{x}\}$ such that in the projections, the classes are maximally separated
- Choose $\boldsymbol{a}_1$ to maximise Fisher criterion:

$$J_F(\boldsymbol{a}_1) = \frac{\boldsymbol{a}_1^T \boldsymbol{S}_B \boldsymbol{a}_1}{\boldsymbol{a}_1^T \boldsymbol{S}_W \boldsymbol{a}_1}$$

- Maximize between class variance

  Minimize within class variance



- Solution: eigen-analysis on $\boldsymbol{S}_W^{-1}\boldsymbol{S}_B$

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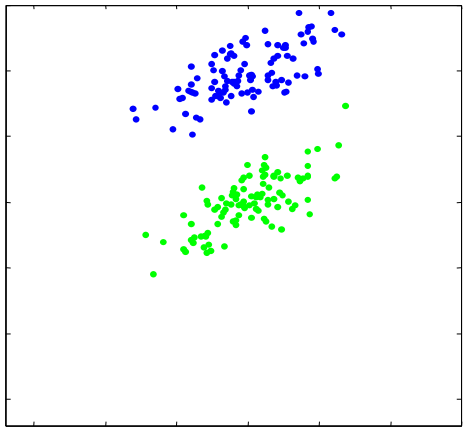
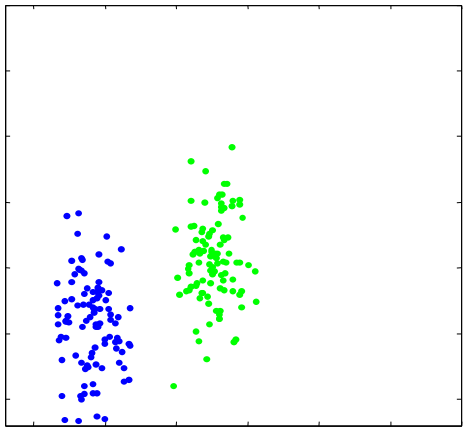
Fisher mapping (2)



Original



Decorrelated

Decorrelation:

1. we assume that the classes have a similar and normal distribution
2. we ROTATE the dataset such that the class conditional densities are uncorrelated (decorrelated)

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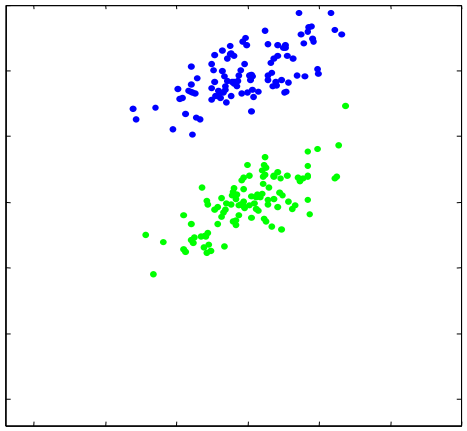
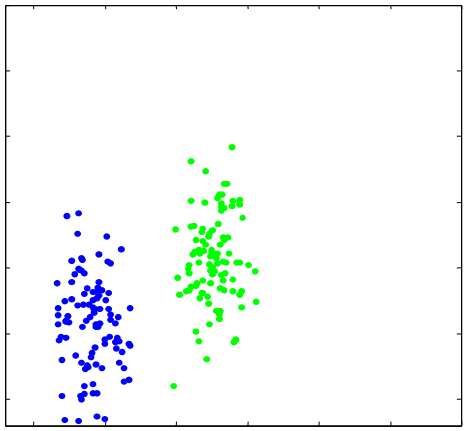
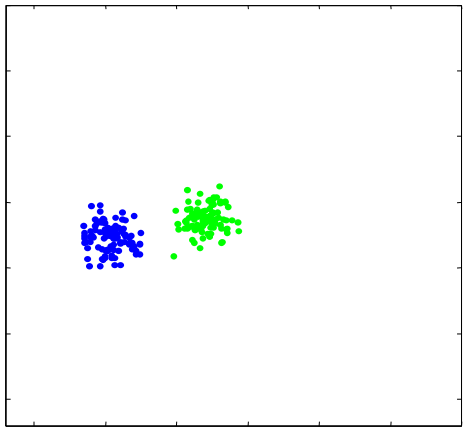
Fisher mapping (2)



Original



Decorrelated



Sphered ($\boldsymbol{S}_W^{-1}$)

Sphering:

1. we assume that the classes have a similar and normal distribution
2. use the within-class scatter matrix to sphere the class conditional distributions

(Class-conditional effects have been removed now)

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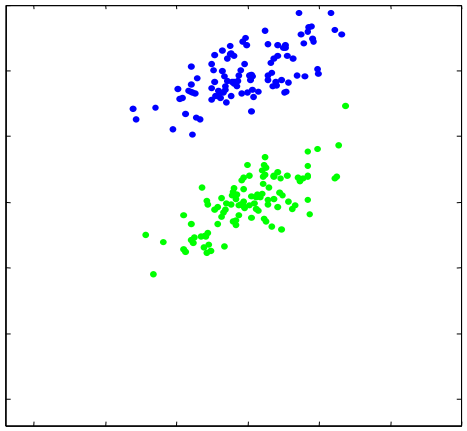
Fisher mapping (2)



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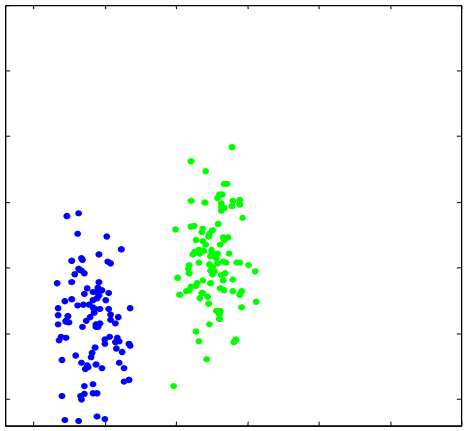
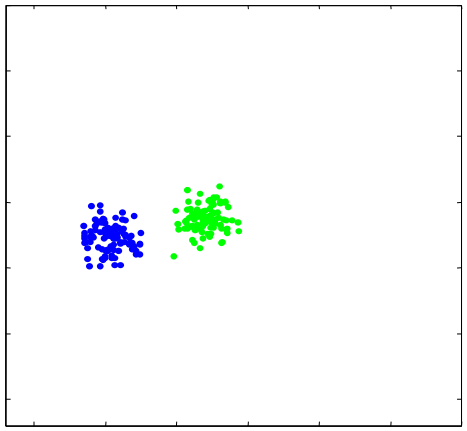
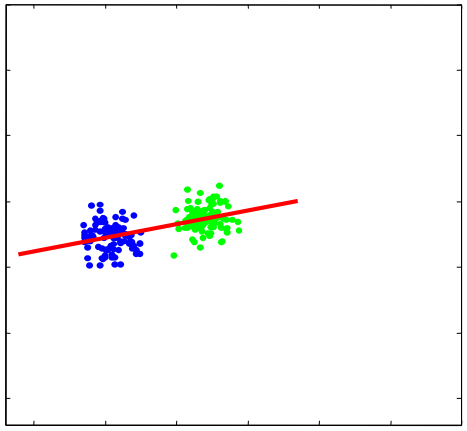


Decorrelated



Sphered (S_W^{-1})



PCA on means (S_B)

PCA on means:

1. Perform PCA on the means (S_B)
2. For c classes, extract c-1 dimensions

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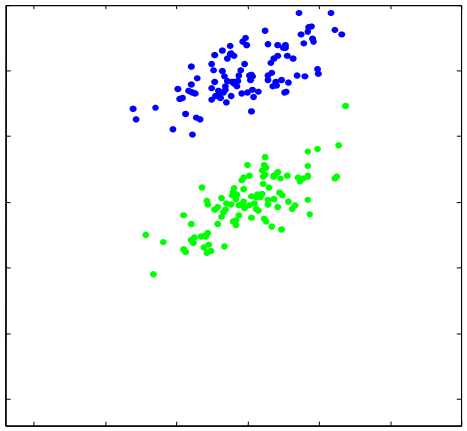
Fisher mapping (2)



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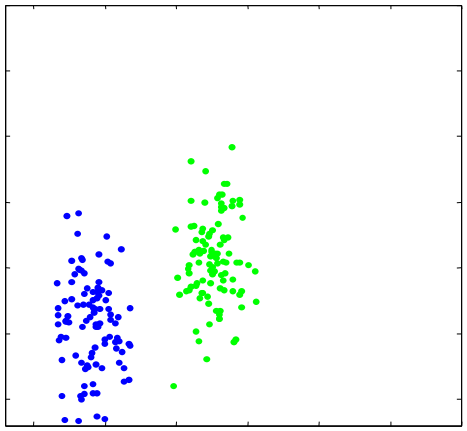
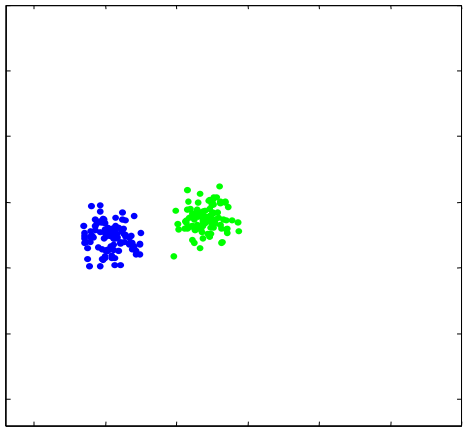
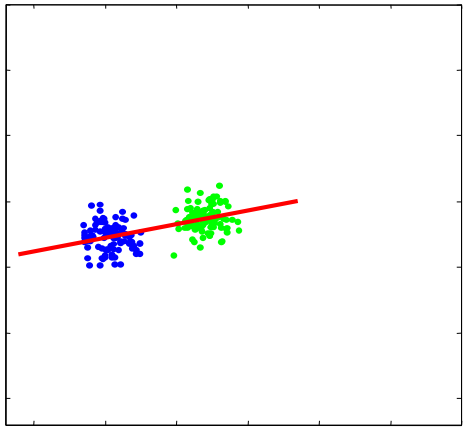


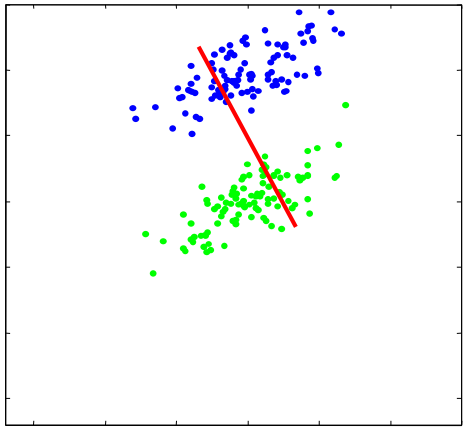
Decorrelated



Sphered (S_W^{-1})



PCA on means (S_B)



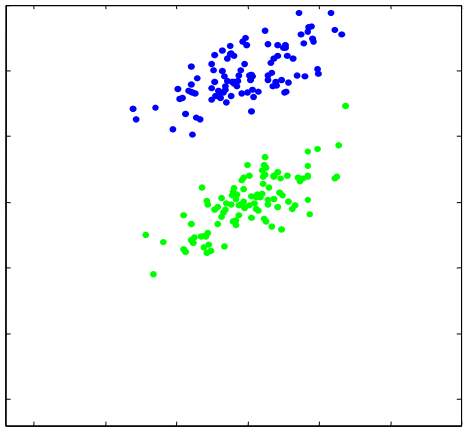
Restored

Restoring:

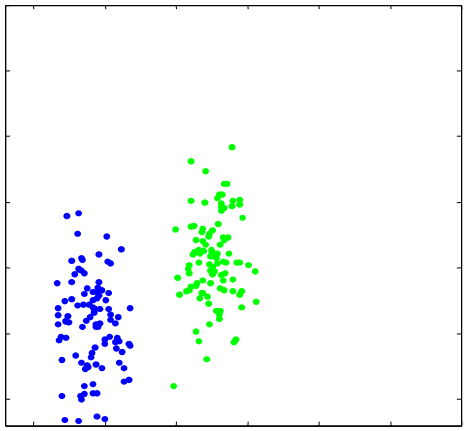
Project this direction back in the original space

BioSB

Fisher mapping (2)



Original



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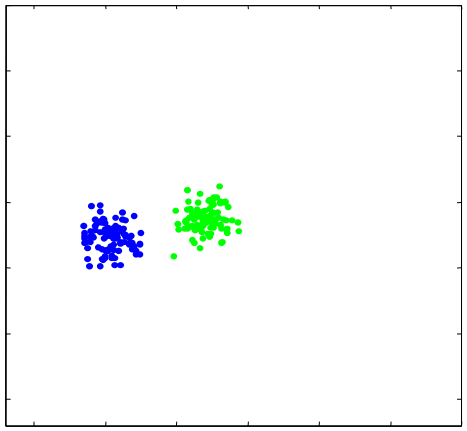

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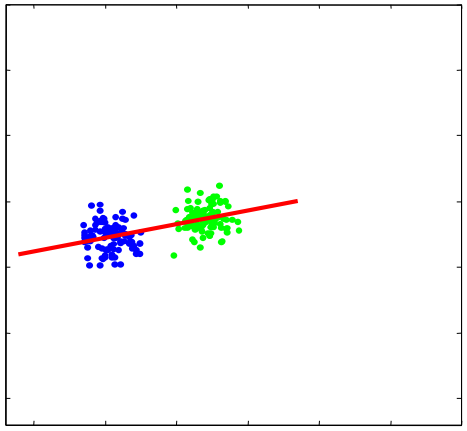

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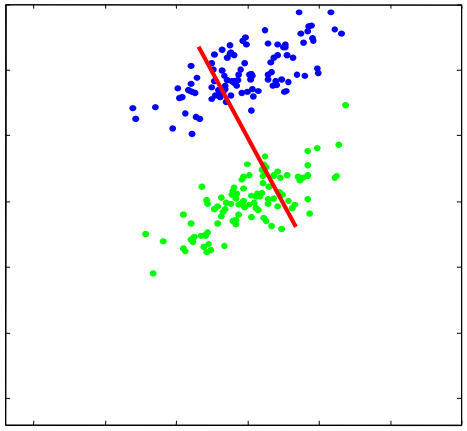

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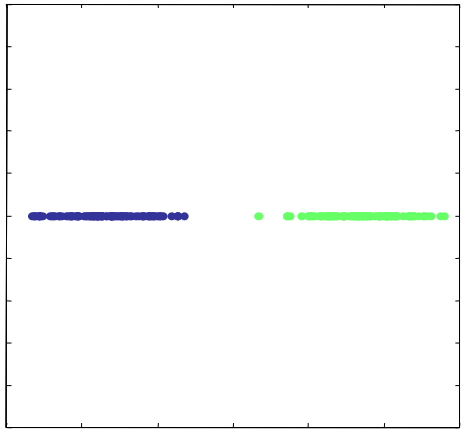


Projected data

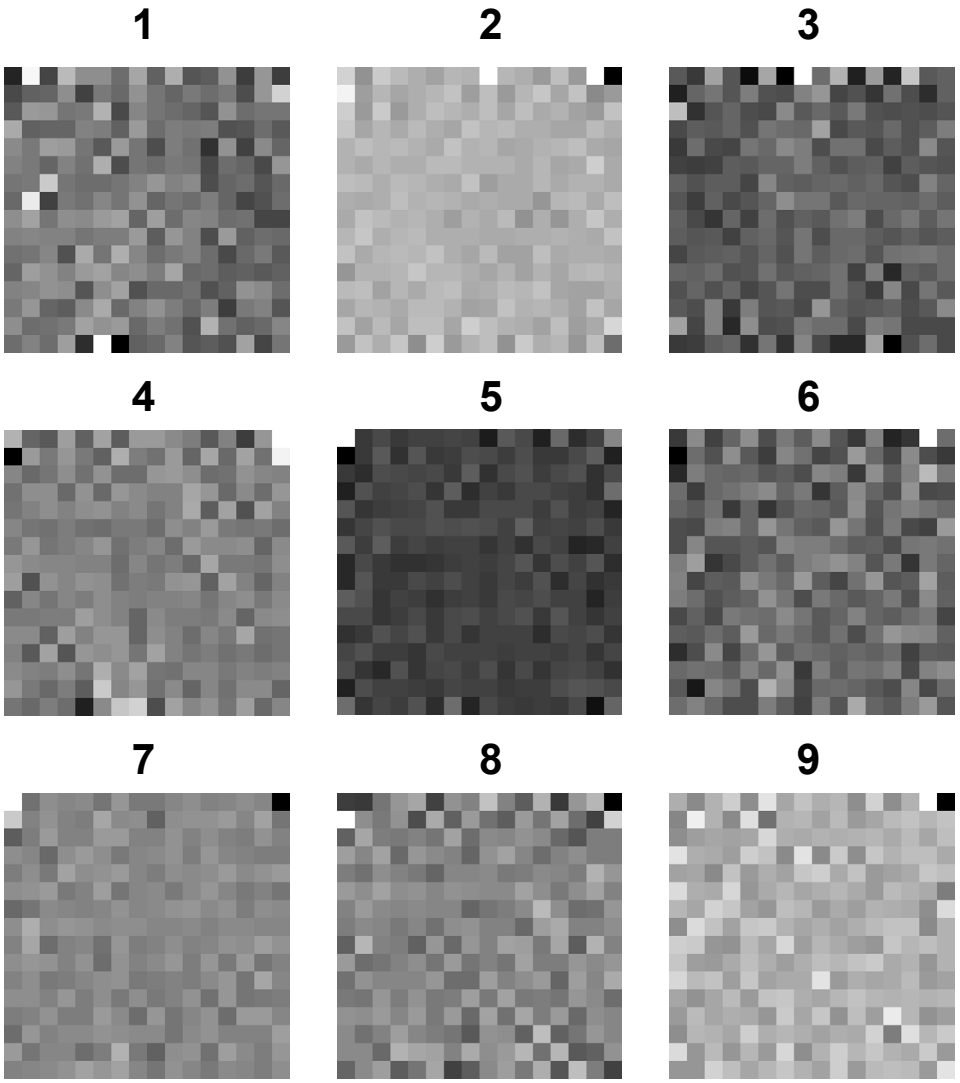
Project:

Project data on projected direction

BioSB

Fisher mapping (3)

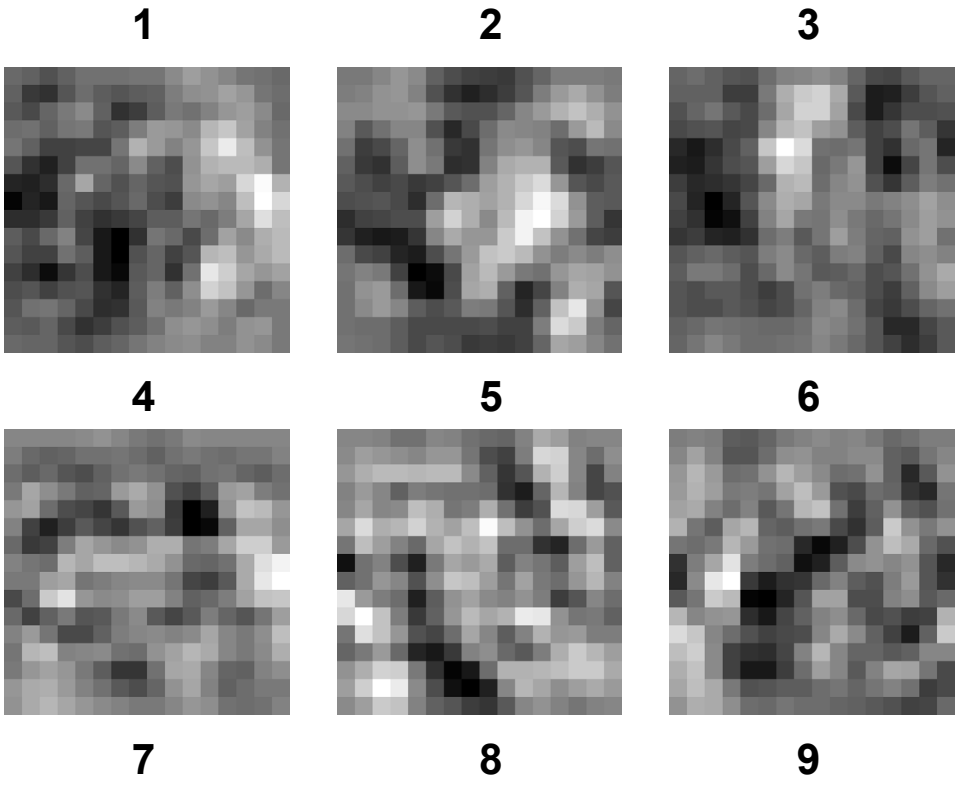
- Map down to a maximum of c - 1 dimensions (why?)
- Example: NIST digits



BioSB

Fisher mapping (4)

- To avoid fitting noise, can do PCA first
- If system underdetermined ($n \leq p$), first doing PCA is required



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Recapitulation

- Discussed:
  - Linear feature extraction
  - Unsupervised: principal component analysis (PCA), widely used linear feature extraction method
  - Supervised: Fisher mapping

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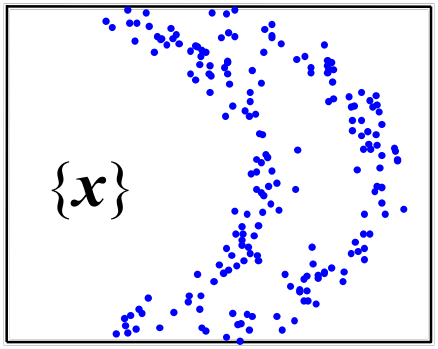
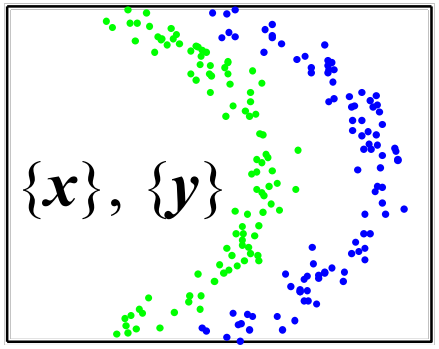
Feature extraction

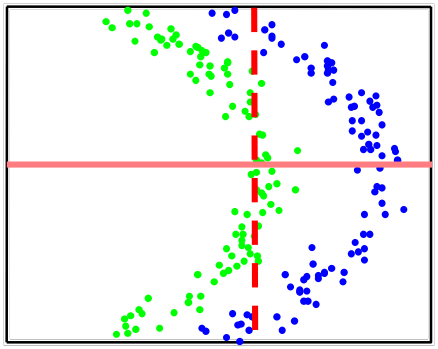
- Main types:



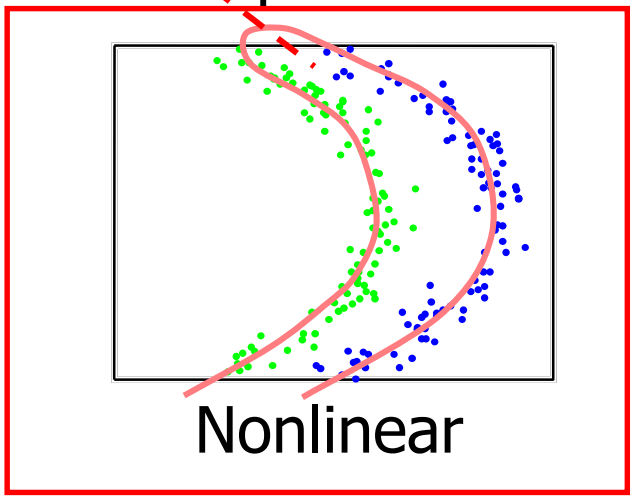
Unsupervised



Supervised



Linear



Nonlinear

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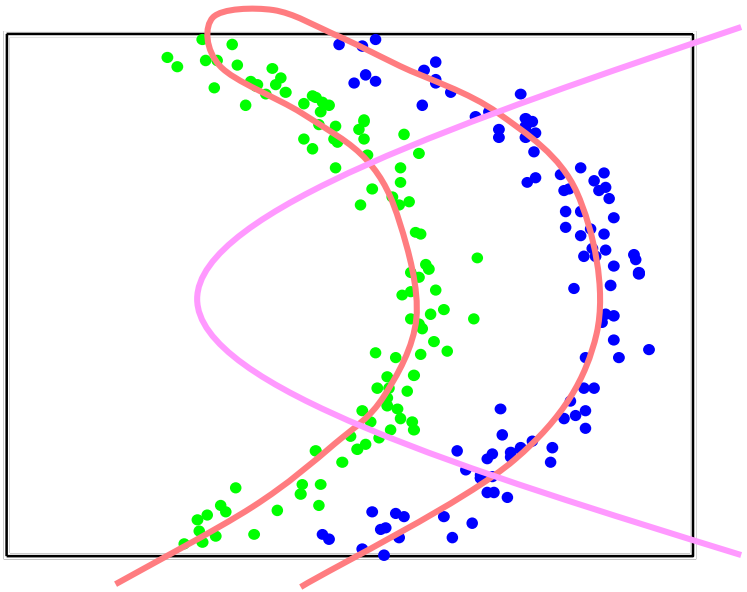
Overview

- Nonlinear feature extraction

- Multidimensional scaling (MDS):
  - Linear: classical scaling
  - Nonlinear:
    - Sammon mapping
    - t-SNE

Nonlinear feature extraction

- Nonlinear mappings:
  a large collection of possible mappings,
  but not all applicable to all problems
- Usually needs an *optimisation algorithm*



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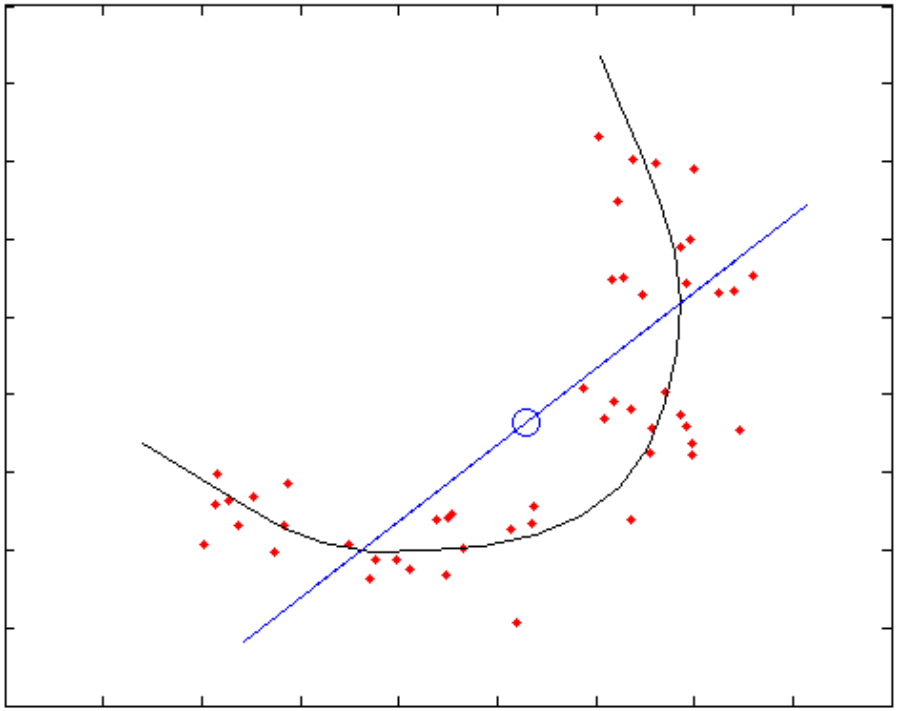
Nonlinear feature extraction (2)

- Example:
  principal curves



- Principal component: minimise deviation from line
- Principal curve: minimise deviation from a curve
  (from a given family of curves)

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Nonlinear feature extraction (3)

Example: embedding

- Find new representation such that distances between samples are preserved as well as possible

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Multidimensional scaling (MDS)

- Criterion: preserve all inter-sample distances
- Needed: *n* x *n* distance matrix between all points
- Map samples to a new (lower dimensional) space

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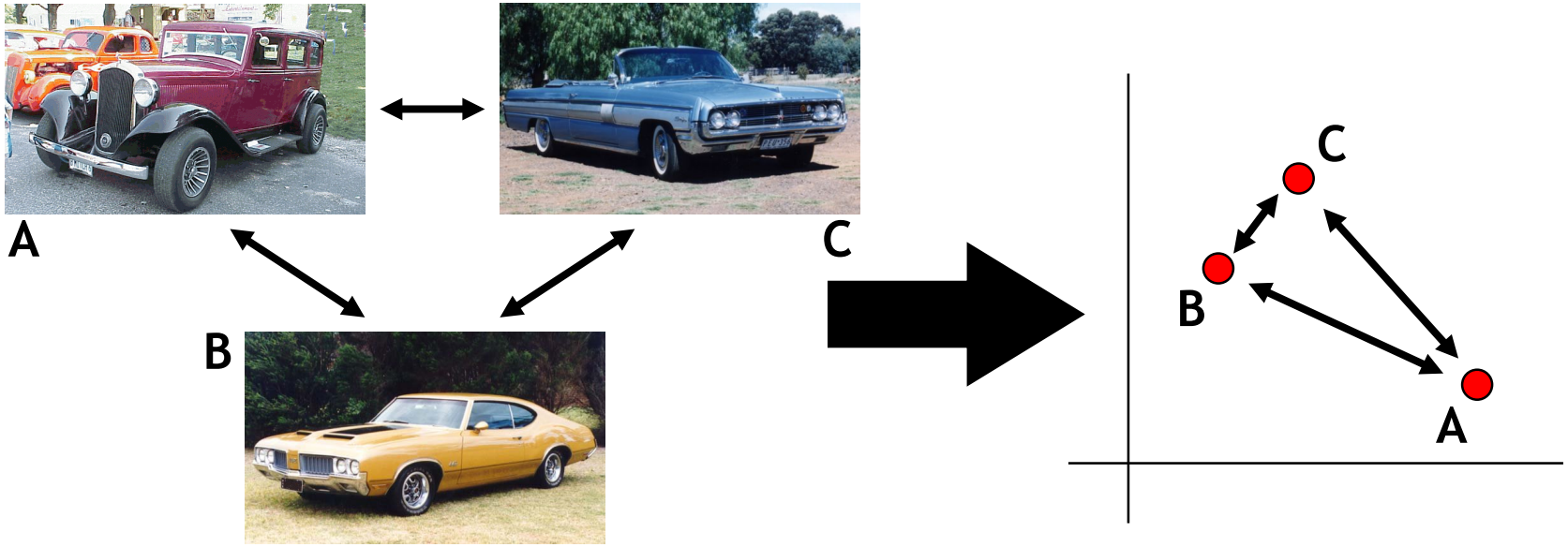

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MDS (2)

- Advantages of using distances:
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  - easy to introduce nonlinearity

- Algorithms should find:
  - new, low-dimensional coordinates for each object
  - the number of dimensions to embed the data in

MDS: Non-linear mappings (5)

- d_{ij} : distance $\| \boldsymbol{x}_i - \boldsymbol{x}_j \|$ in original space (? - dimensional)
- δ_{ij} : distance $\| \boldsymbol{y}_i - \boldsymbol{y}_j \|$ in new space (d - dimensional)

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$$Stress(\boldsymbol{y}) = \frac{1}{\sum_i \sum_{j>i} d_{ij}^{(q+2)}} \sum_i \sum_{j>i} d_{ij}^{q} (\delta_{ij} - d_{ij})^2$$

- weight factor $q = \ldots, -2, -1, 0, 1, 2, \ldots$

  $q < 0$: emphasise short distances

  $q > 0$: emphasise large distances

  Sammon mapping: $q = -1$

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  $q < 0$: emphasise short distances
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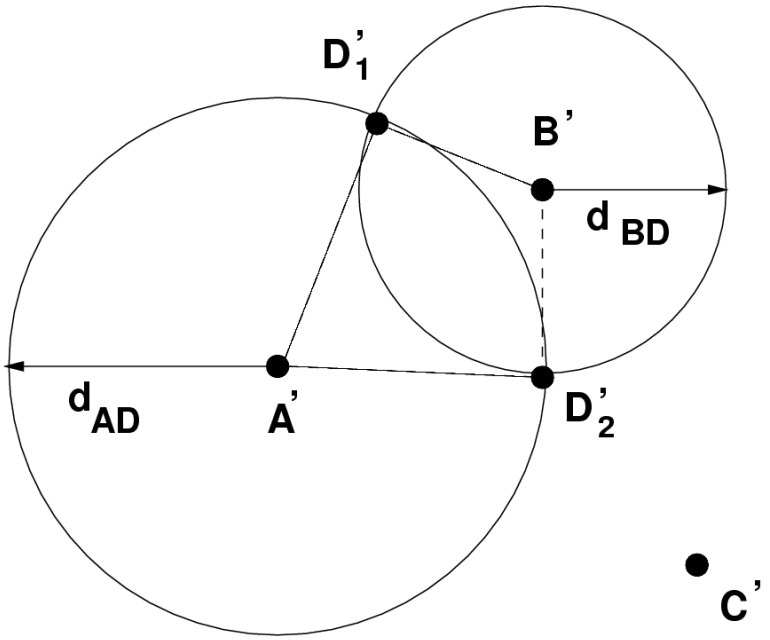
- Minimise as function of $\boldsymbol{y}$, using your favourite minimizer, e.g. gradient descent:

$$\boldsymbol{y}' = \boldsymbol{y} - \alpha \frac{\partial Stress(\boldsymbol{y})}{\partial \boldsymbol{y}}$$

Embedding new points

- Problematic: re-run entire algorithm...
- Sub-optimal solution: triangulation
  - Embed new point **D**
  - **D** has **A** and **B** as neighbors in original space
  - Preserve distance to two embedded neigbours **A'**, **B'** exactly
  - Use **C'** to decide which of the two candidates D_1', D_2' to use



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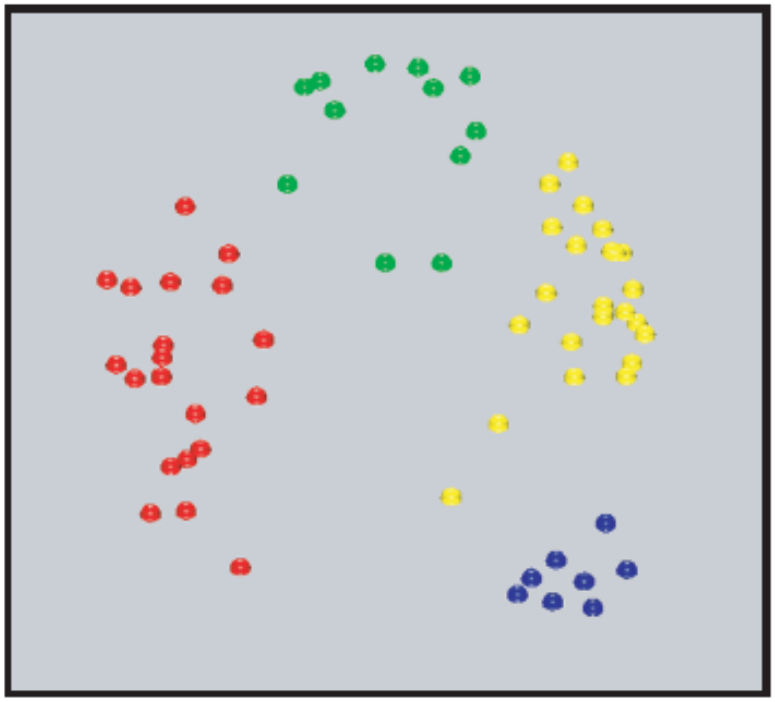
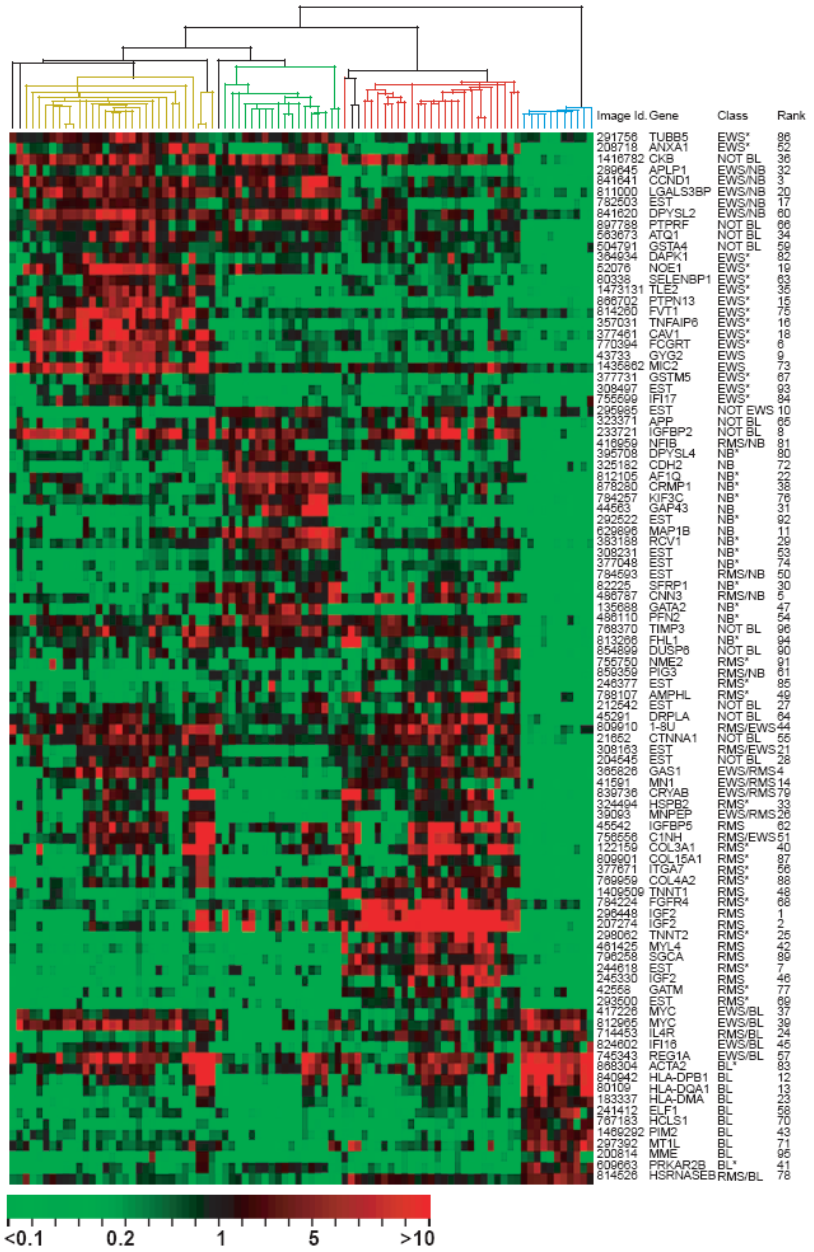
MDS example



- Neuroblastoma (NB)
- Rhabdomyosarcoma (RMS)
- Burkitt lymphoma (BL)
- Ewing family of tumors (EWS),



Khan et al, Nature Medicine, 2001

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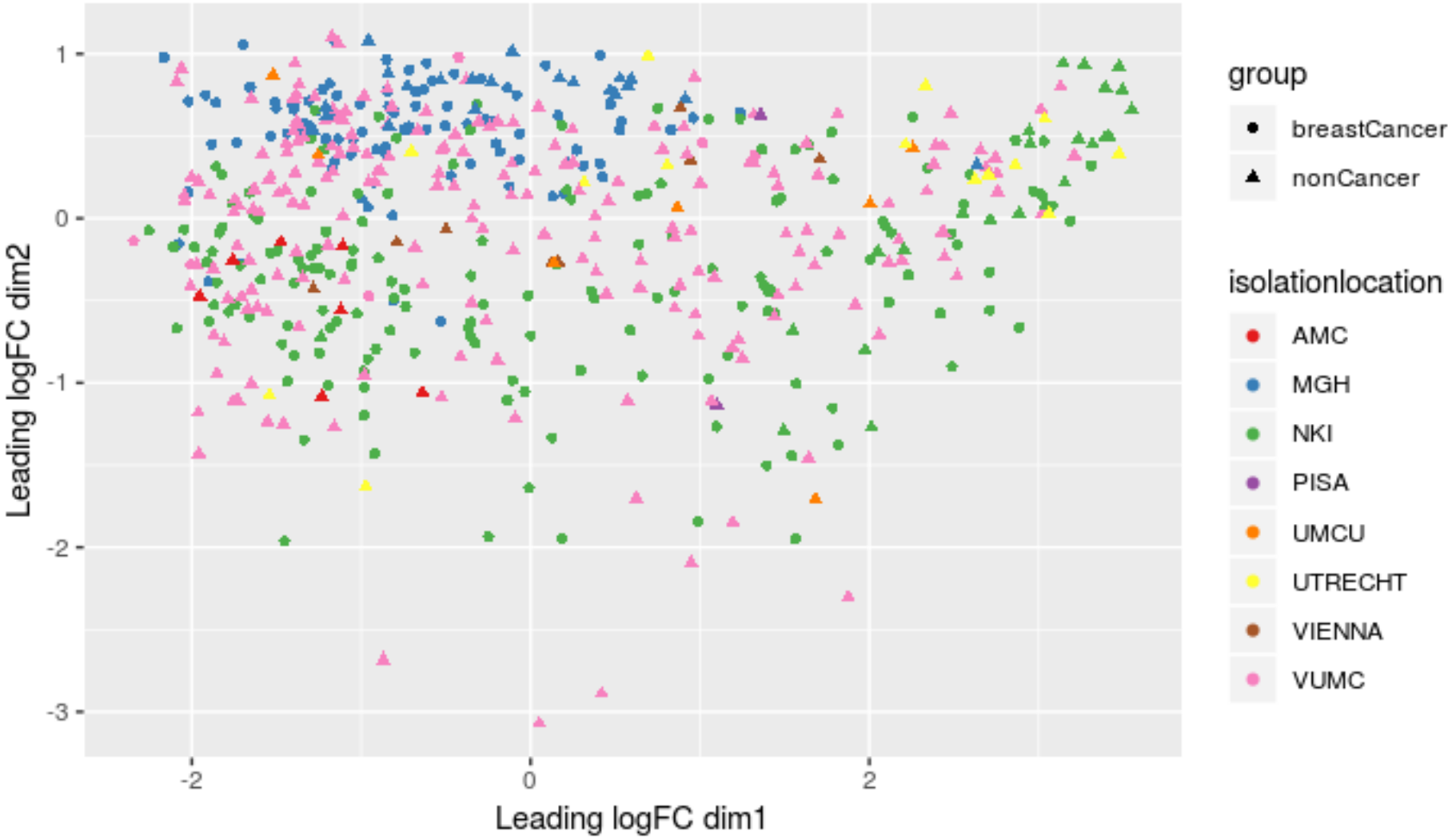
MDS Example: detecting batch effects



t-SNE (t-distributed stochastic neighbor embedding) (van der Maaten et al, 2008)

- **Definitions:**
  - A **data point** is a point x_i in the original data space R^D
  - A **map point** is a point y_i in the map space R^2
  - This space will contain our final representation of the dataset
  - There is a bijection between the data points and the map points
  - Every map point represents one of the data points.

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t-SNE (3)

- **How do we choose the positions of the map points?**
  - We want to conserve the structure of the data
  - data points close $\Longrightarrow$ corresponding map points close

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  - We want to conserve the structure of the data
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- **Similarity of data points**
  - Let $|x_i - x_j|$ be the Euclidean distance between two data points
  - The conditional similarity between the two data points is:

$$p_{j|i} = \frac{\exp\left(-|x_i - x_j|^2 / 2\sigma_i^2\right)}{\sum_{k \neq i} \exp\left(-|x_i - x_j|^2 / 2\sigma_i^2\right)}$$

BioSB

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  - Assuming a Gaussian distribution around x_i with variance σ_i^2

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t-SNE (4)

- The conditional similarity between the two data points is:

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- This represents the likelihood of x_j given x_i
- Assuming a Gaussian distribution around x_i with variance σ_i^2
- σ_i^2 is different for every point
  - dense areas are given a smaller variance
  - sparse areas are given a larger variance
- Similarity is symmetrized form:

$$p_{ij} = (p_{j|i} + p_{i|j})/2N$$

t-SNE (5)

- **Similarity of map points:**
  - Let $|y_i - y_j|$ be the Euclidean distance between the map points

$$q_{ij} = \frac{f(|y_i - y_j|)}{\sum_{k \neq i} f(|y_i - y_k|)}$$

    with

$$f(z) = 1/(1 + z^2)$$

  - Same as for the data points, but different distribution:
  - t-Student with one degree of freedom, or Cauchy distribution

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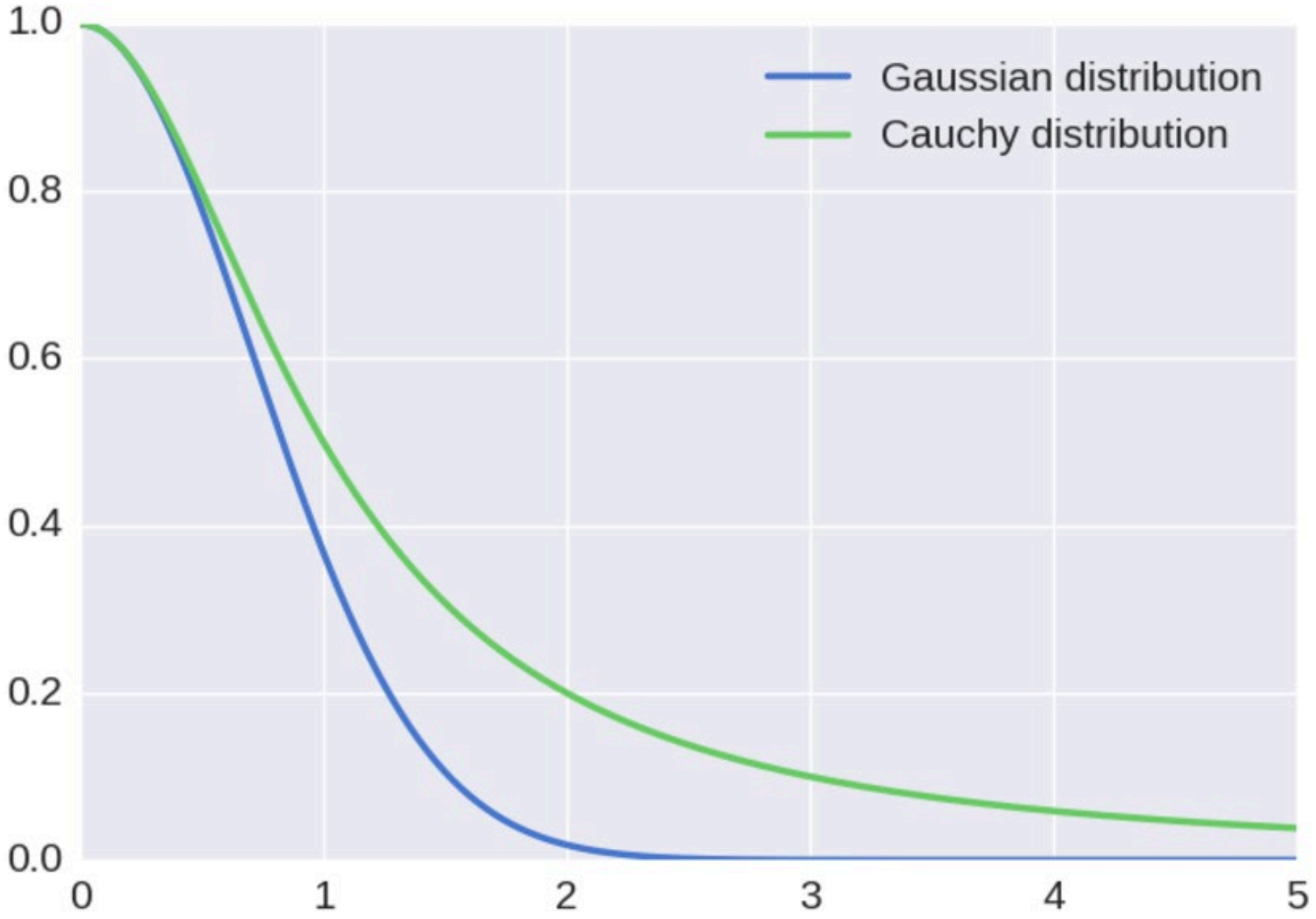
t-SNE (10): Cauchy and Gaussian distribution



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t-SNE (6)

- **How do we choose the positions of the map points?**
  - Data similarity matrix (p_{ij}) is fixed
  - Map similarity matrix (q_{ij}) depends on the map points
  - Get two matrices as similar as possible
  - Idea: similar data points yield similar map points

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t-SNE (7)

- **Algorithm**
  - Minimizing the Kullback-Leibler divergence between p_{ij} and q_{ij}:

$$KL(P,Q) = \sum_{i,j} p_{ij} \log(p_{ij}/q_{ij})$$

  - $KL(P,Q)$ measures the distance between our two distributions

t-SNE (7)

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$$KL(P,Q) = \sum_{i,j} p_{ij} \log(p_{ij}/q_{ij})$$

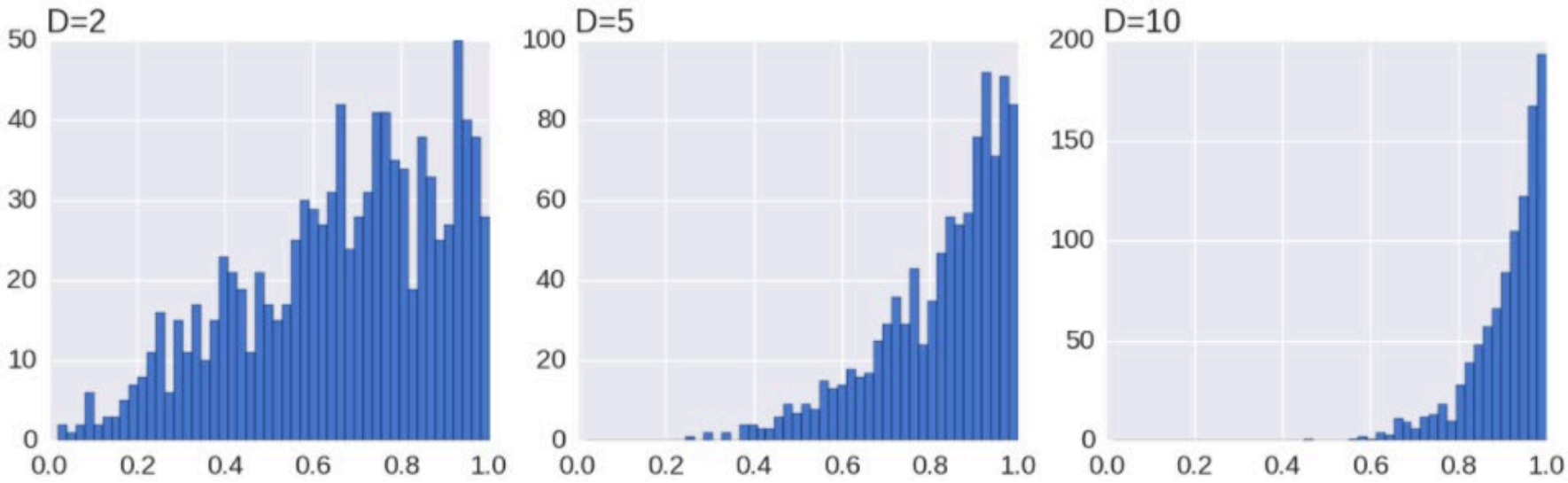
  - $KL(P,Q)$ measures the distance between our two distributions
  - To minimize this score, we perform a gradient descent
  - The gradient can be computed analytically:

$$\frac{\partial KL(P,Q)}{\partial y_i} = 4 \sum_j (p_{ij} - q_{ij}) f(|y_i - y_j|)$$

    where $f(z) = z/(1+z^2)$
  - The gradient expresses the sum of all spring forces applied to map point i.

t-SNE (8)

- **Why the t-Student distribution?**
  - The volume of the N-dim. ball of radius r scales as r^N
  - For large N, random points are close to the surface, not in center



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t-SNE (9)

- **Why the t-Student distribution?**
  - We go from high dimensionality to low dimensionality
  - If we use the same distribution in data and map space
  - There is an imbalance in the distribution of the distances of a point's neighbors.
  - As distances are so different between a high-D and low-D space
  - Yet, t-SNE tries to reproduce the same distances in the two spaces
  - Result: excess of 'attraction forces' (gradient) that move map space points
  - t-SNE compensates this by the heavier tail of the t-distribution in low-D
  - Larger distances in low-D get more weight so match high-D

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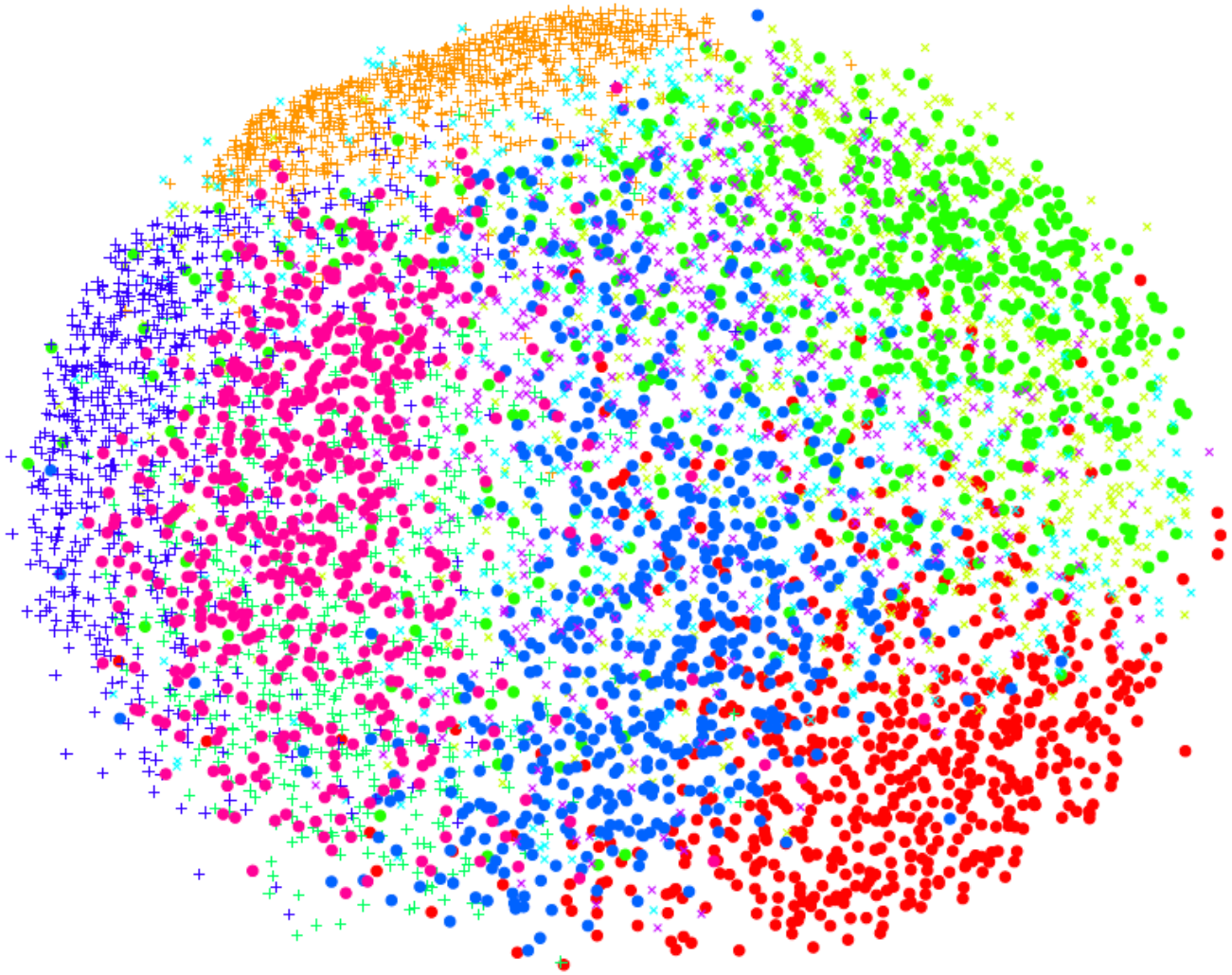
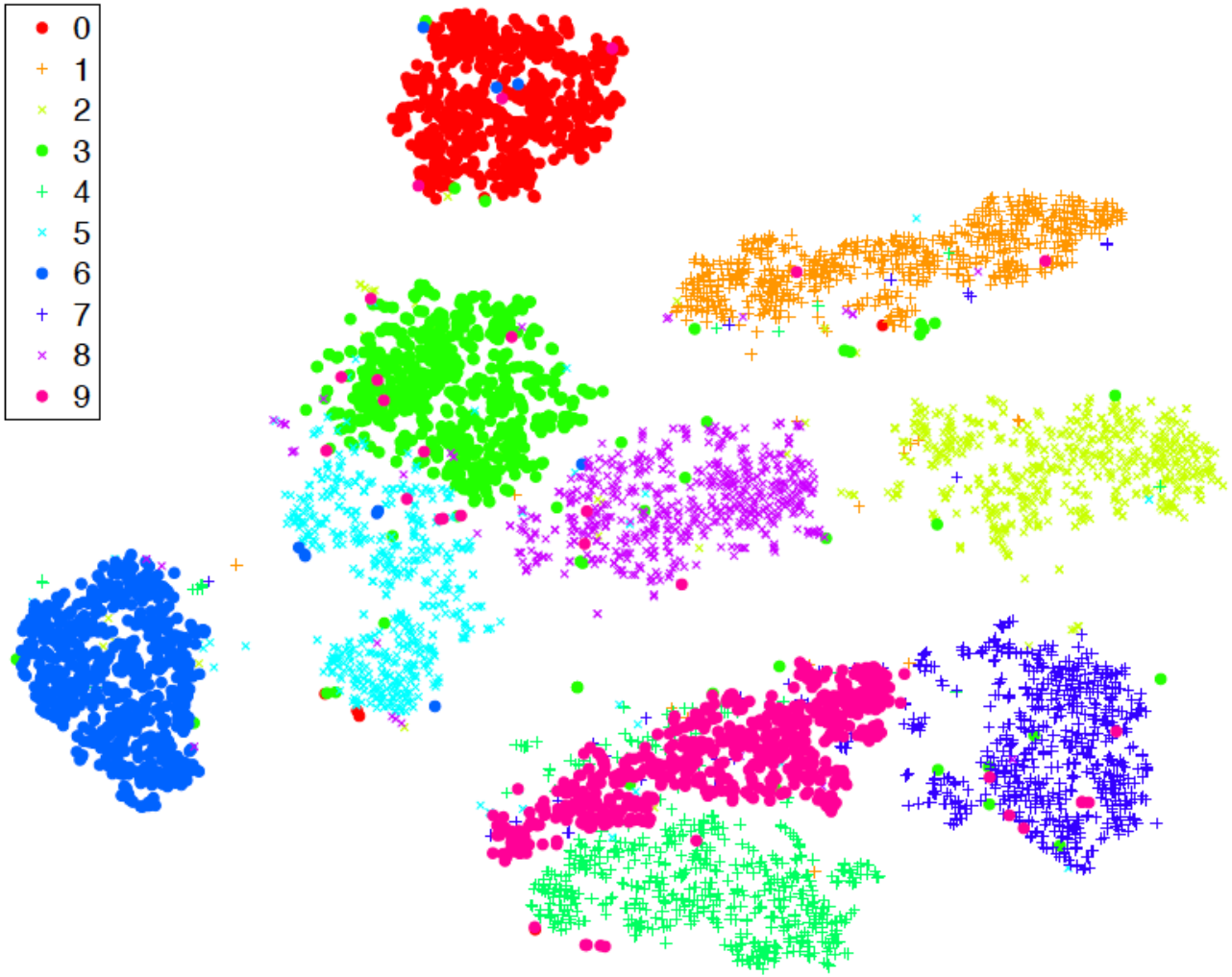
t-SNE (11): Sammon map of digit data



BioSB

t-SNE (12): t-SNE map of digit data



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MDS conclusions

- Experts or measurements give distances
- Optimise a *stress-function* (MDS) or KL distance (t-SNE)
- Important:
  - *the distance measure used*: is it representative?
  - *the weighting of distances* (q): can influence outcome heavily.
  - t-SNE run with defaults is quite reliable
- Largest risk:
  seeing structure in the data that is not really there
- Remaining problem: embedding new data points

Feature selection

- For feature selection, we need:
  - A **criterion** function
    e.g. error, class overlap, information loss
  - A **search algorithm**
    e.g. pick the best single feature at each time

Criteria

1. **Wrapper**: exact performance measure
    - base performance estimate on classifier;
    - estimate performance using cross-validation:
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Criteria

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   - base performance estimate on classifier;
   - estimate performance using cross-validation:
   - very expensive!

Note:
we should never use the training set to calculate performance; this will give a biased estimate!

2. **Filter**: approximate performance predictors:
   - calculate the performance of an easy-to-use model;
   - this gives an indication of how well a more powerful model may perform but
   - is much faster to compute.

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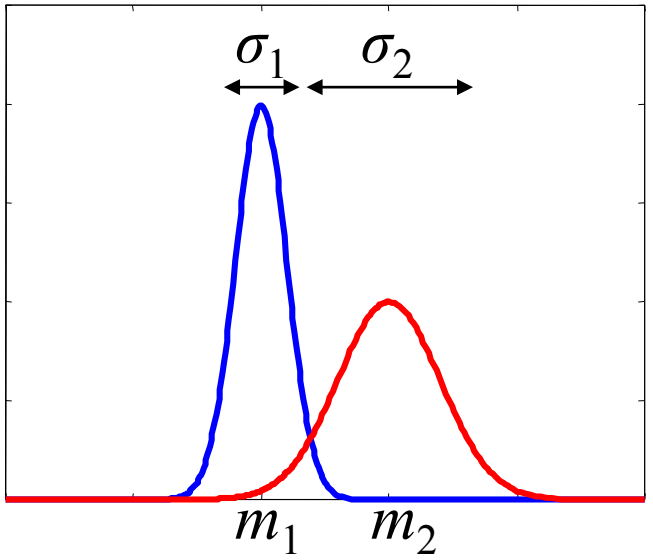
Criteria (2)

- Example
  - Simple measure of the ‘separability’ of classes given a feature
  - 1D case: Signal-to-Noise Ratio (SNR) or Fisher criterion:

$$J_F = \frac{|m_1 - m_2|^2}{\left(\sigma_1^2 + \sigma_2^2\right)}$$



BioSB

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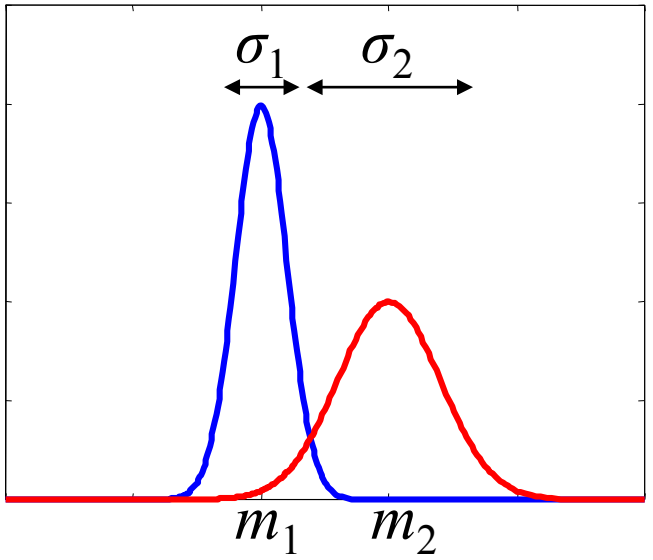
  - 1D case: Signal-to-Noise Ratio (SNR) or Fisher criterion:

$$J_F = \frac{|m_1 - m_2|^2}{\left(\sigma_1^2 + \sigma_2^2\right)}$$



  - If J_F is large: good separability
  - If J_F is small: poor separability

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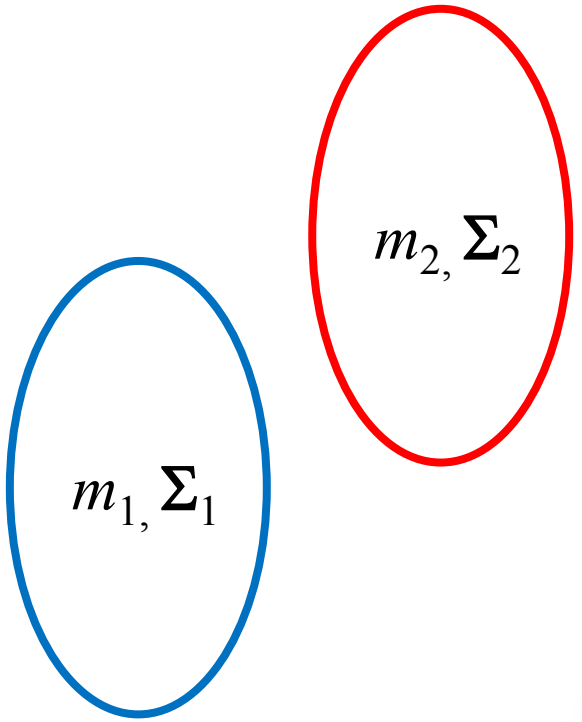
Criteria (4)

- The multi-variate equivalent of Fisher criterion is the
- Mahalanobis distance:
  - assumes
    - Gaussian distributions with
    - equal covariance matrix Σ:

$$D_M = (m_1 - m_2)^T \Sigma^{-1} (m_1 - m_2)$$

$$\Sigma = \sum_{i=1}^{C} \frac{n_i}{n} \Sigma_i$$



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Criteria (5)

- Recall

$$\boldsymbol{S}_w = \sum_{i=1}^{C} \frac{n_i}{n} \boldsymbol{\Sigma}_i \qquad \boldsymbol{S}_B = \sum_{i=1}^{C} \frac{n_i}{n} (\boldsymbol{m}_i - \boldsymbol{m})(\boldsymbol{m}_i - \boldsymbol{m})^T$$

- Scatter-based classification performance indicators:

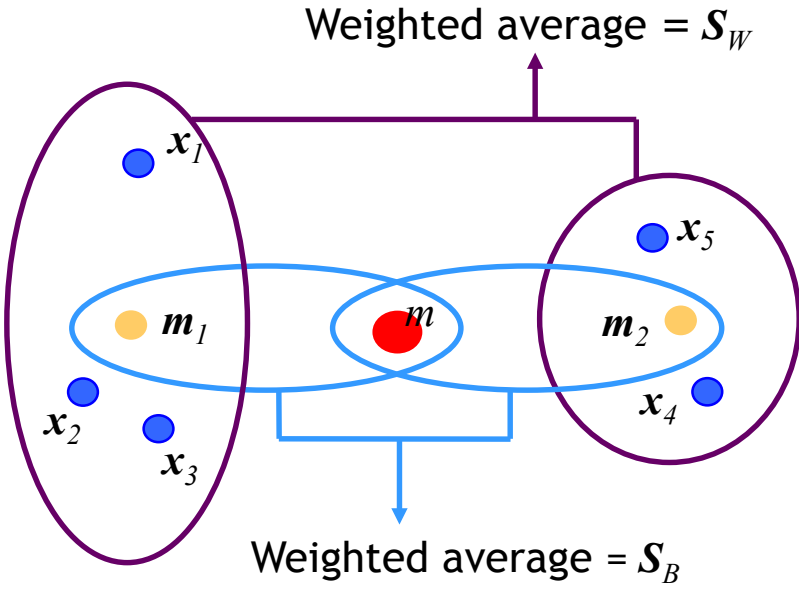
$J_1 = \text{trace}\,(\boldsymbol{S}_W + \boldsymbol{S}_B) = \text{trace}\,(\boldsymbol{\Sigma})$

$J_2 = \text{trace}\,(\boldsymbol{S}_B / \boldsymbol{S}_w)$

$J_3 = \det\,(\boldsymbol{\Sigma}) / \det\,(\boldsymbol{S}_w)$

$J_3 = \text{trace}\,(\boldsymbol{S}_W) / \text{trace}\,(\boldsymbol{S}_B)$

(trace = sum of diagonal elements)



- These are all just approximations!

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Search algorithms

- **Feature selection**: select a subset of d out of p measurements which optimises the criterion

- Simplest solution: look at all possible subsets

- Problem: there are $\binom{p}{d} = \frac{p!}{(p-d)!d!}$ subsets

- *e.g.* $p = 50$ measurements, $d = 2$: 1225 subsets
  $d = 5$: 2.1×10^6 subsets
  $d = 25$: 1.3×10^{14} subsets

BioSB

Search algorithms (2)

- Sub-optimal algorithms: select or deselect one feature (or a few features) at a time

- Simplest: best individual d
  but these are not necessarily the best d !

- Demonstration: two Gaussians;
  select 2 features out of 3 for classification

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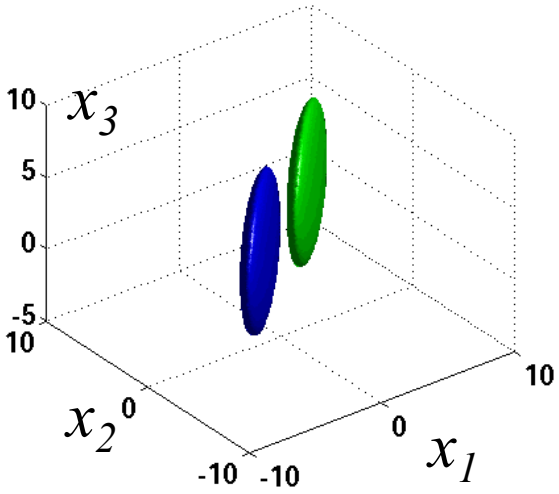
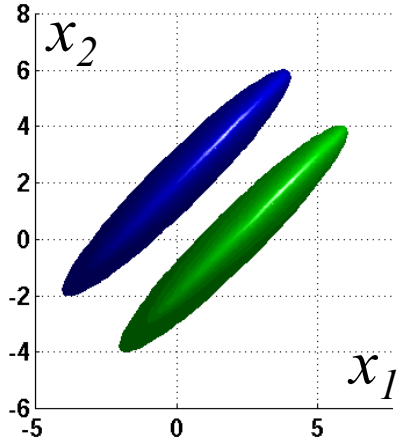
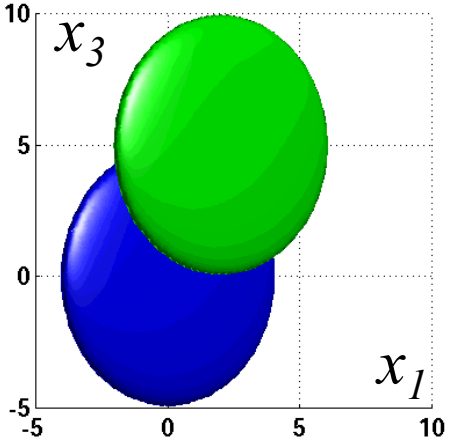
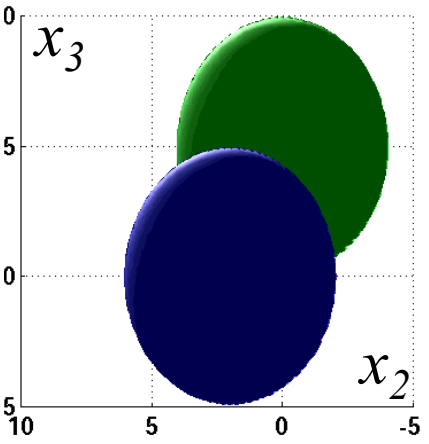
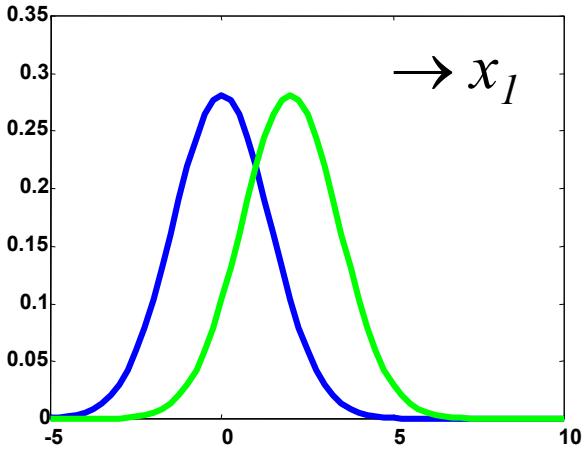
Search algorithms (3)

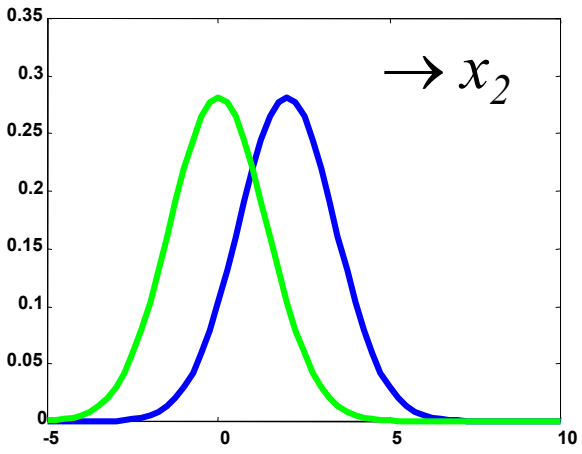


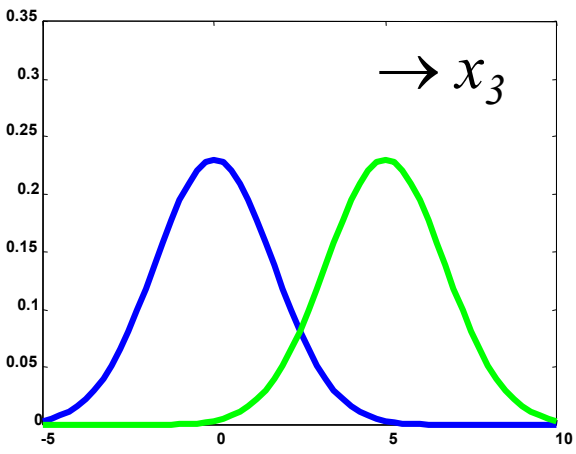












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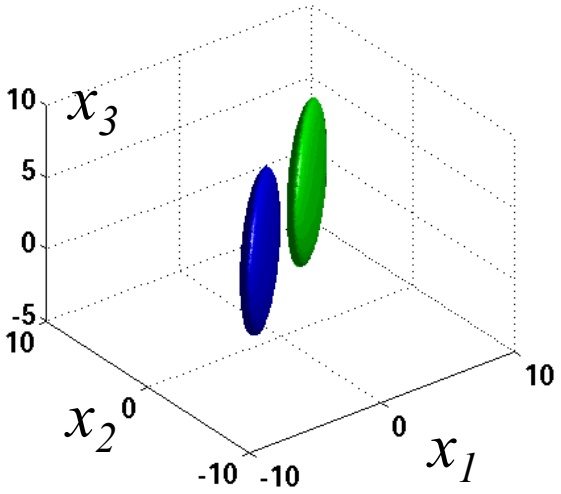
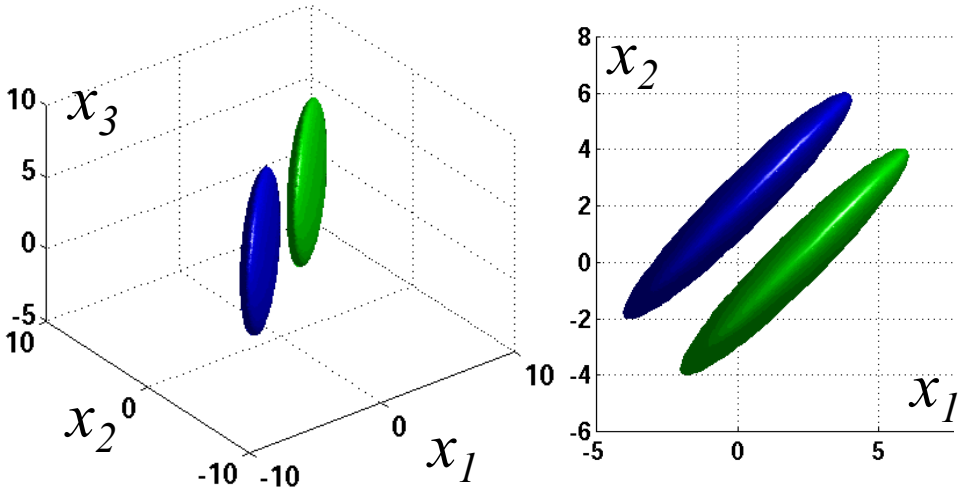
Search algorithms (3)



Search algorithms (3)



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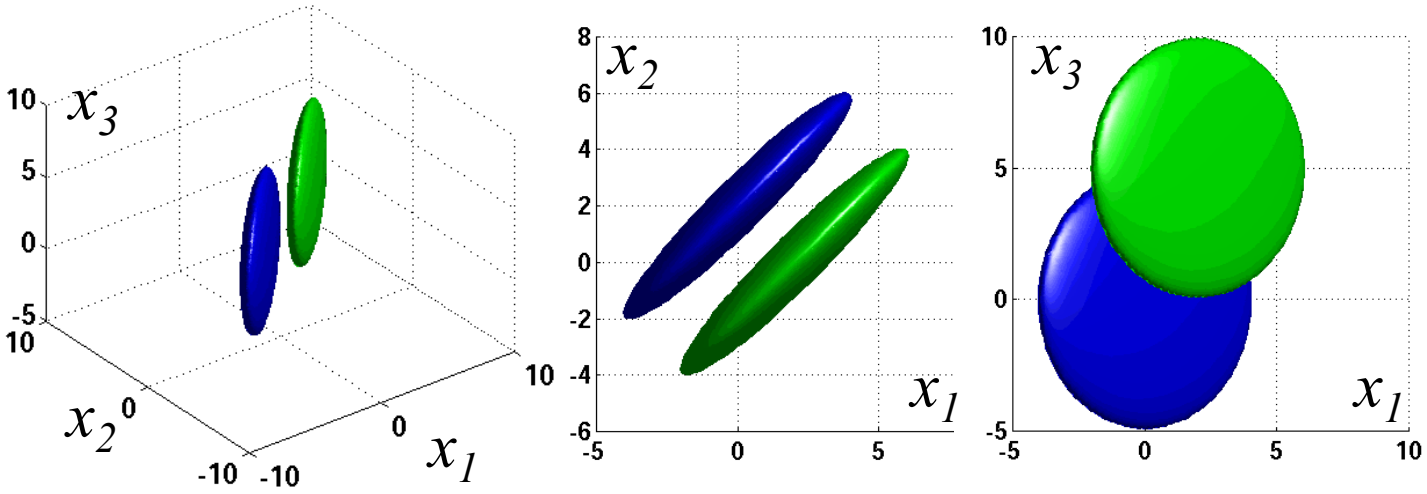

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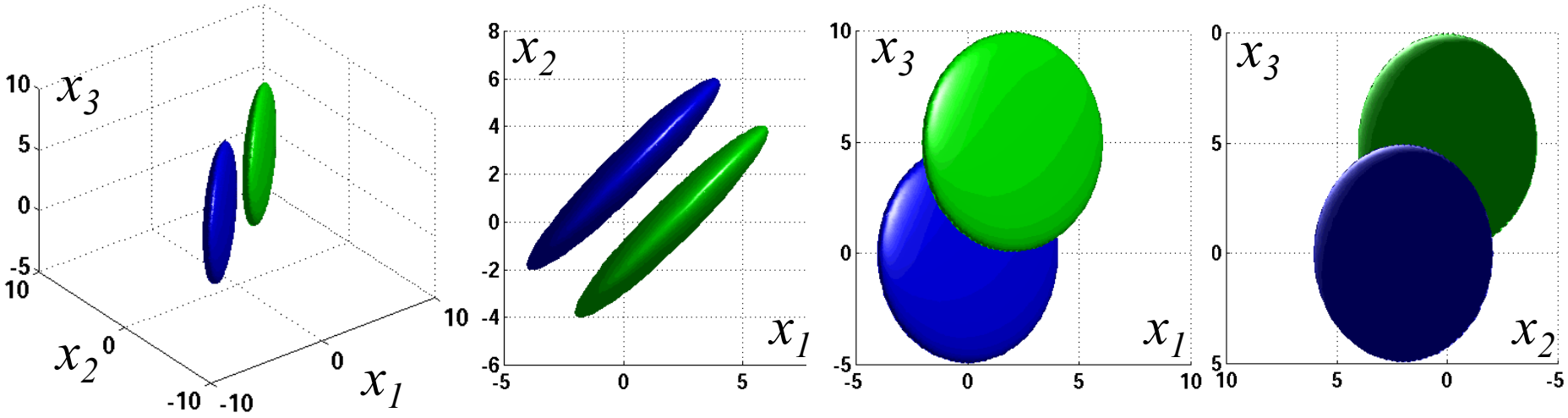
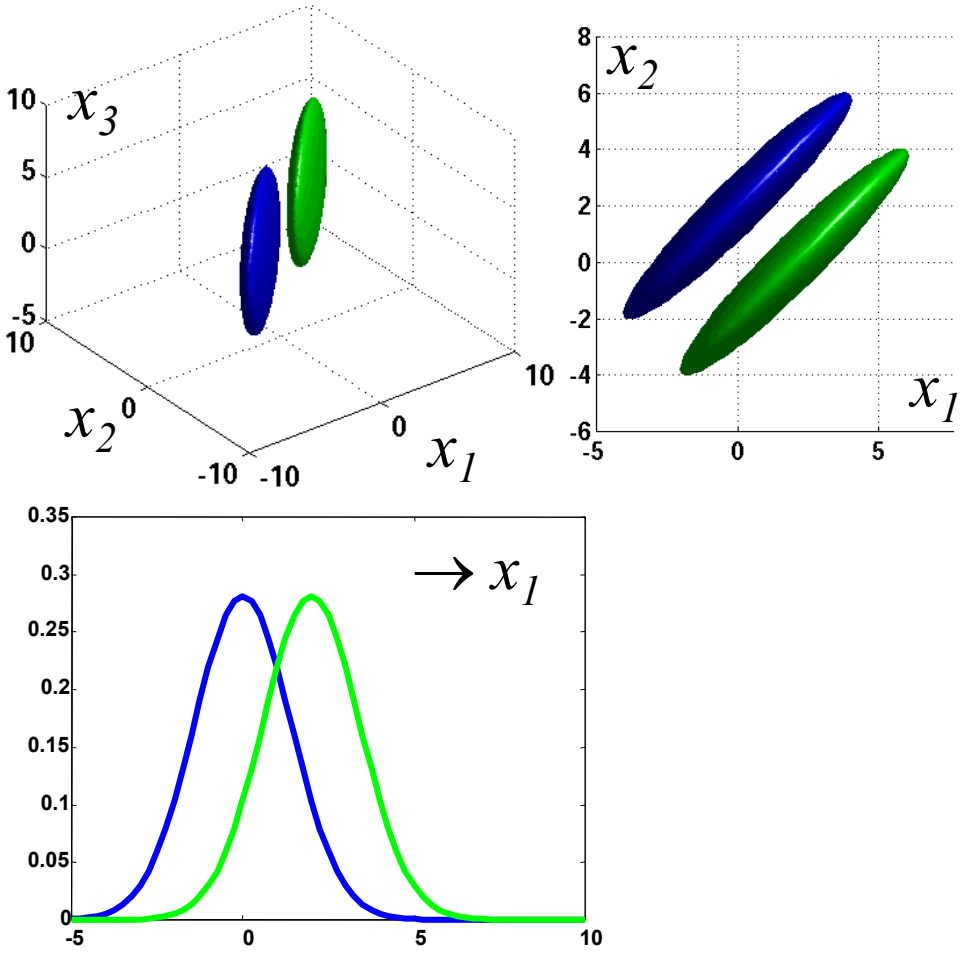
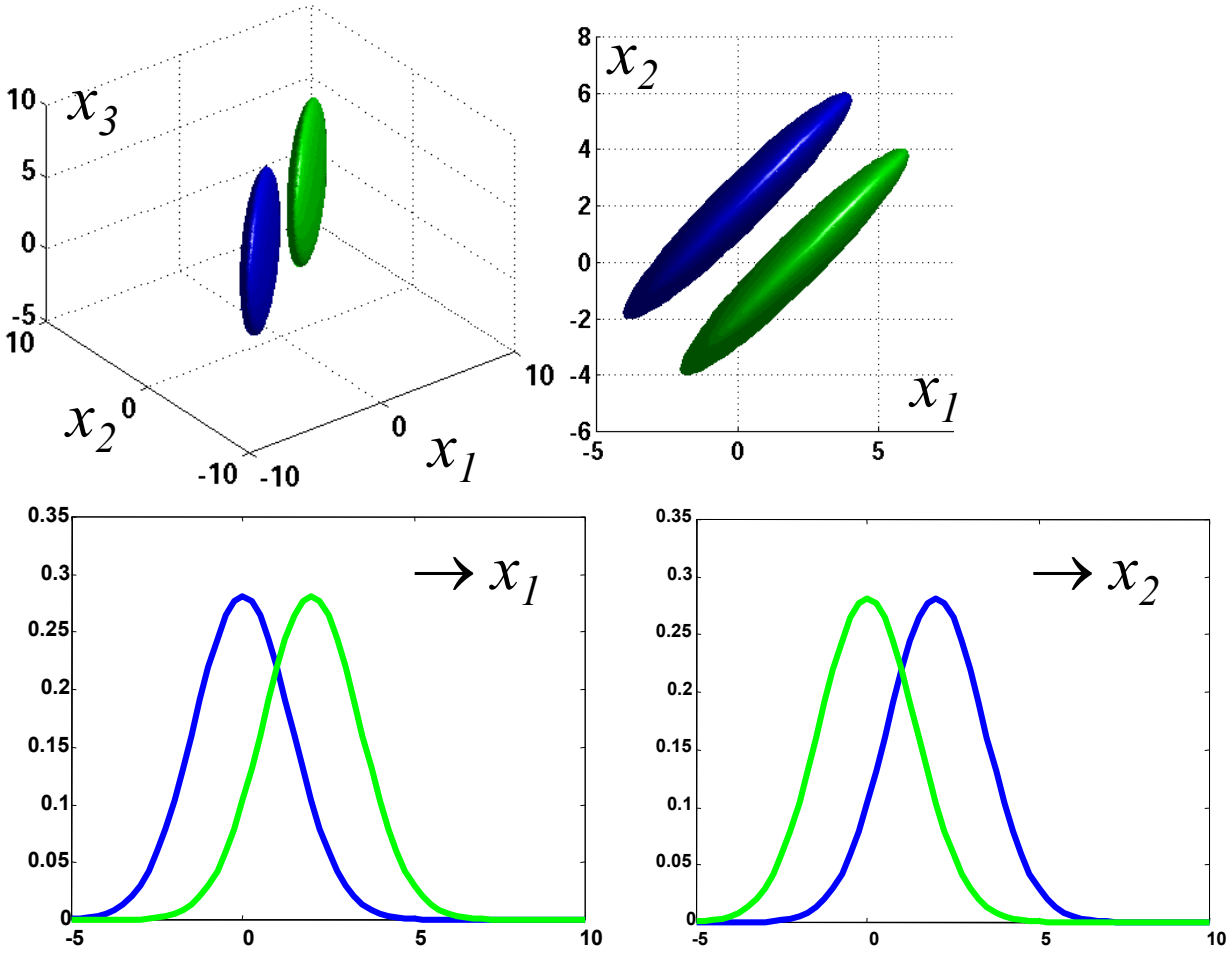


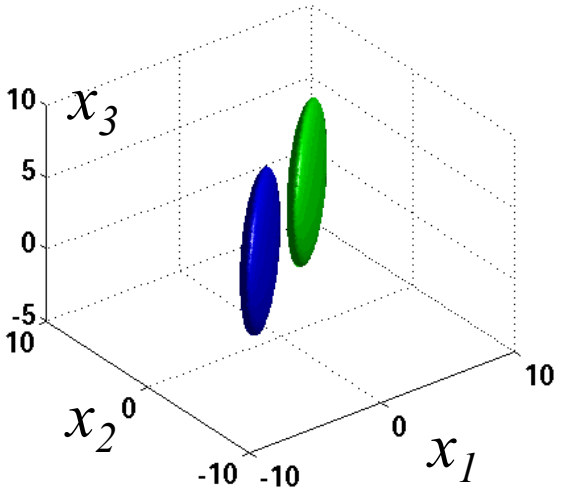
Search algorithms (3)

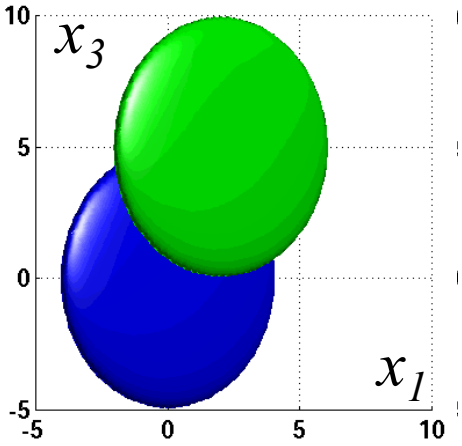


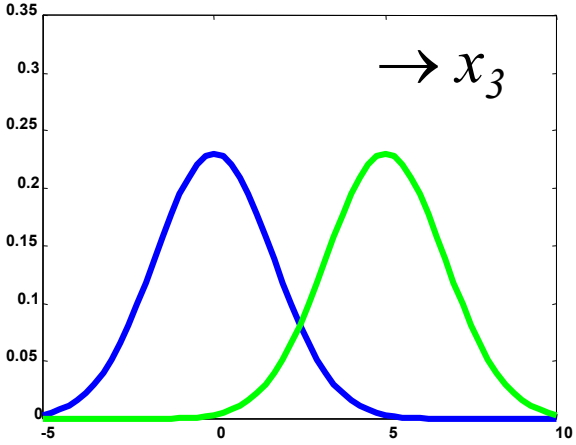
Search algorithms (3)



Search algorithms (3)







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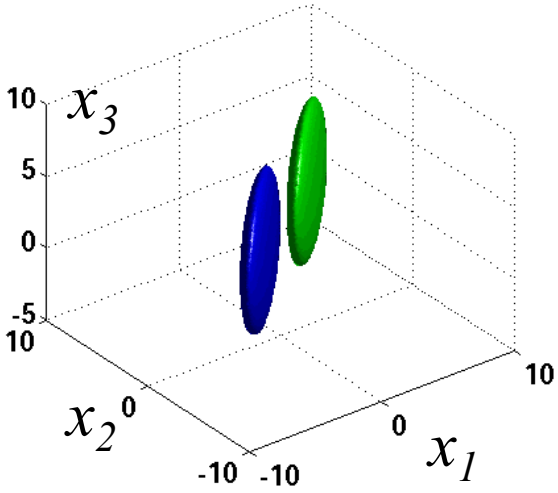
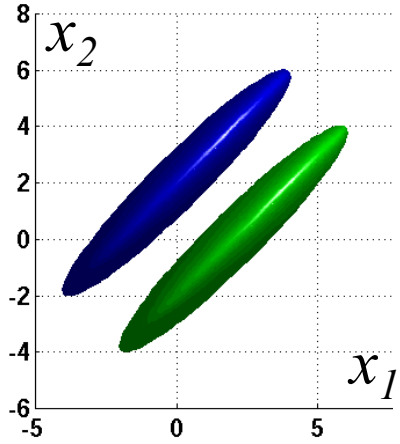
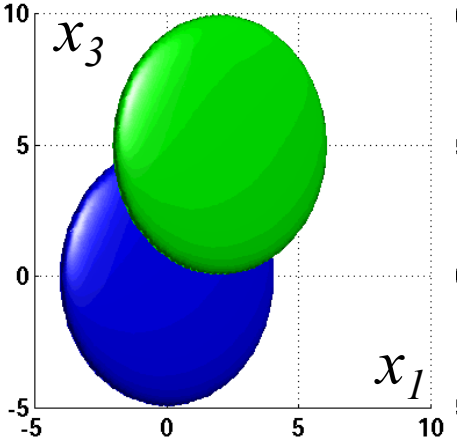
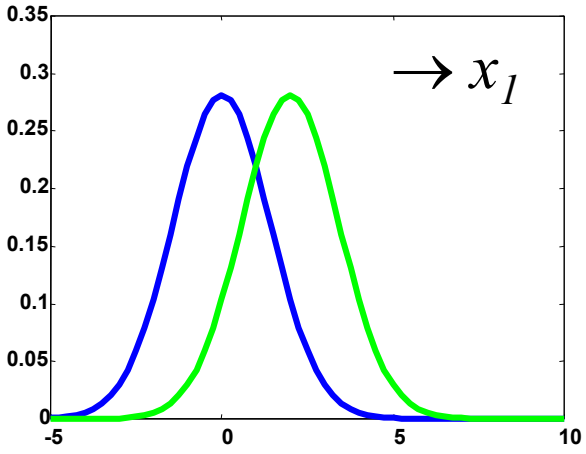
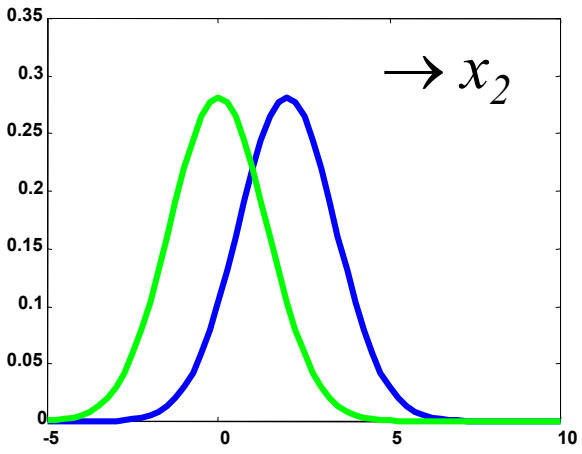
Search algorithms (3)

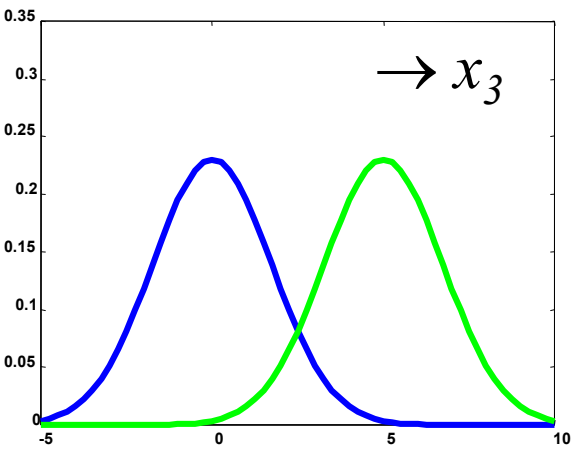












Search algorithms (4)

- Other sub-optimal algorithms:
  - Forward selection (for when d is low)
    - start with empty set
    - keep adding one feature at a time
      so that the entire subset so far performs best

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Search algorithms (4)

- Other sub-optimal algorithms:
  - Forward selection (for when d is low)
    - start with empty set
    - keep adding one feature at a time
      so that the entire subset so far performs best
  - Backward selection (for when d is high)
    - start with entire set
    - keep removing one feature at a time
      so that the entire subset so far performs best
  - Plus-l-takeaway-r (may be slightly better)
    - start with empty set (if $l > r$) or entire set (if $l < r$)
    - keep adding best l and removing worst r

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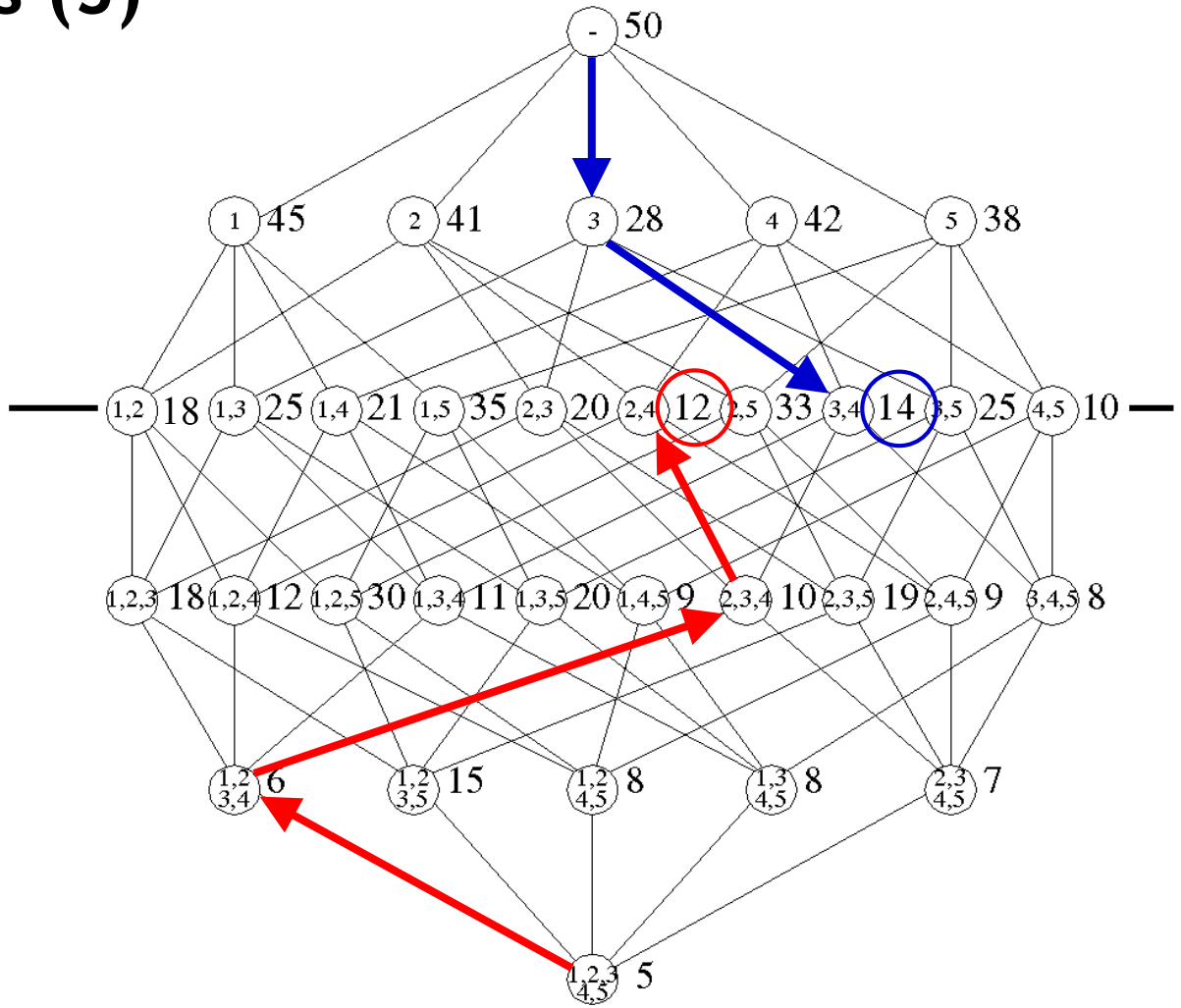
Search algorithms (5)

- Select $d = 2$ out of $p = 5$ features
- Sub-optimality illustrated:
  - forward
  - backward



Feature subset

Criterion value

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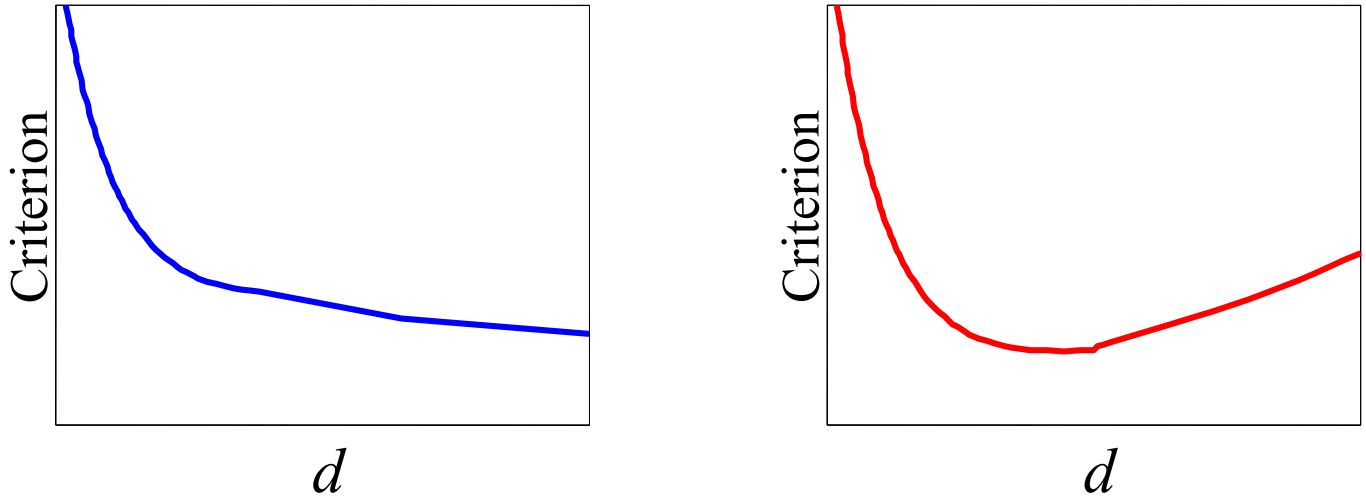
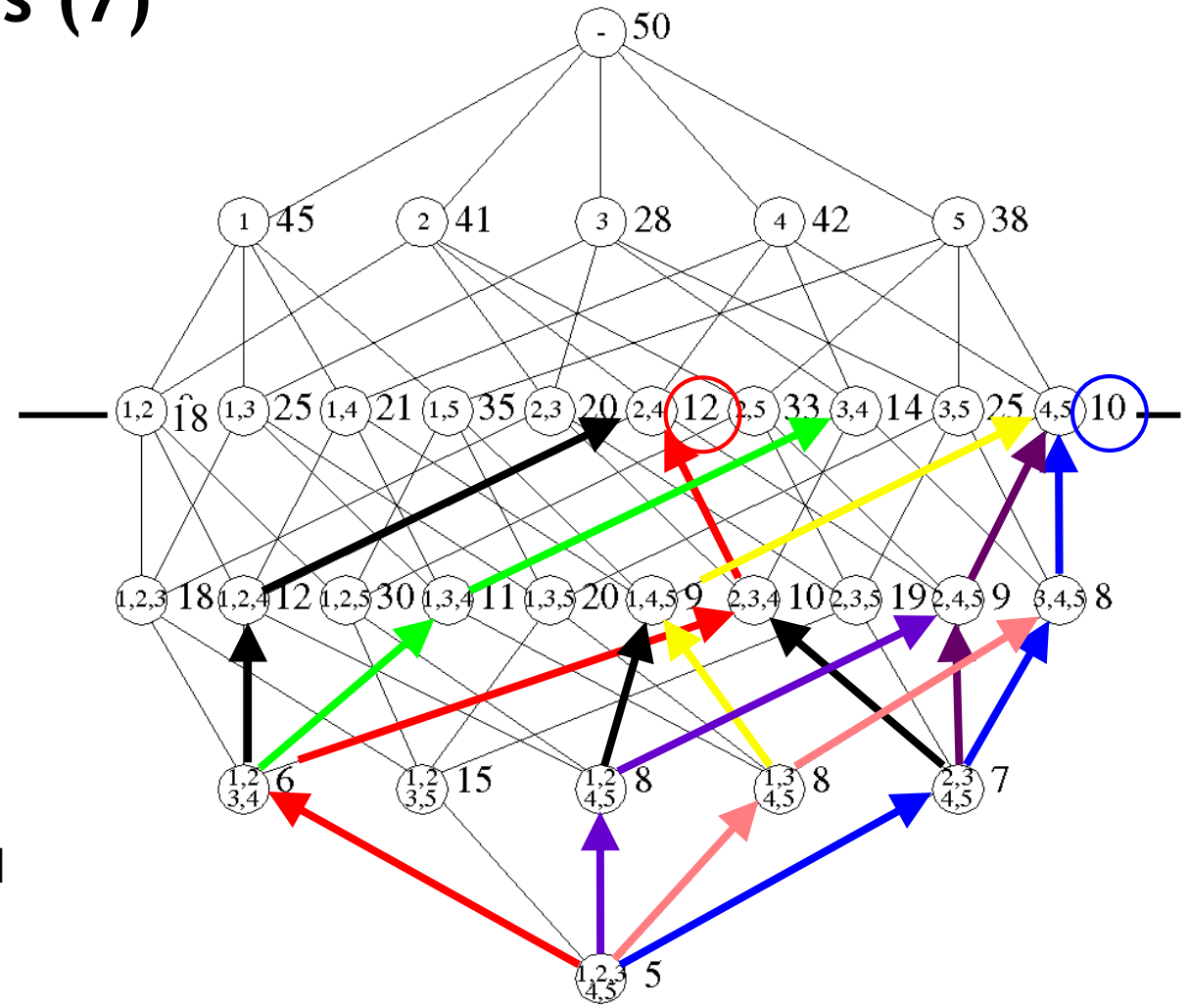
Search algorithms (6)

- Branch & bound: backtracking
- Optimal when criterion is monotonic in the number of features d



Search algorithms (7)

- Branch & bound
  - Use backward search to find preset number of features
  - Set *bound*, backtrack (*branch*) and use backward search again, considering just sets with criterion values better than the bound



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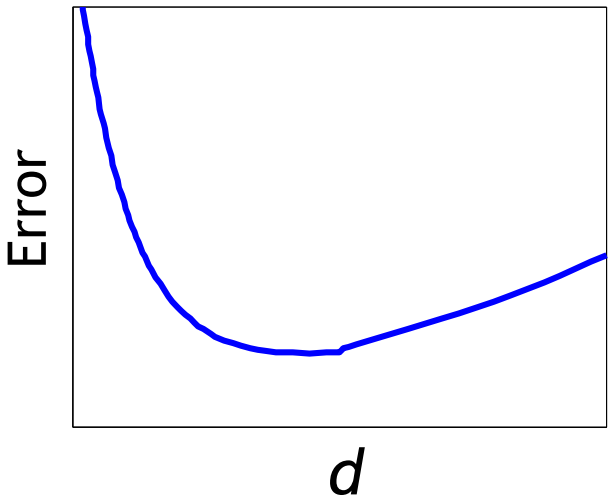
Search algorithms (8)

- When should we stop?
  - Due to estimation problems (*e.g.* covariance matrix), we may be overtraining on training set (in cross validation)
  - This is revealed by increasing error on the test set



  - Otherwise (with very large sample sizes), we will have to specify a desired number of measurements

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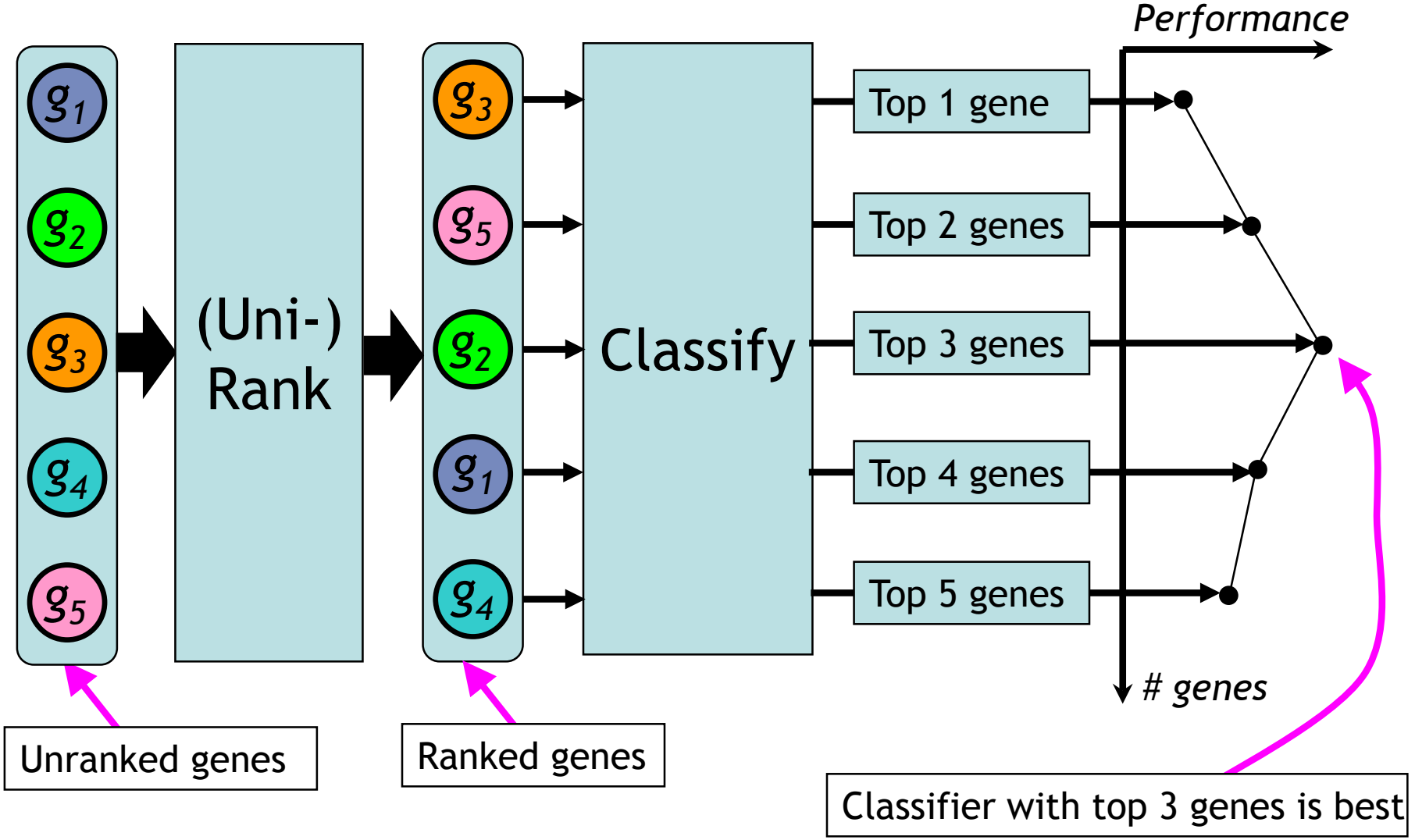
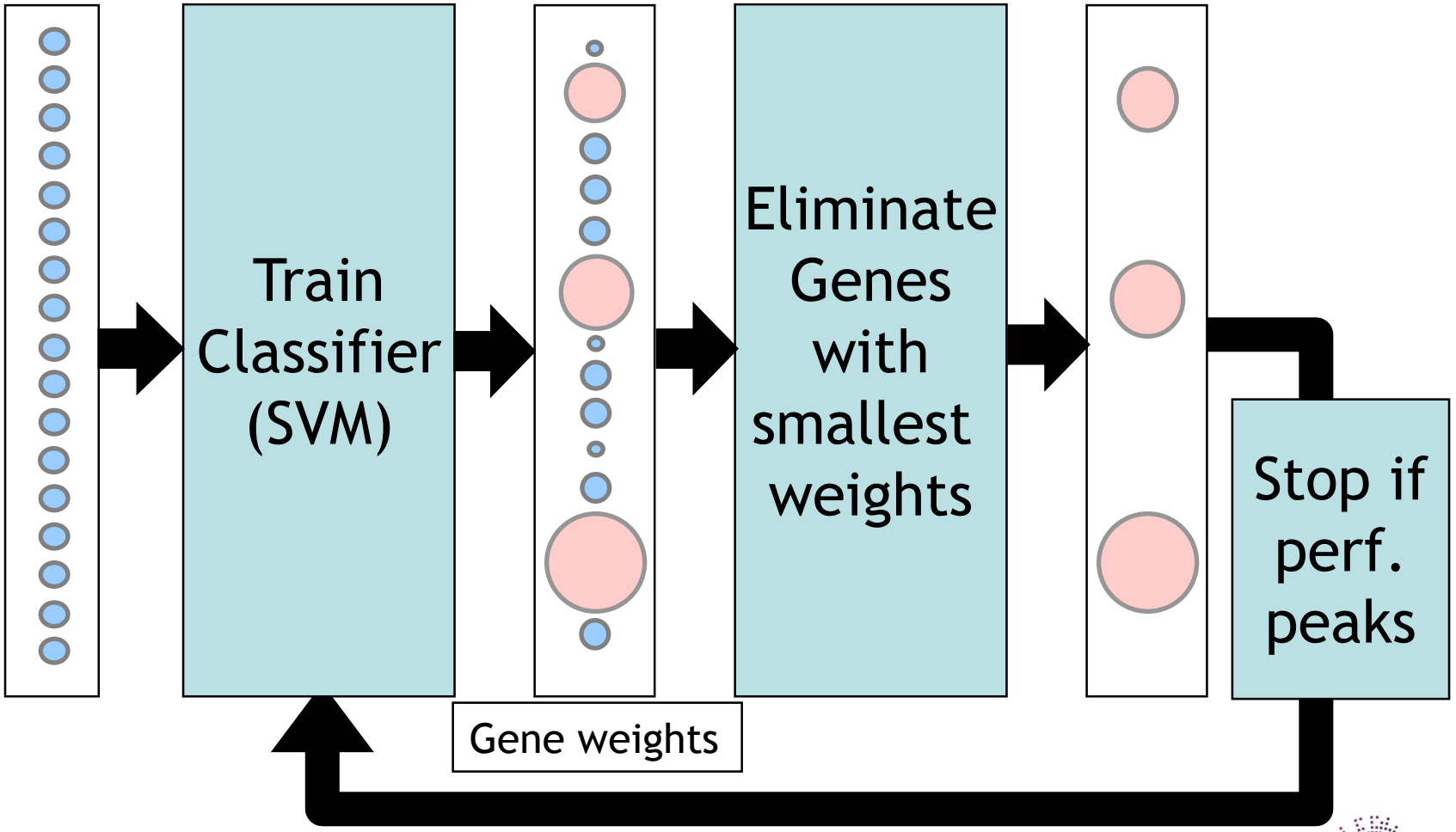
Example: Filtering (forward selection)



Example: Recursive feature elimination (RFE)

Wrapper, Backward search



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What can go wrong?

Selection bias...

- Guyon et al. (2002). Machine Learning **46**, 389 – 422.
- Ambroise and McLachlan (2002). PNAS **99**, 6562-6566.

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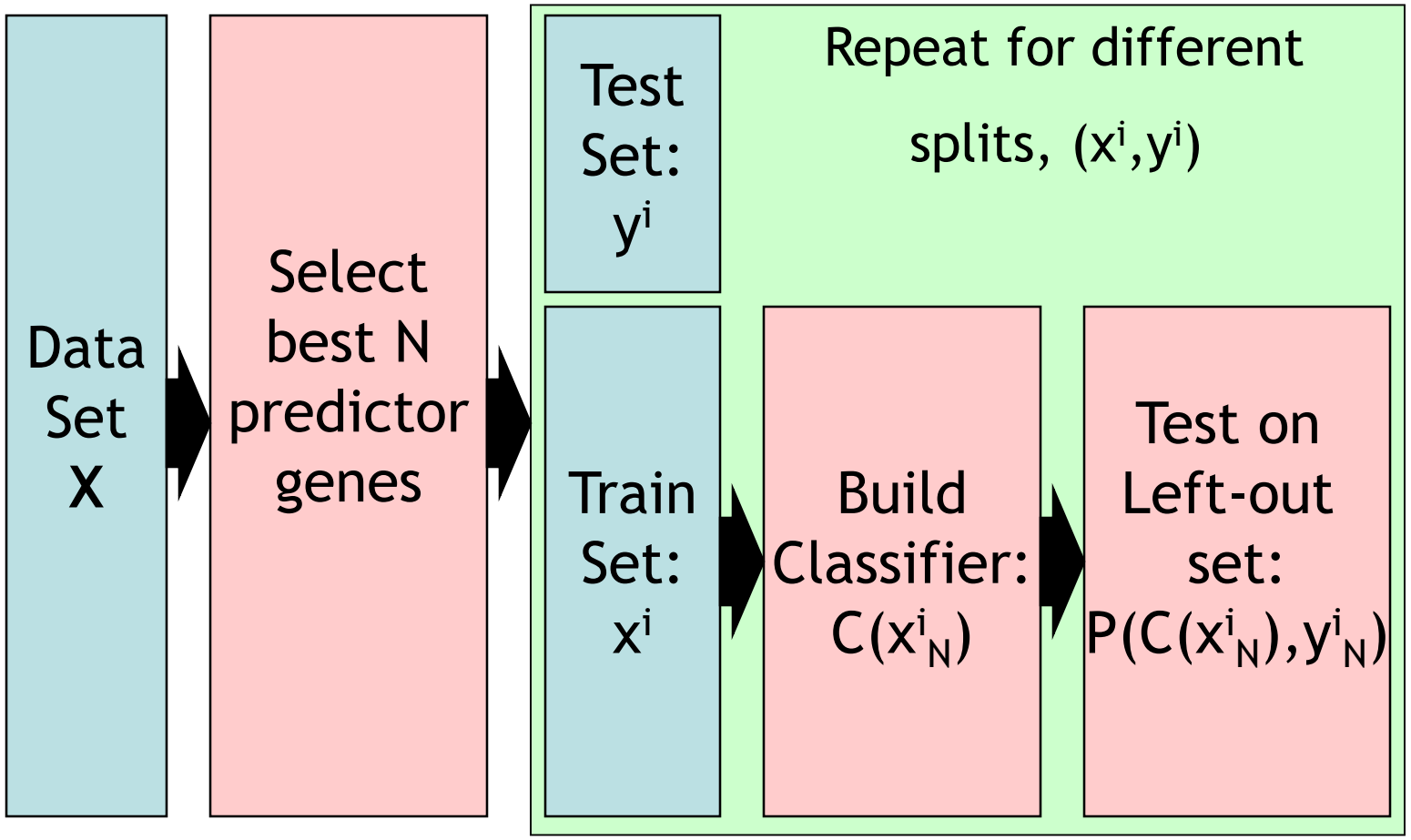
Biased selection



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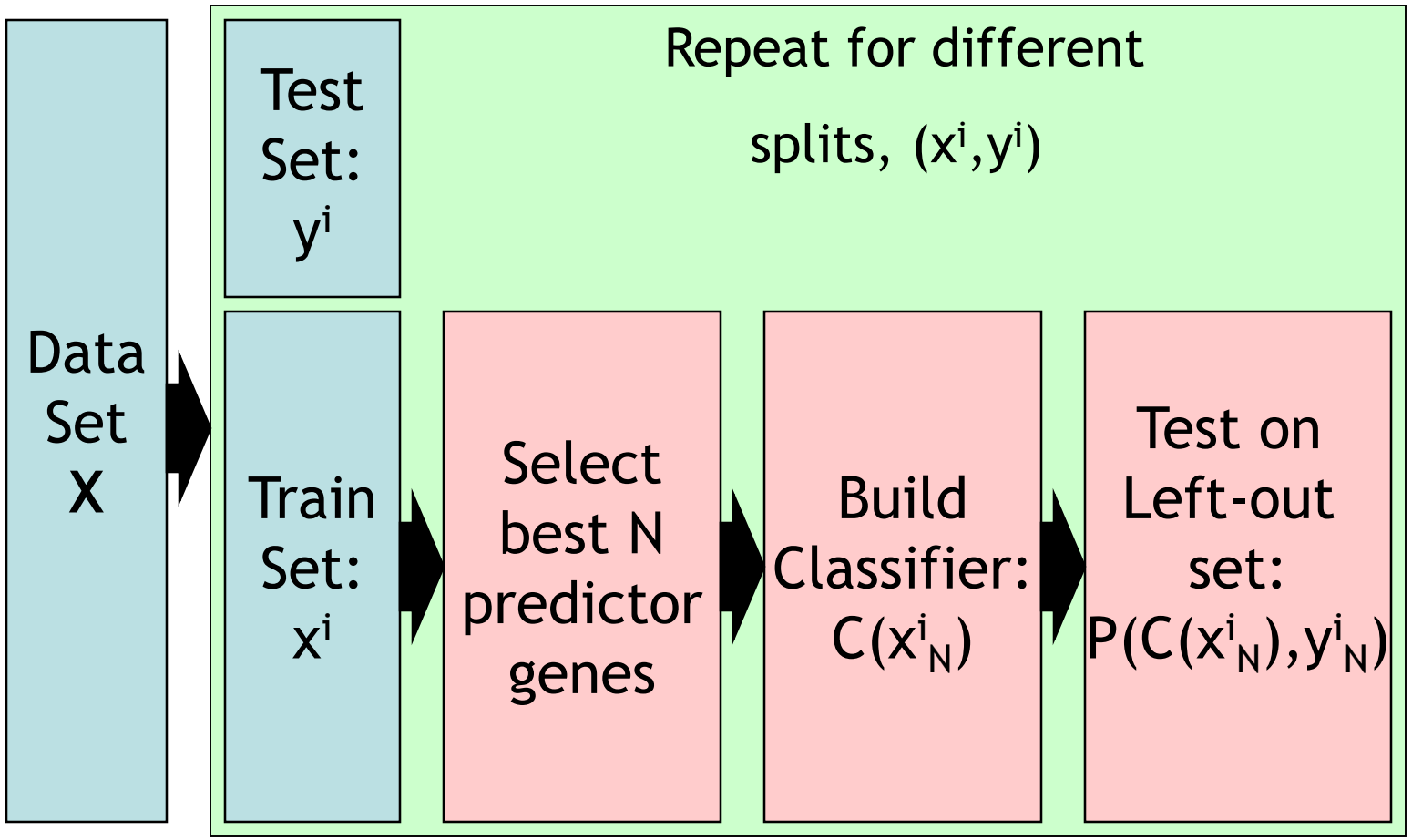
Unbiased selection



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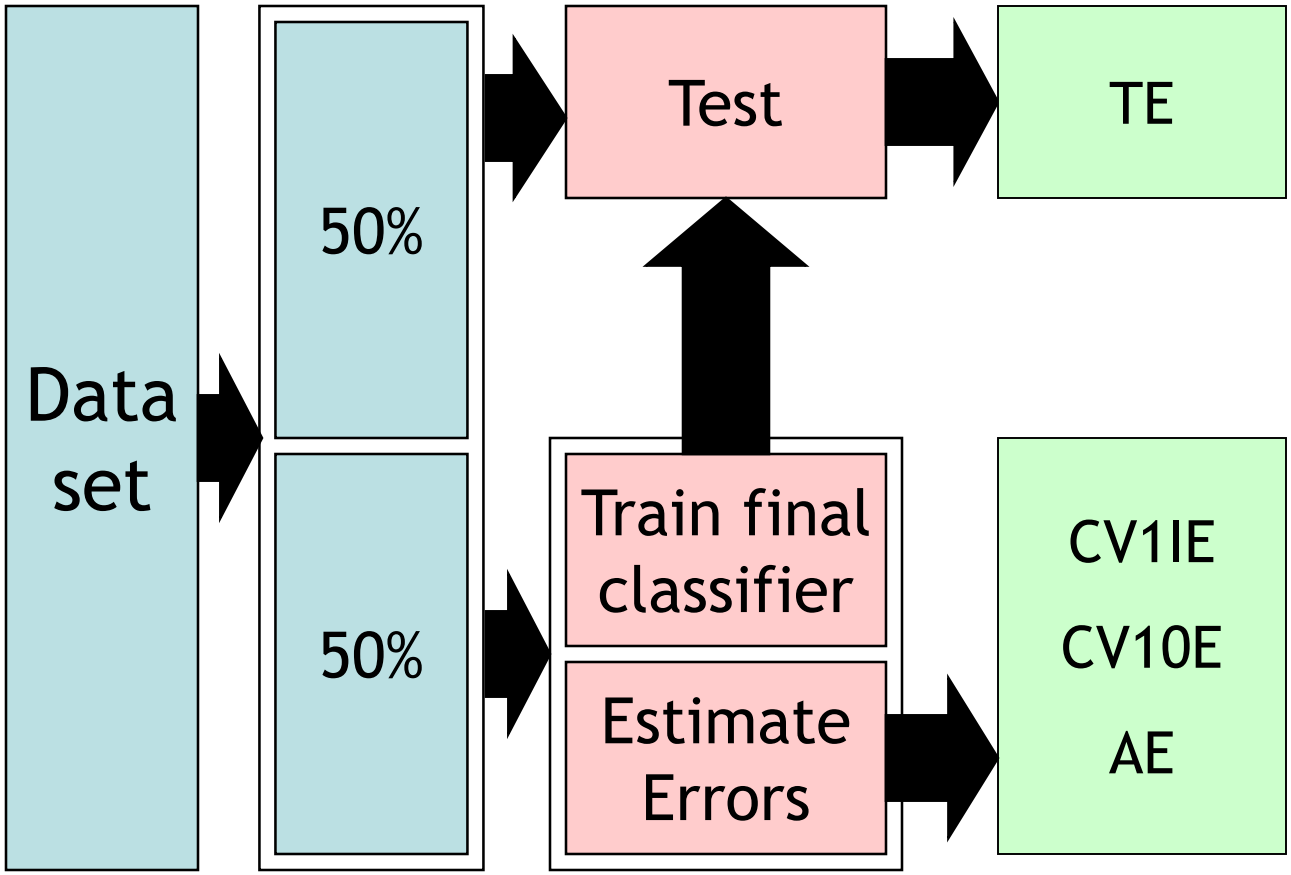
Ambroise & McLachlan experiments



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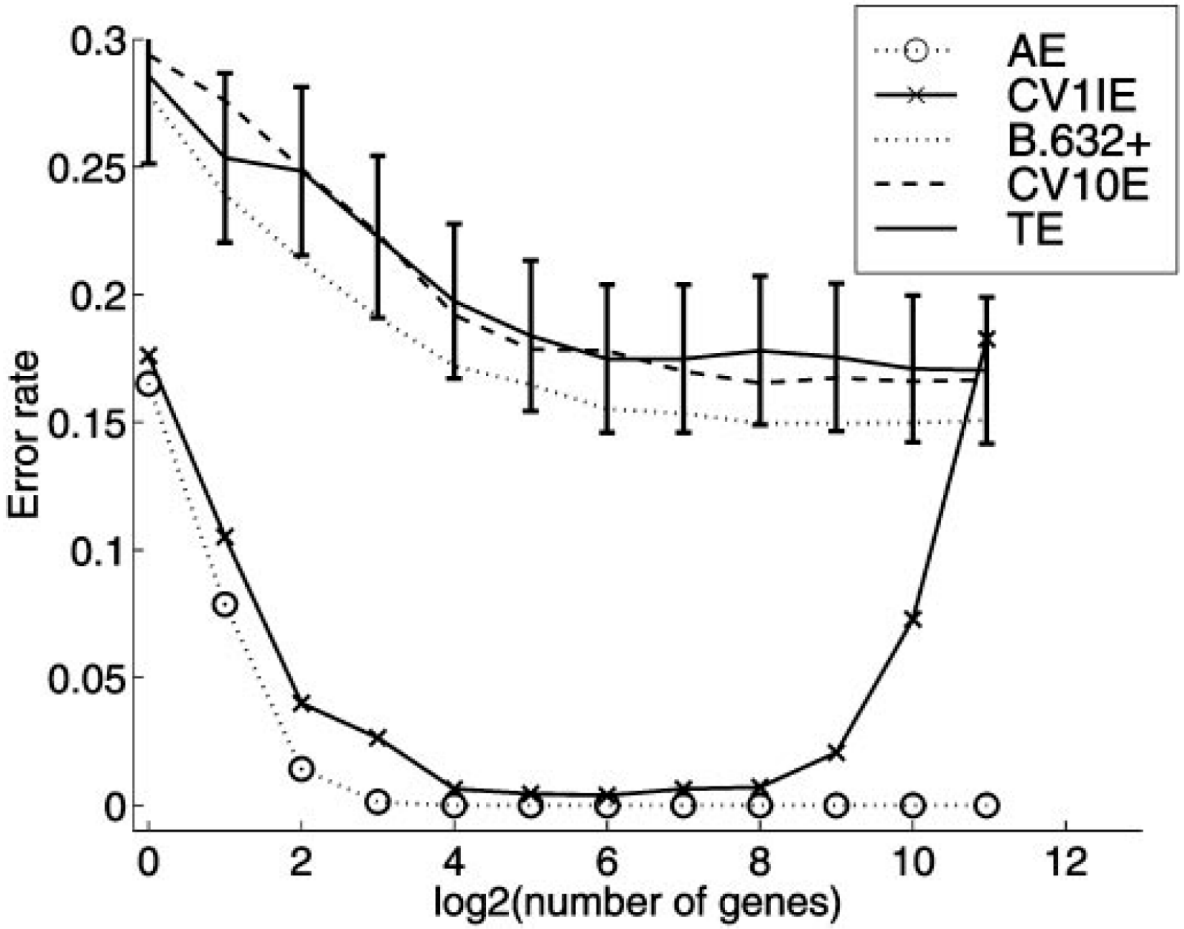
Ambroise & McLachlan experiments

Colon vs. normal data



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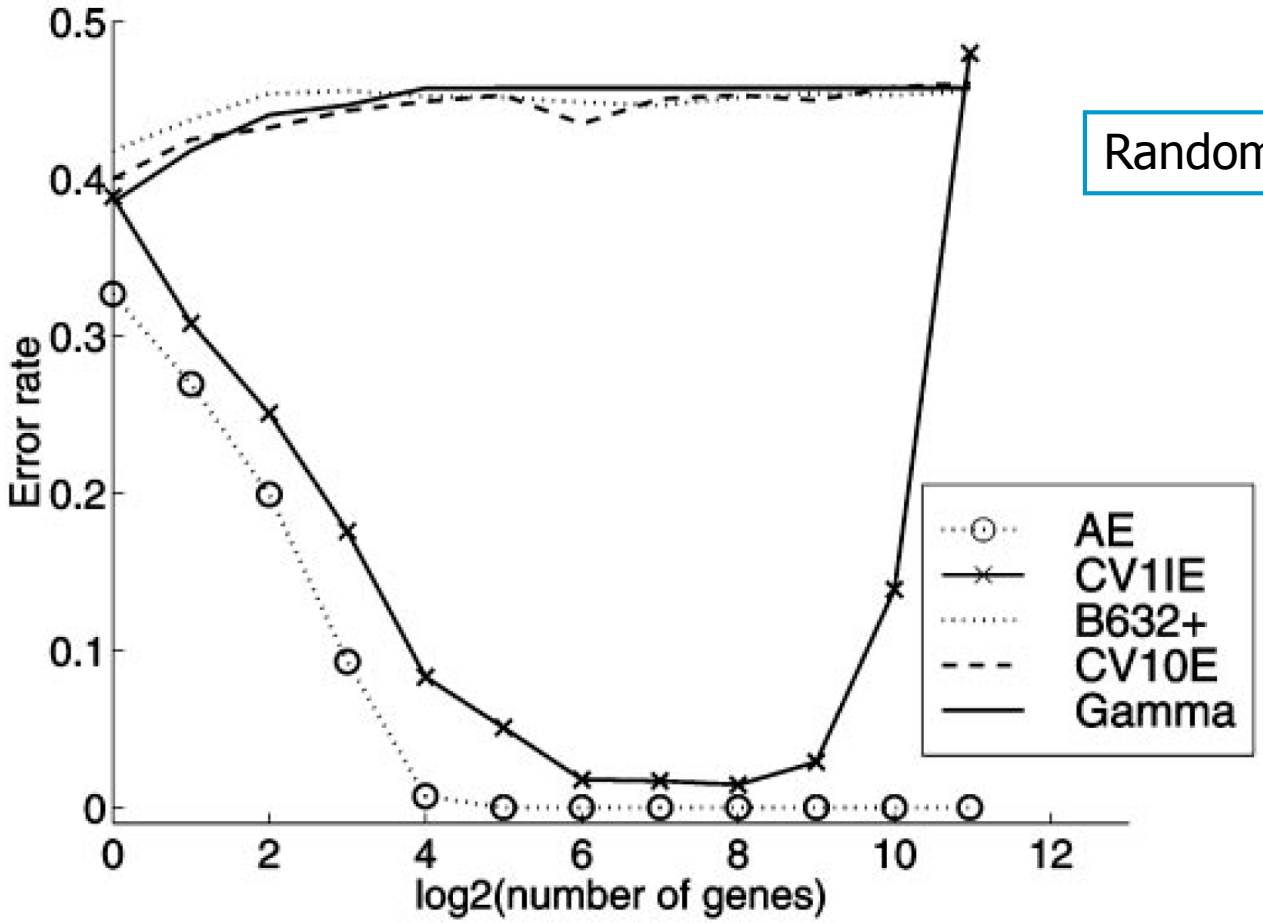
Ambroise & McLachlan experiments

Random data



Random data

Cross-validation

- Remember:

Note:
we should never use the training set to calculate performance; this will give a biased estimate!

  - for small sample size: use cross-validation
- Cross-validation should be applied to *every choice* made, including:
  - the number of features to use
  - the features to use
  - the type of classifier to use
  - …

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Feature selection: summary

- Feature selection can improve performance and help interpretation
- Requirements: a criterion and a search algorithm
- Methodology (cross-validation) is very important, especially for RNAseq data (‘p >> n’)
- There seems to be some evidence that the simplest methods (individual selection) work best

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Shrinkage

- Feature selection: selects a subset of features (1/0)
- Feature extraction: combinations of features are constructed based on variance and accuracy arguments
- Regularization 1: 'shave off' genes based on individual quality and control degree of 'shaving' with error
- Regularization 2: combines accuracy (error) and penalty on large weights (= simple models) in one criterion.

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Shrunken centroids

- Same principle as forward filtering
- Genes are evaluated *individually*
- BUT, do not start with the best and keep adding;
- RATHER, start removing worst genes from the back
- In PAM* genes can participate ‘partially’, in forward filtering a gene is either 100% in or out.

* PAM: Prediction analysis of micro-arrays
R. Tibshirani, T. Hastie, B. Narasimhan and G. Chu. Diagnosis of multiple cancer types by shrunken centroids of gene expression. PNAS 99(10):6567 6572, 2002.

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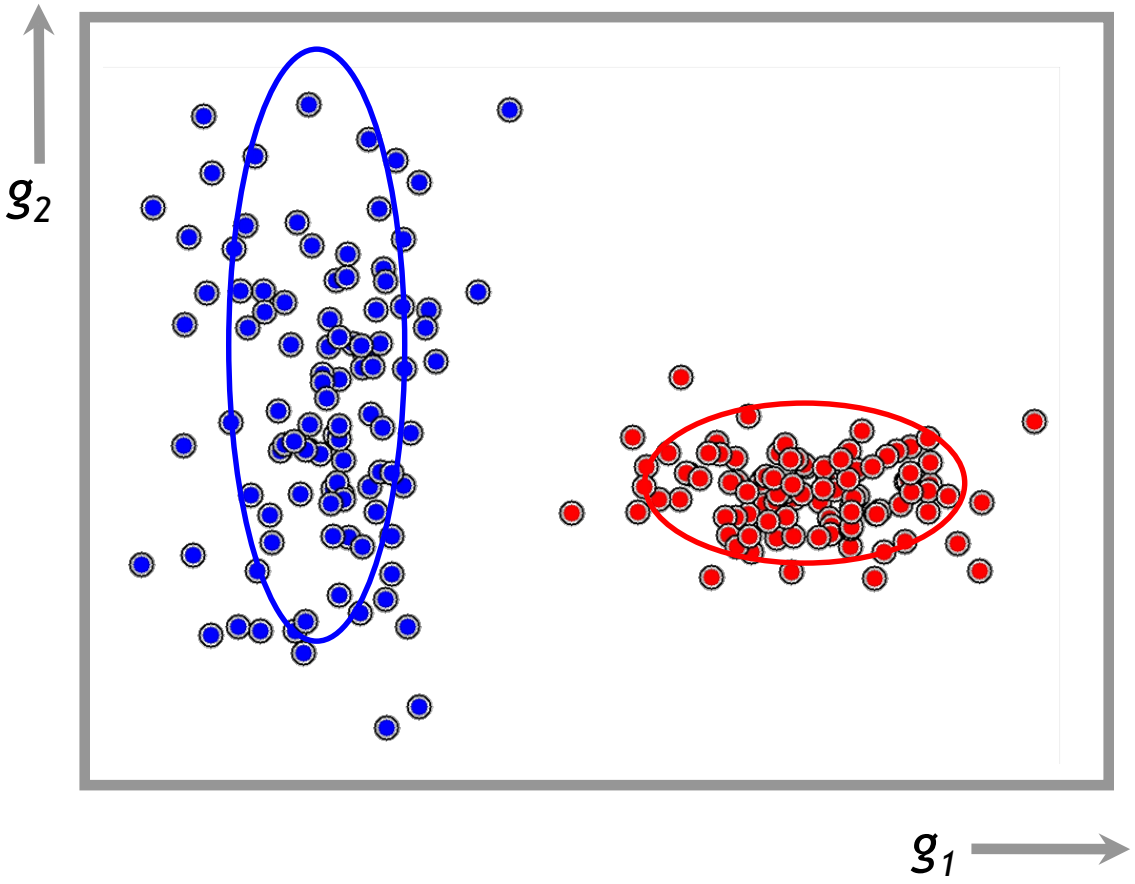
Shrunken centroids in 2D (1)



Which is the best marker gene?

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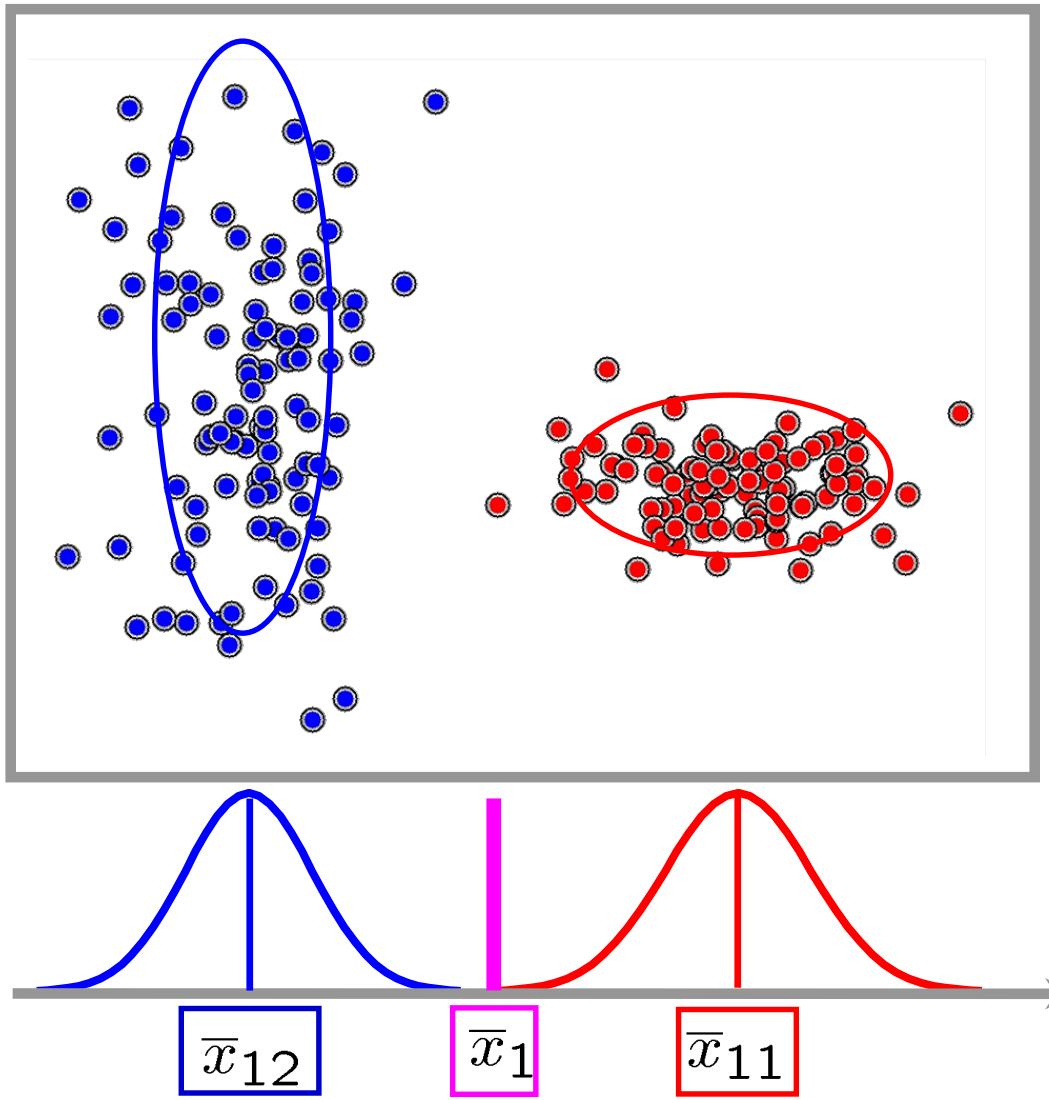
Shrunken centroids in 2D (1)



$$\overline{x}_i = \sum_{j=1}^{n} x_{ij}/n$$

$$\overline{x}_{ik} = \sum_{j \in C_k} x_{ij}/n_k$$

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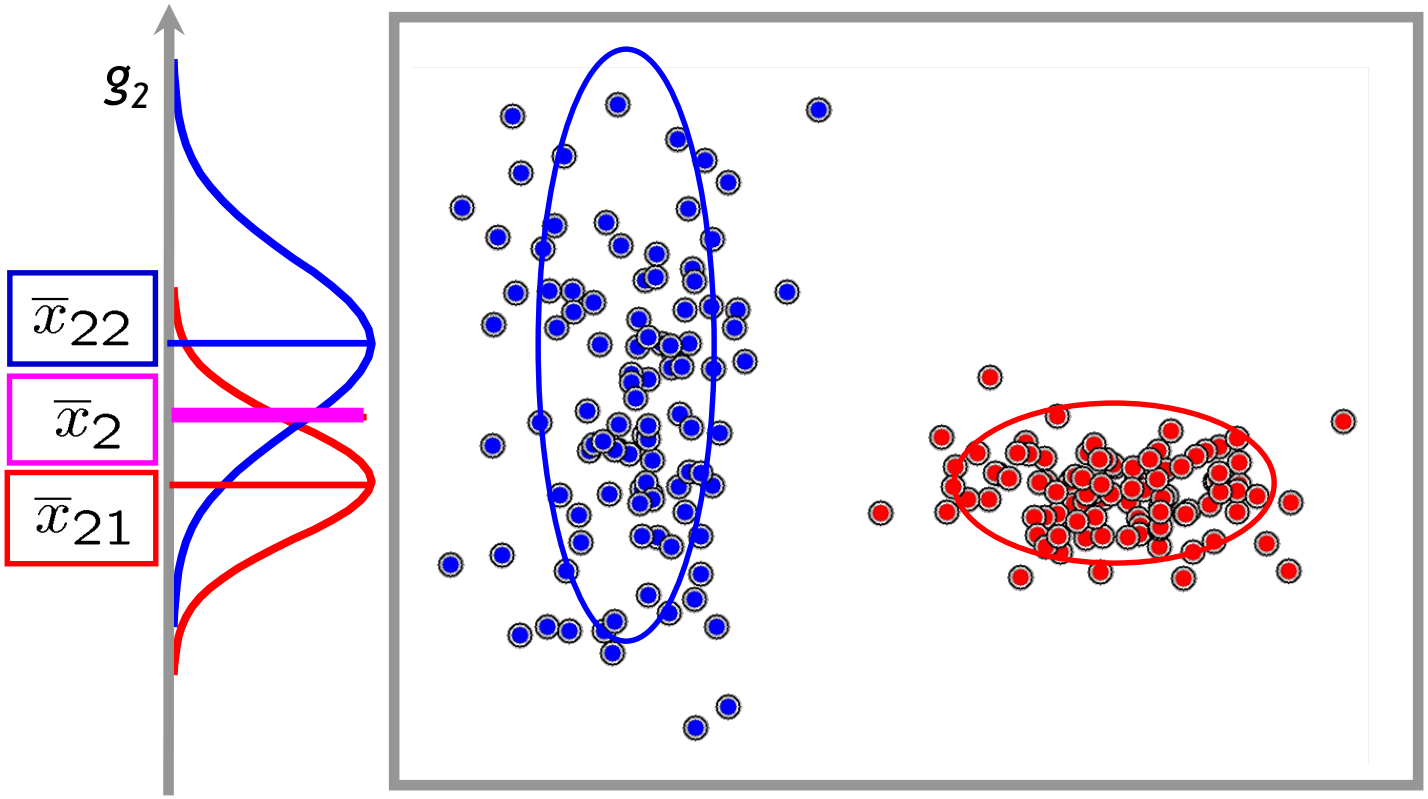
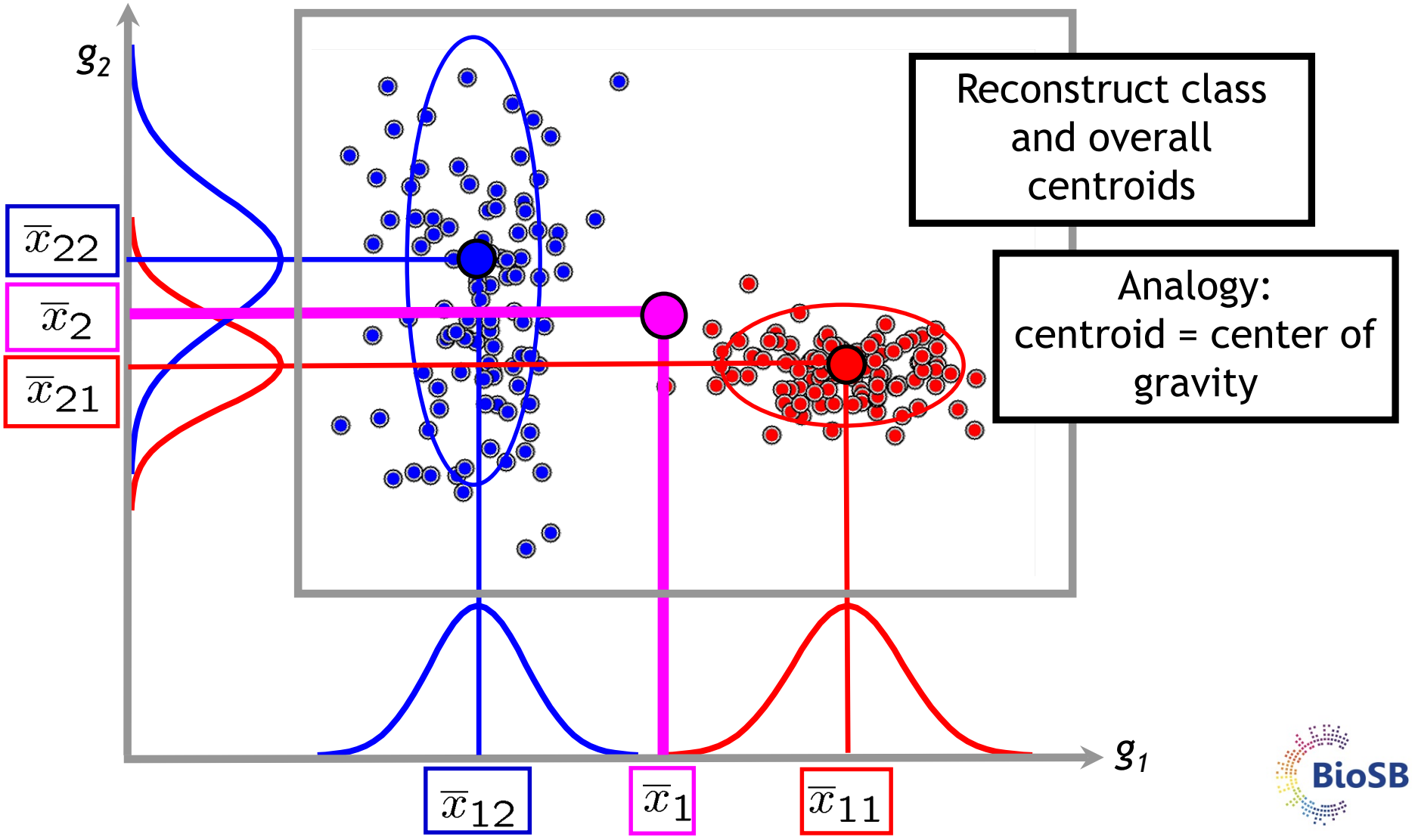
Shrunken centroids in 2D (2)



$$\overline{x}_i = \sum_{j=1}^{n} x_{ij}/n \qquad \overline{x}_{ik} = \sum_{j \in C_k} x_{ij}/n_k$$

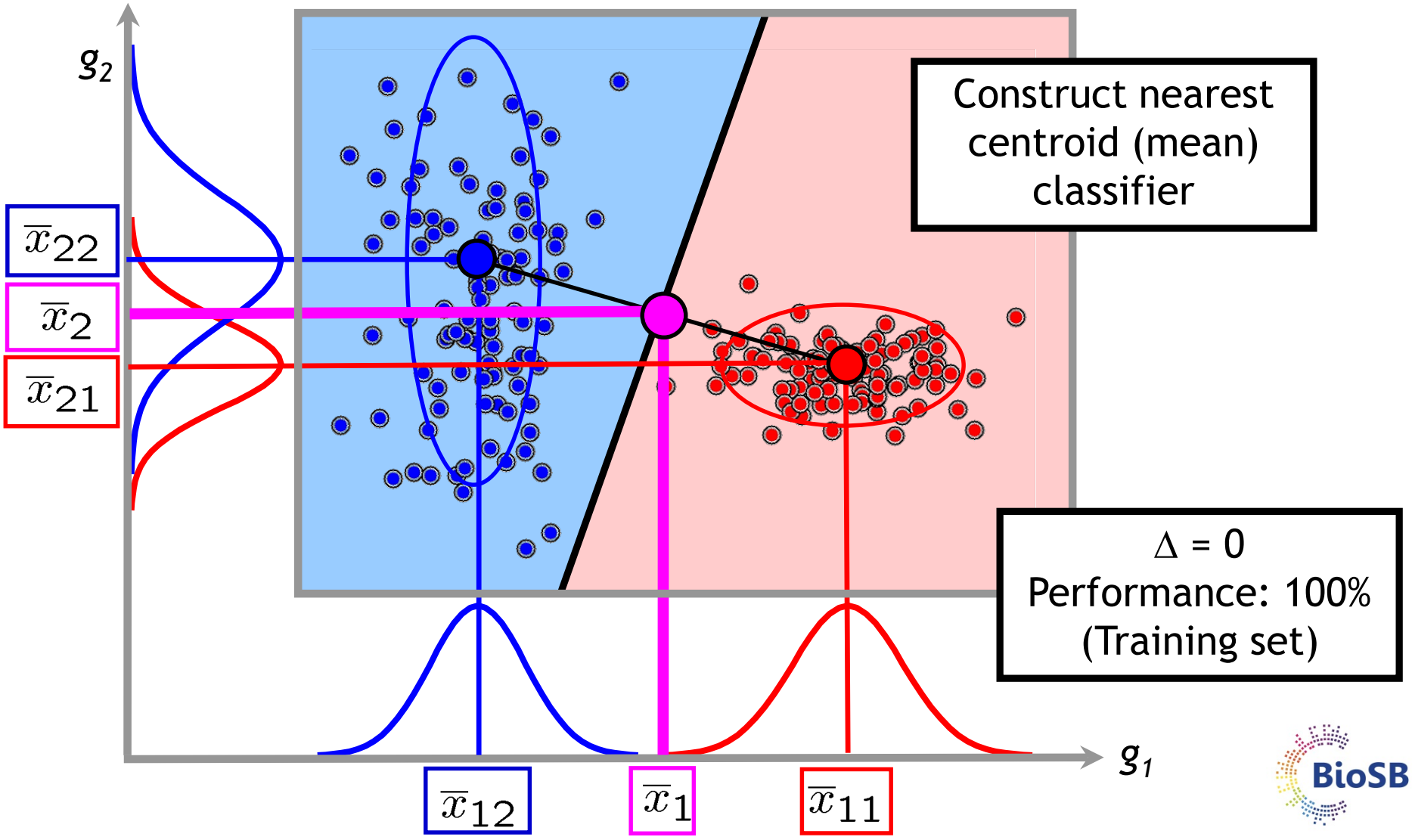
BioSB

Shrunken centroids in 2D (3)



BioSB

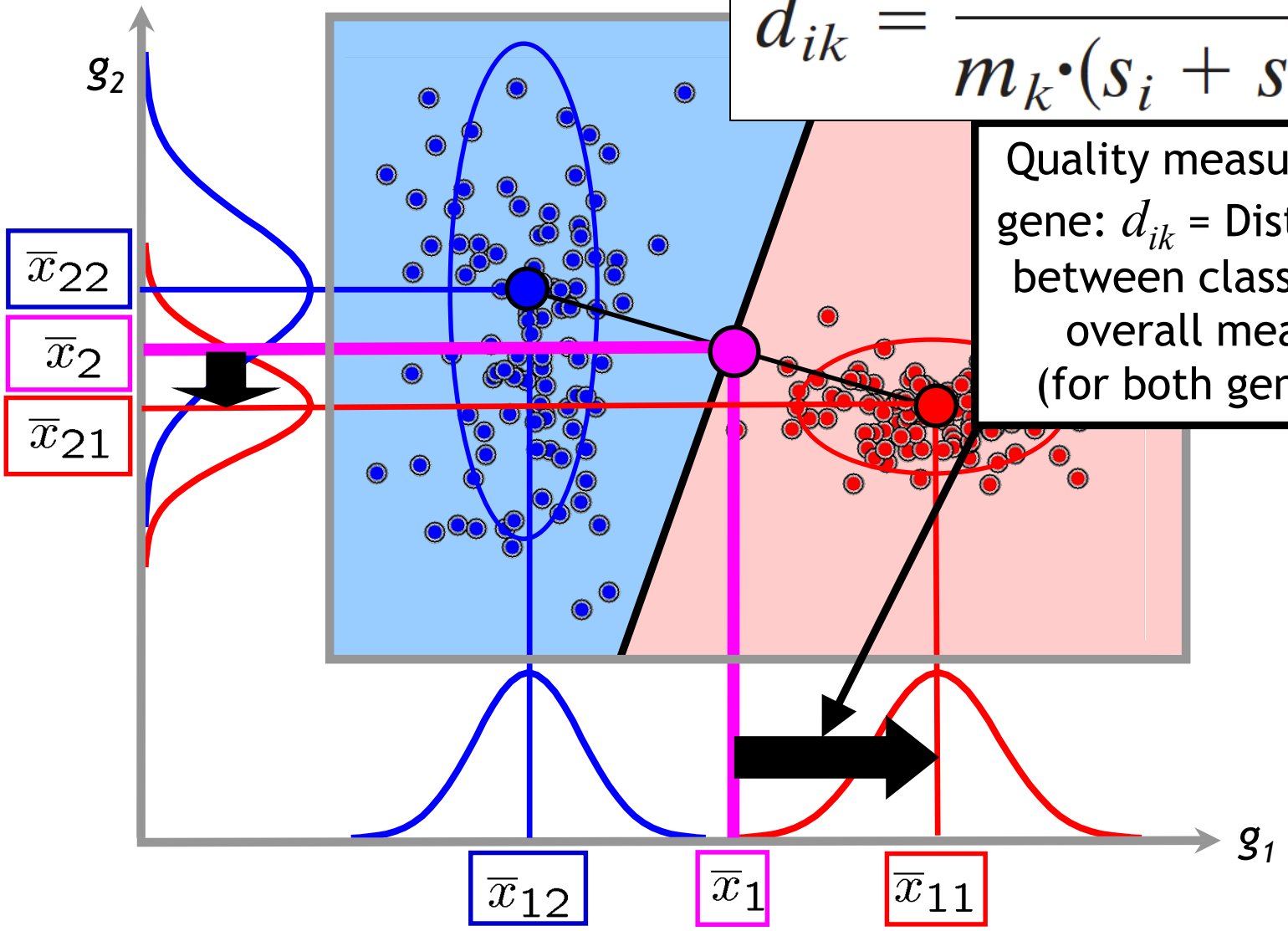
Shrunken centroids in 2D (4)



BioSB

Shrunken centroids in 2D (5)

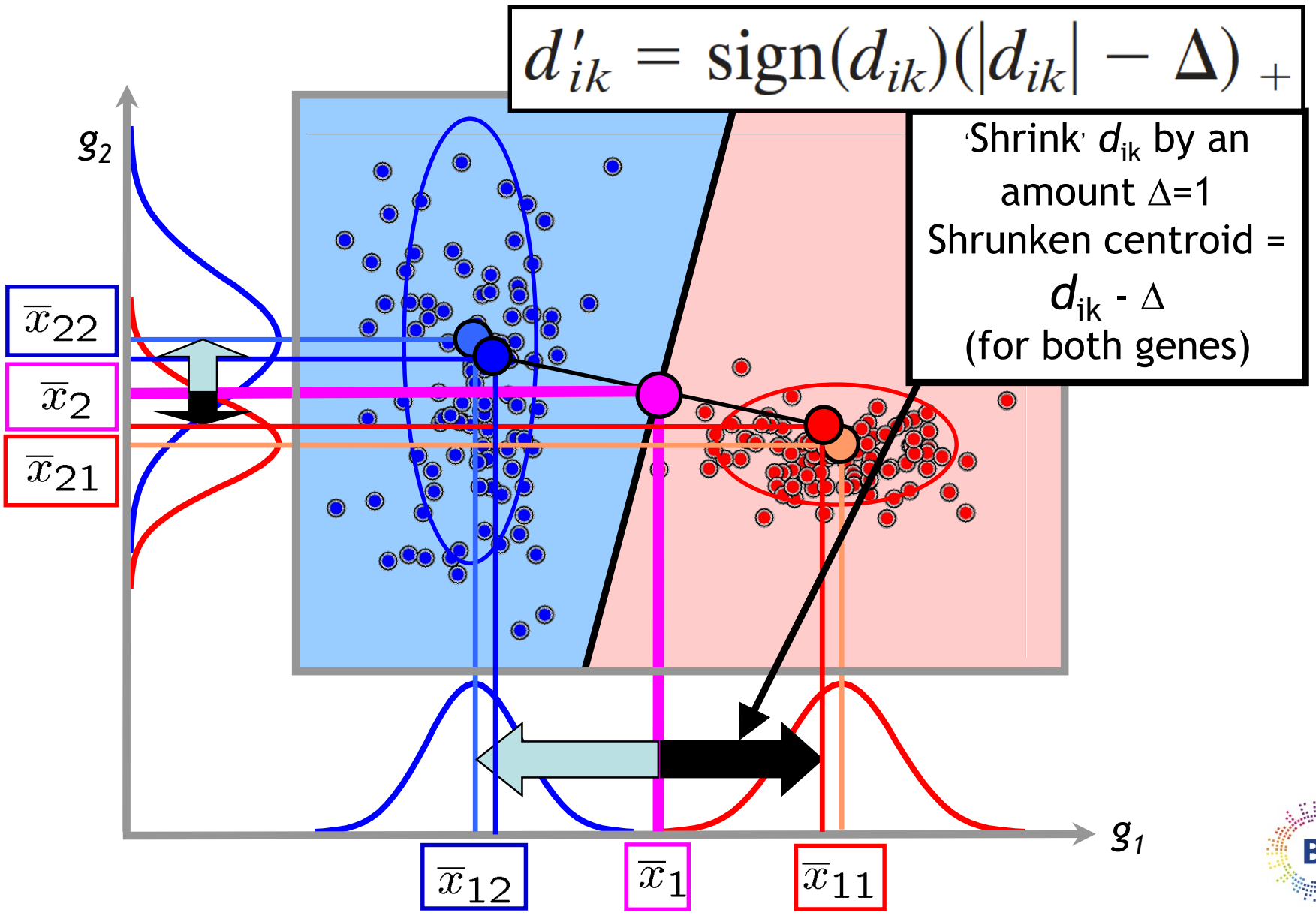
$$d_{ik} = \frac{\bar{x}_{ik} - \bar{x}_i}{m_k \cdot (s_i + s_0)}$$



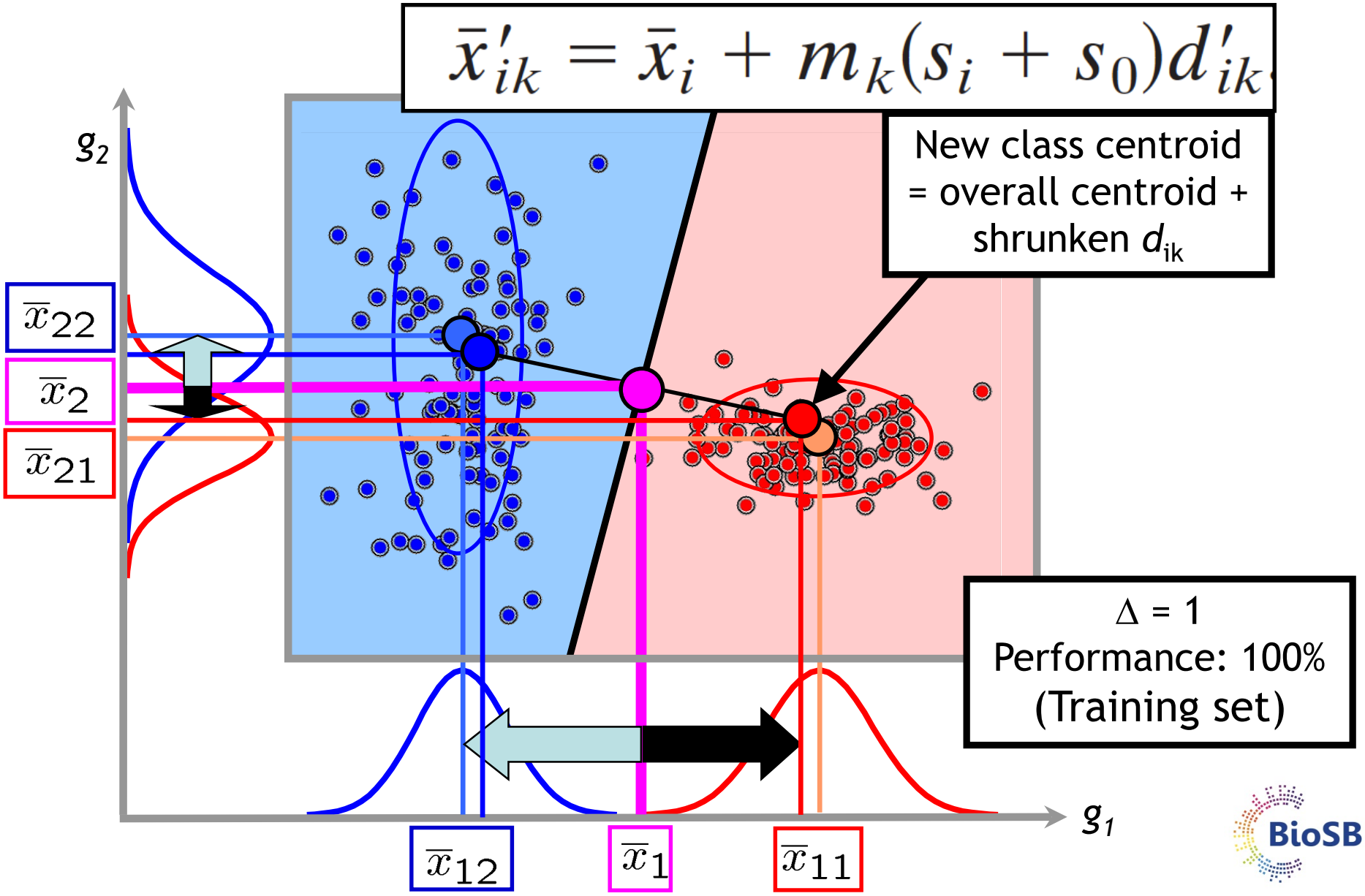
Quality measure of gene: d_{ik} = Distance between class and overall mean (for both genes)

BioSB

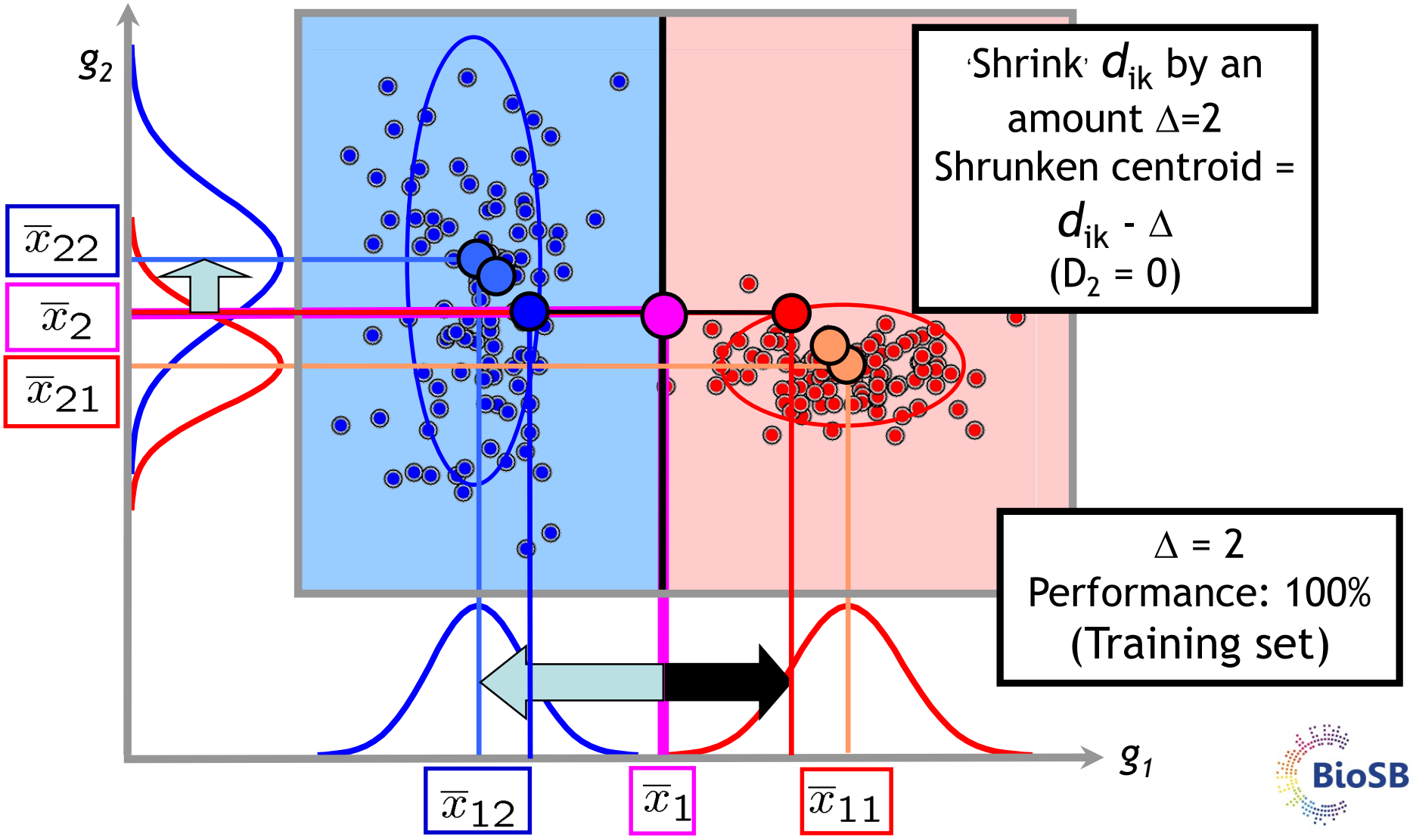
Shrunken centroids in 2D (6)



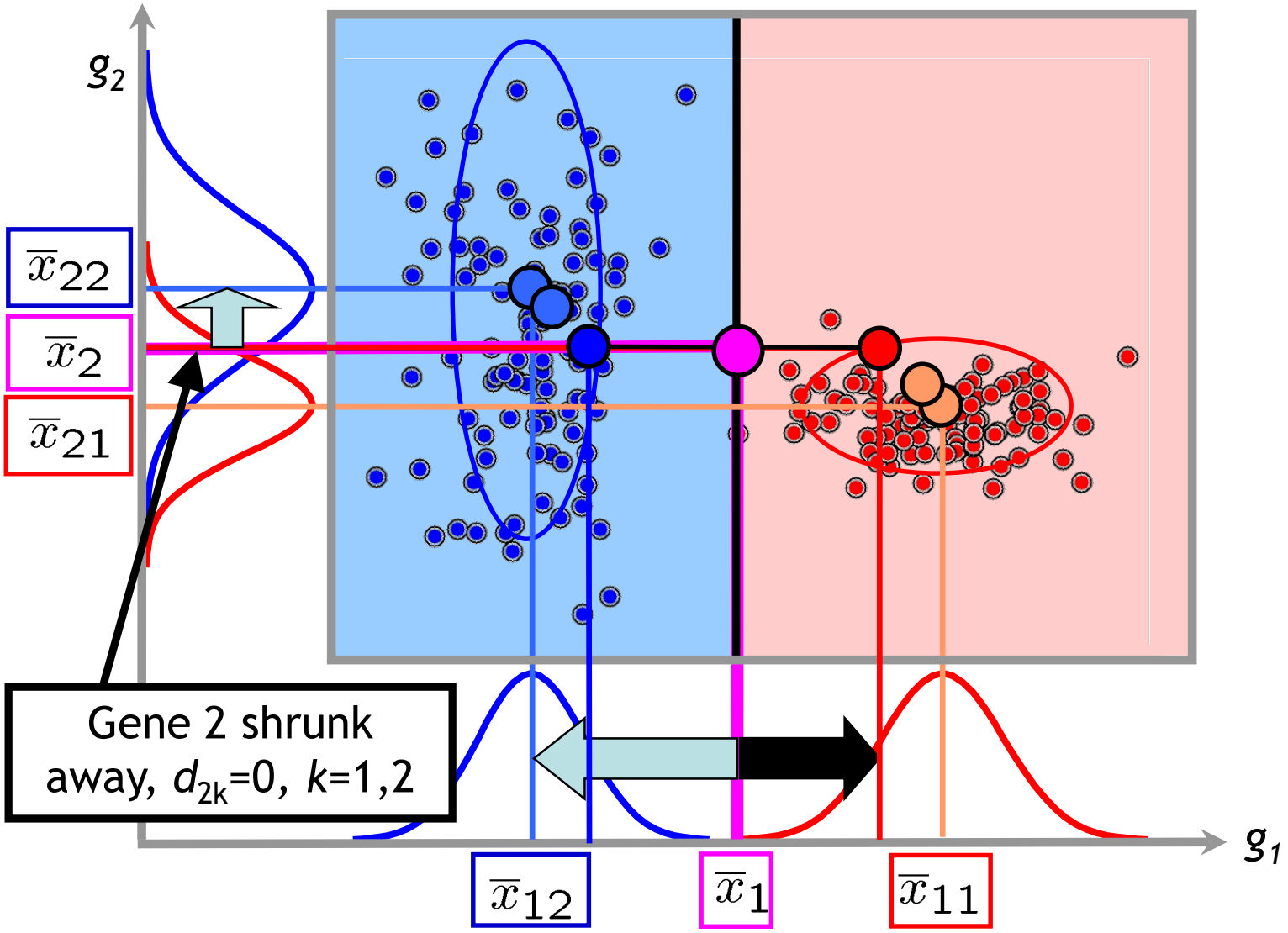
Shrunken centroids in 2D (6)



Shrunken centroids in 2D (7)

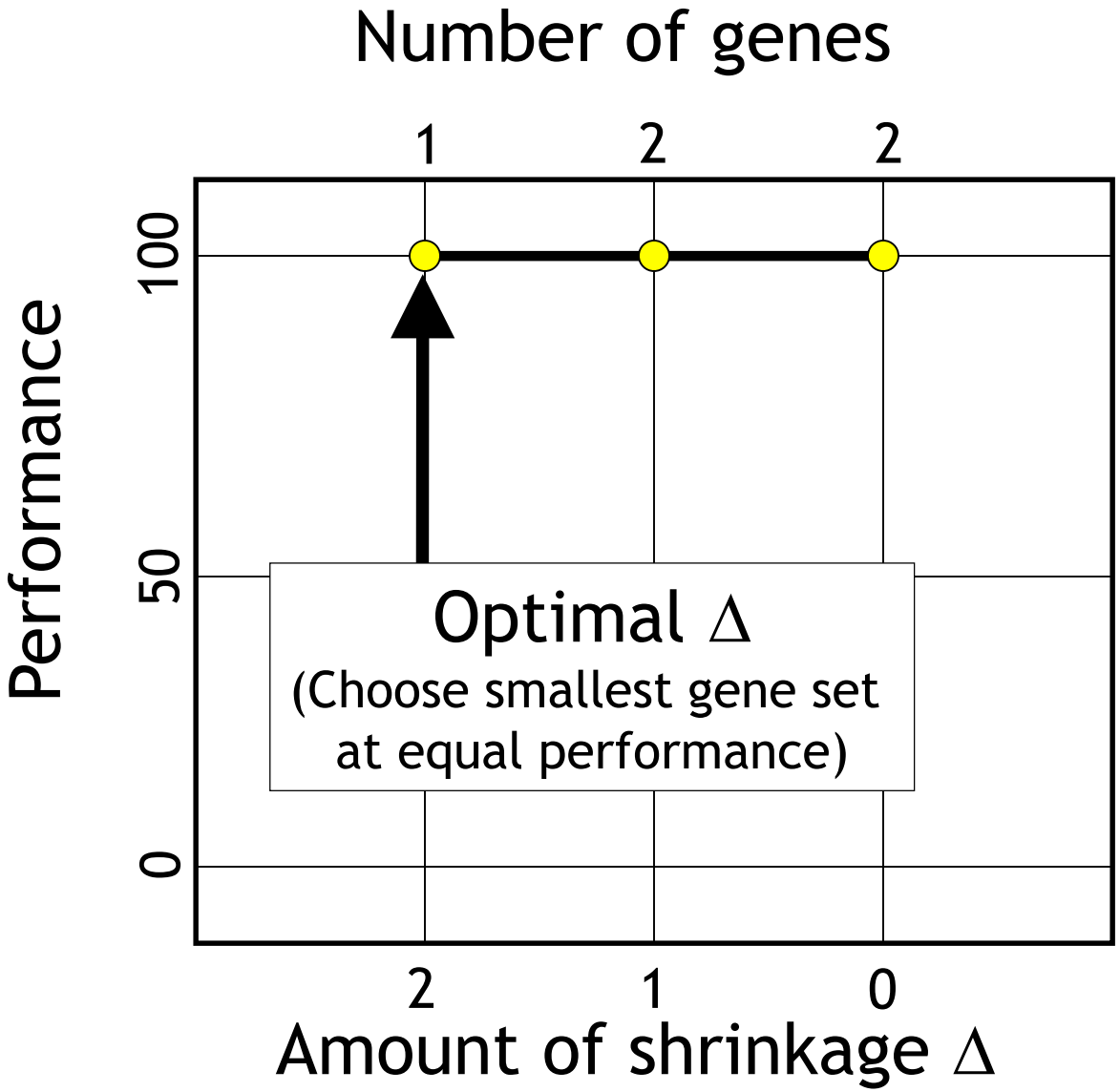


Shrunken centroids in 2D (8)



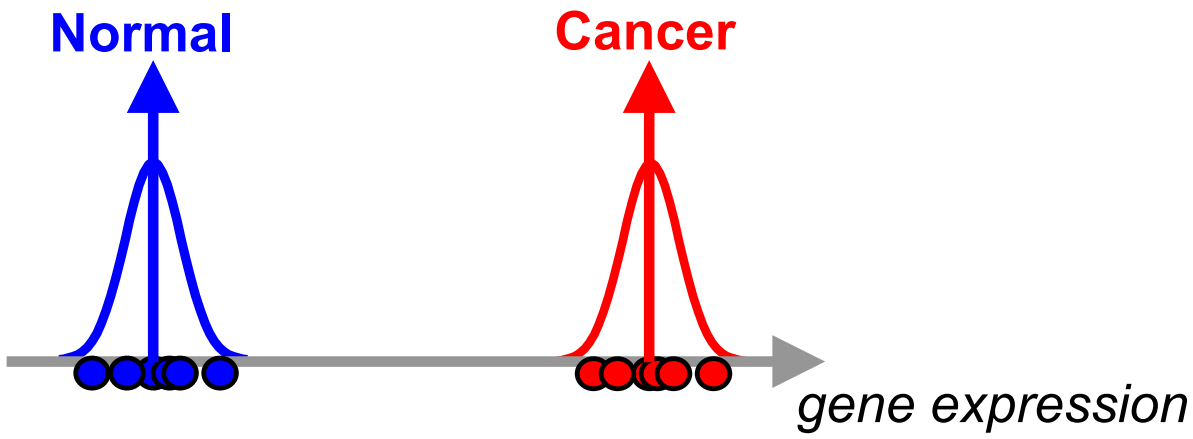
BioSB

Results: number of genes selected

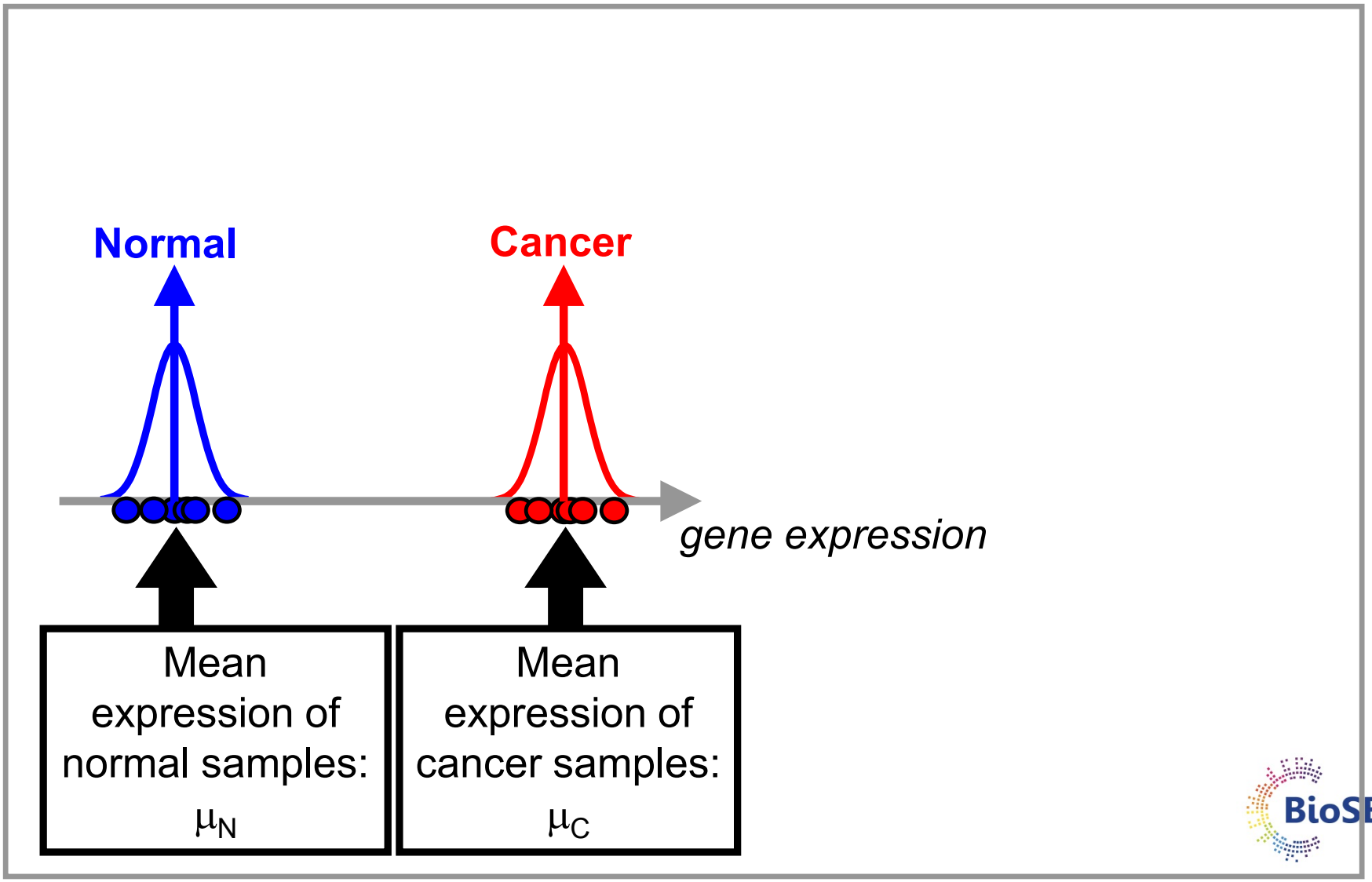


Shrunken centroids: alternative view

Shrunken centroids: D-measure (1)

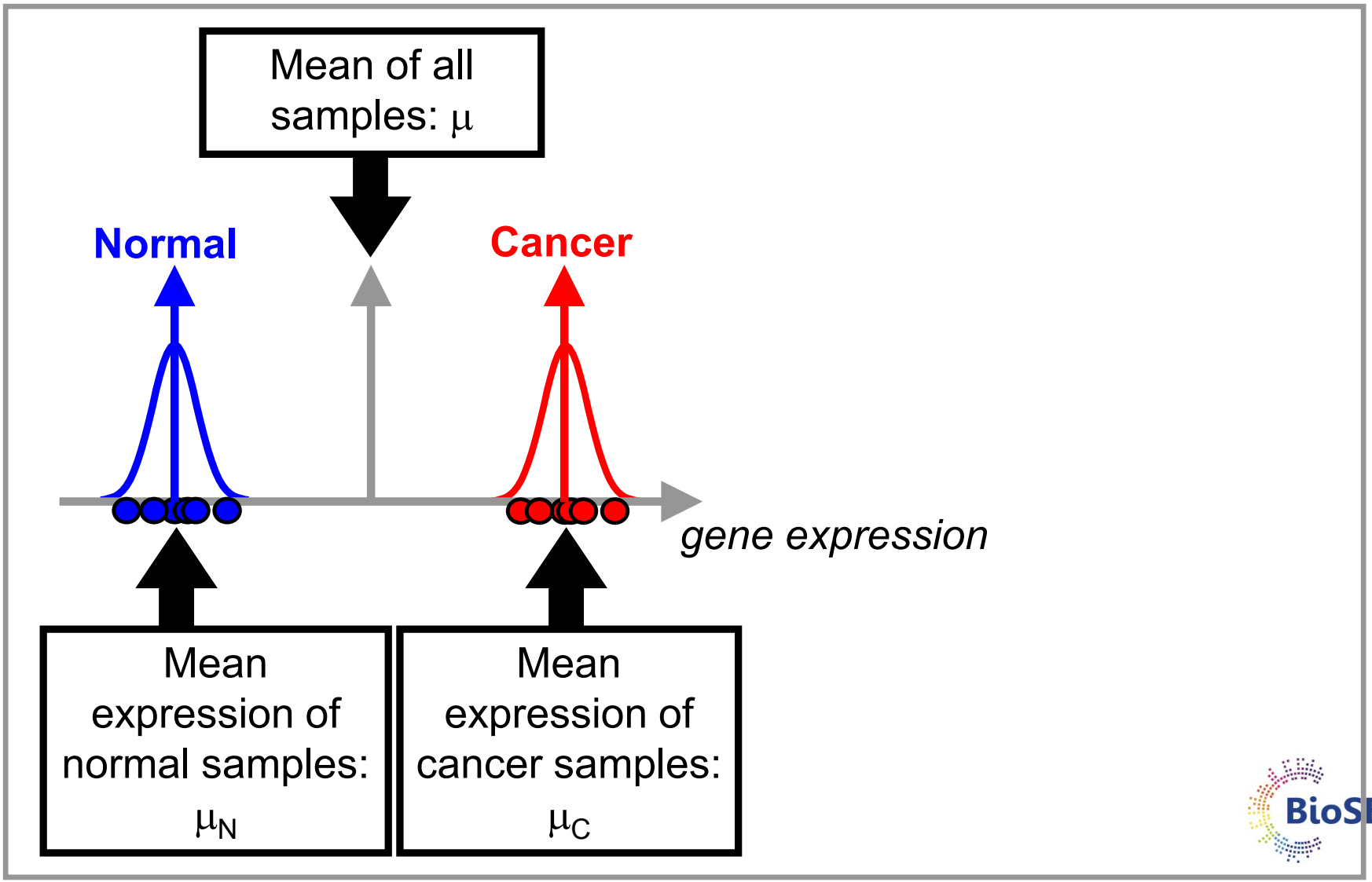


Shrunken centroids: D-measure (2)



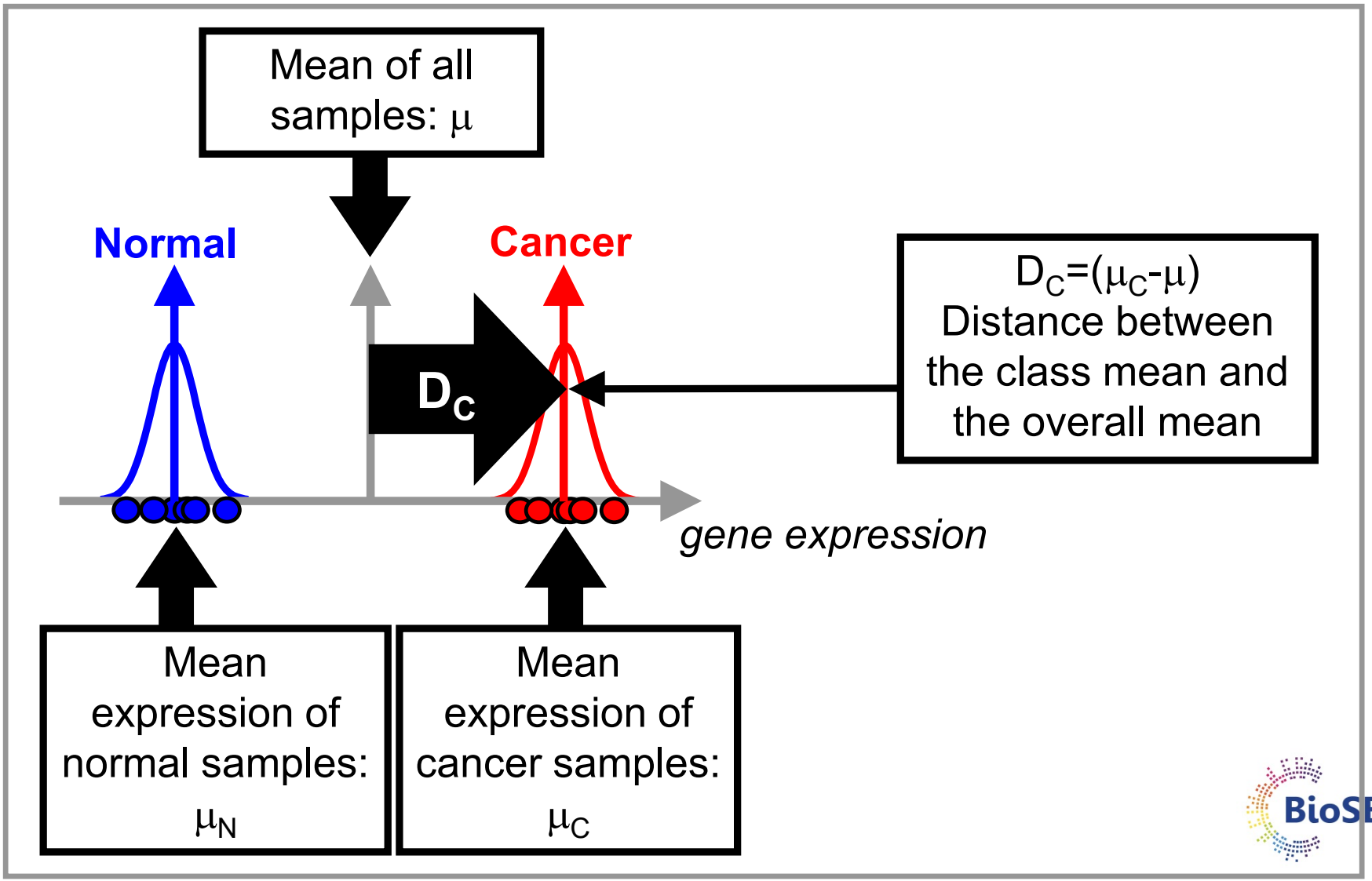
BioSB

Shrunken centroids: D-measure (3)

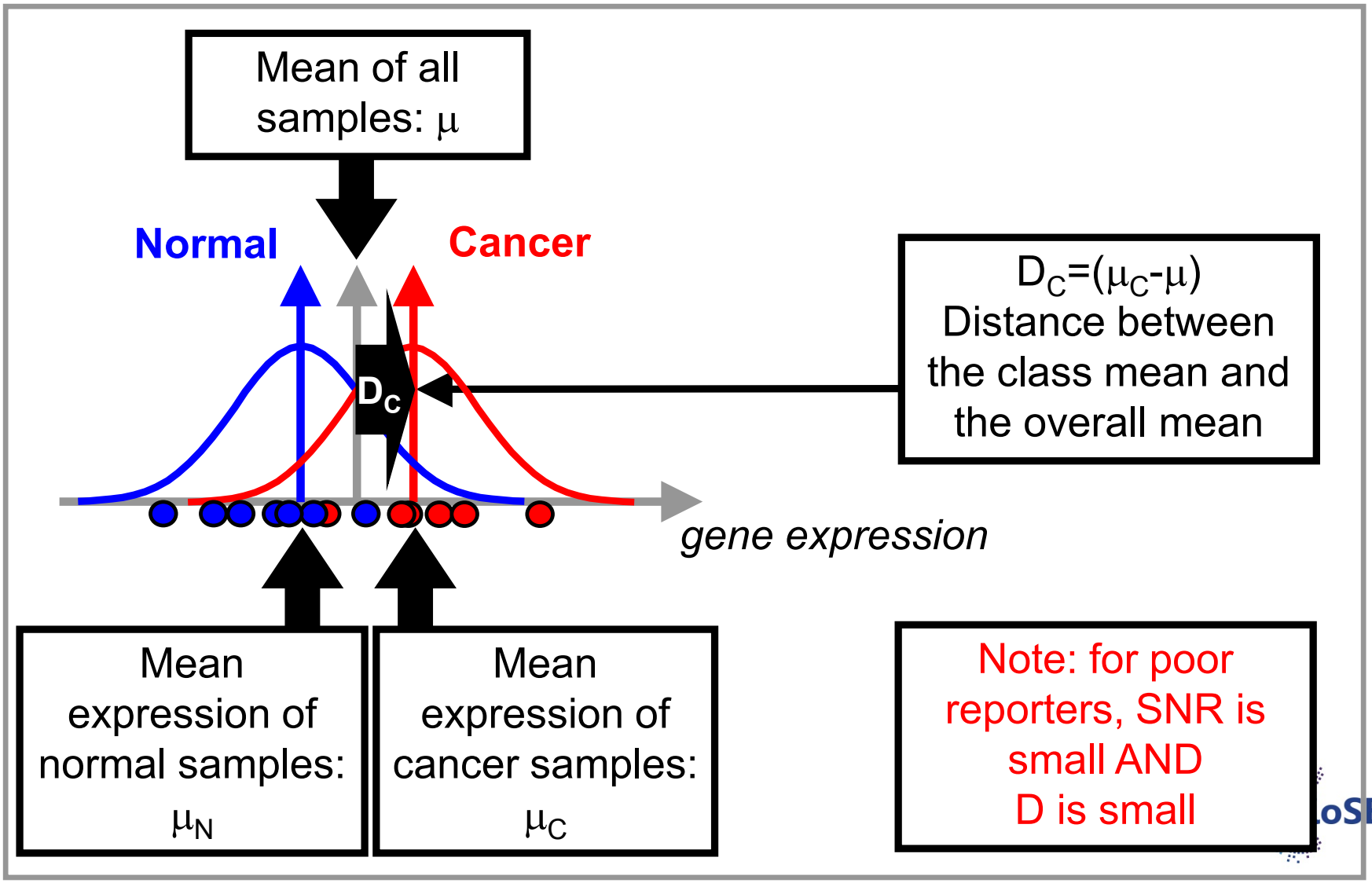


BioSB

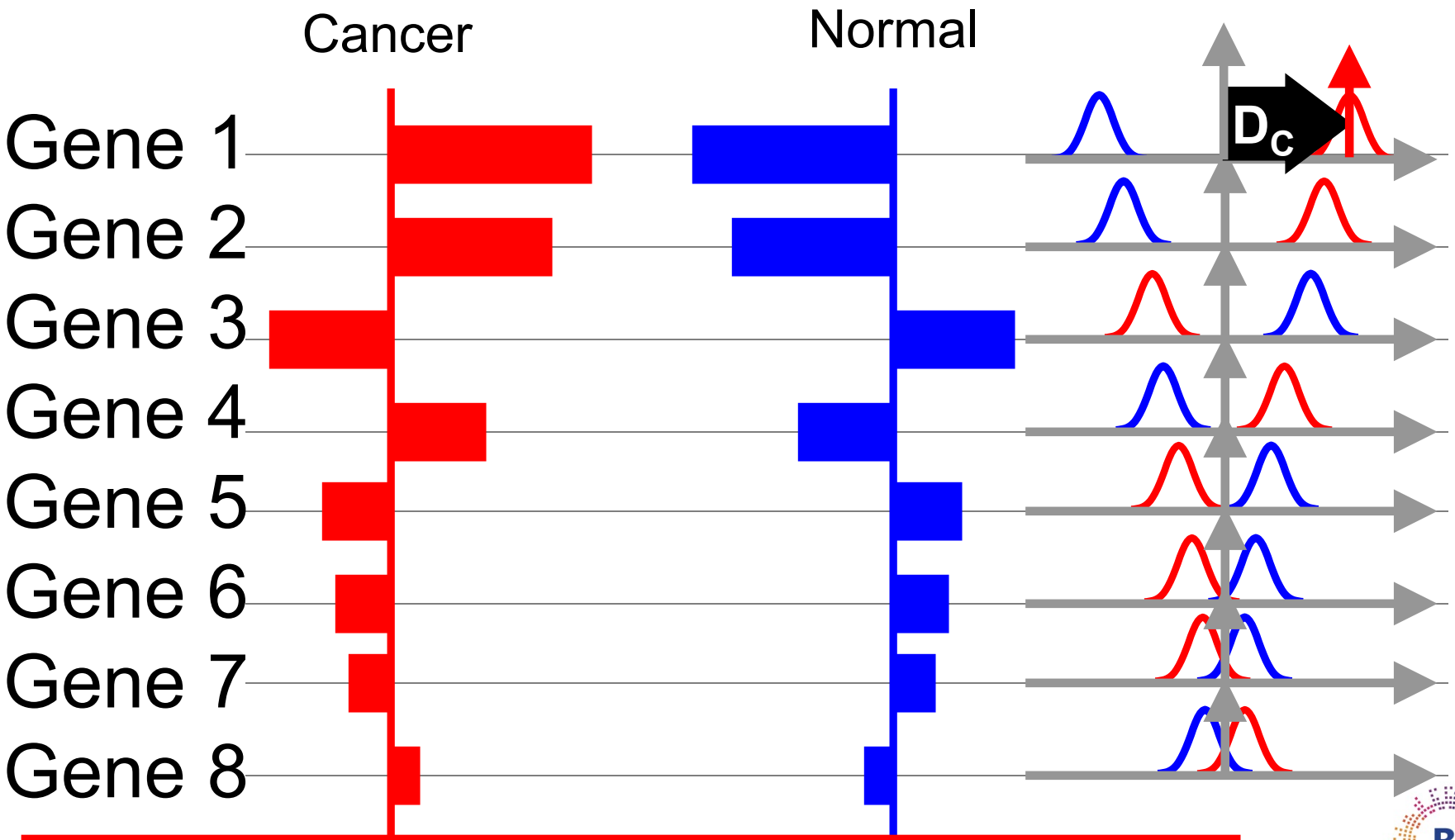
Shrunken centroids: D-measure (4)



Shrunken centroids: D-measure (5)



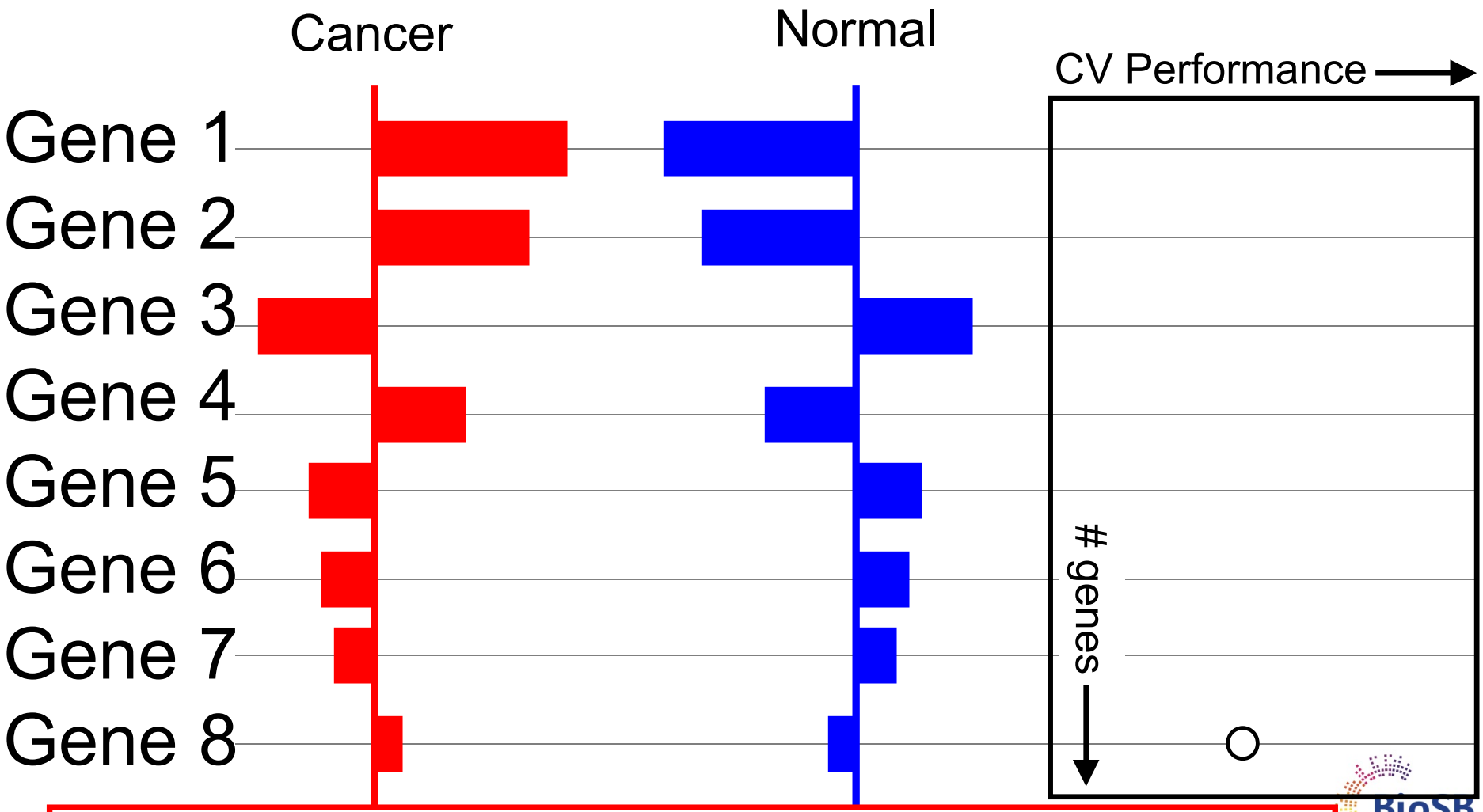
Shrunken centroids: selecting the genes



Genes sorted based on D-measure: best to worse

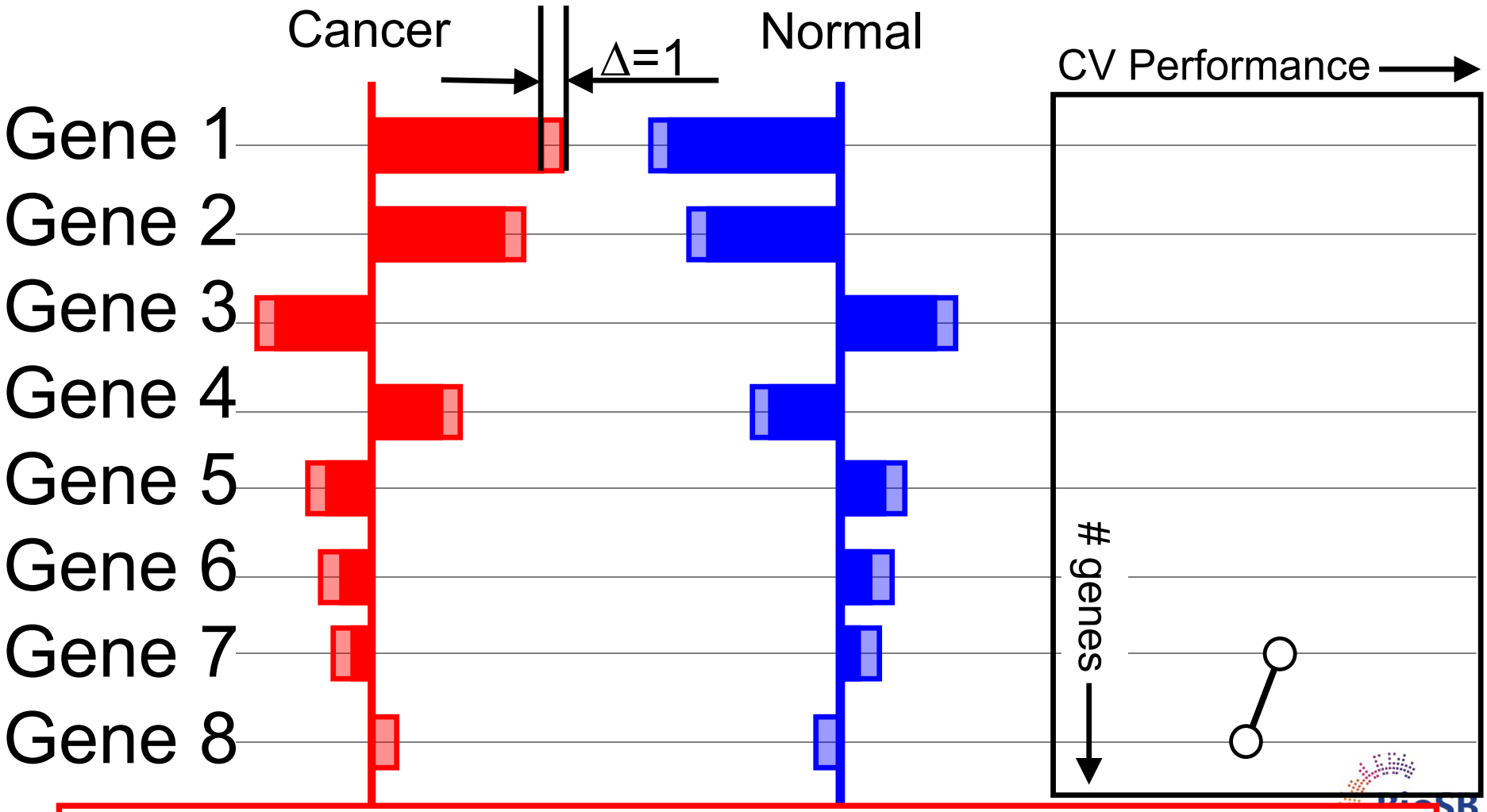
BioSB

Shrunken centroids: selecting the genes



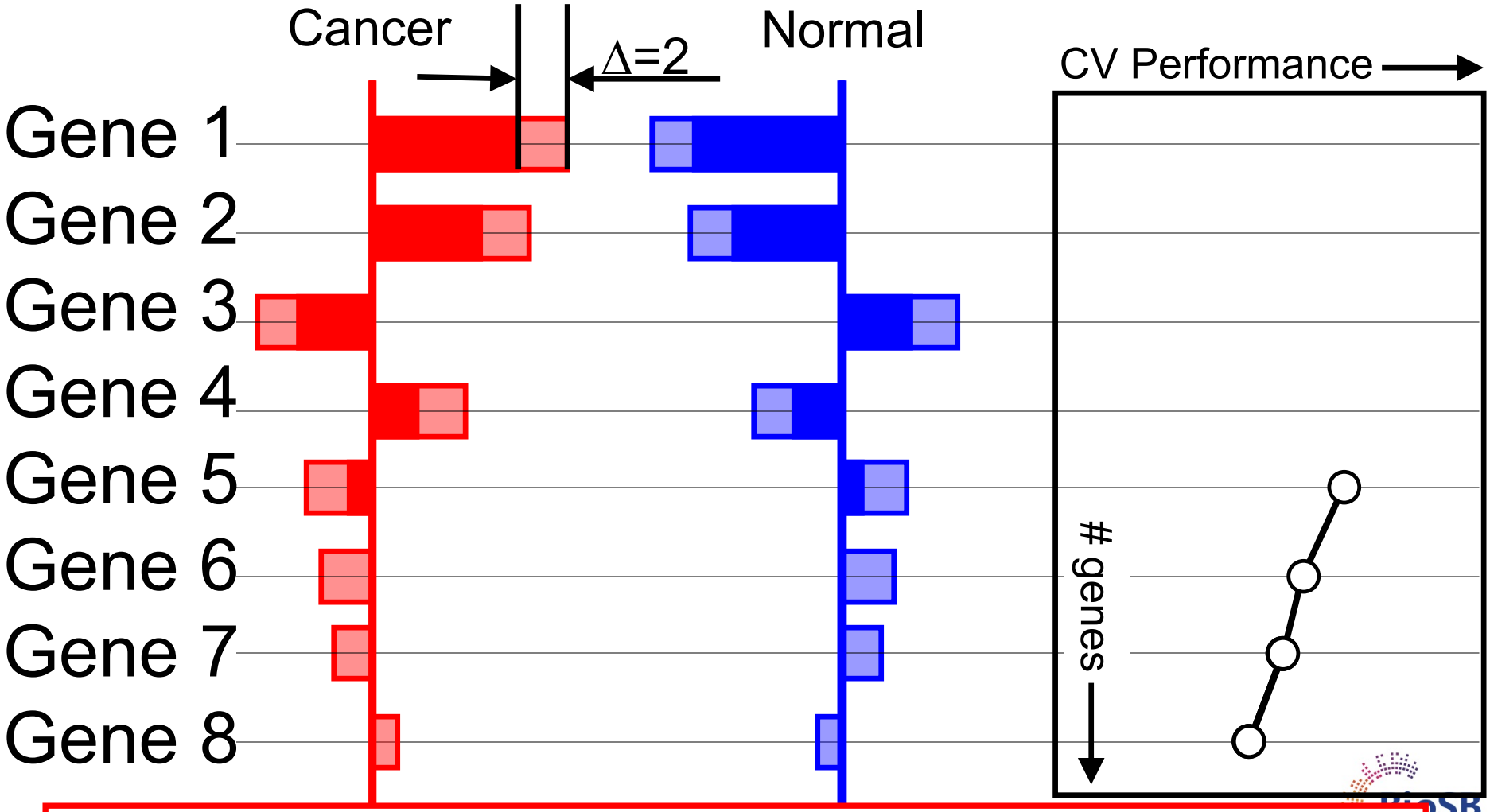
Train classifier on all 8 genes; estimate CV performance

Shrink all D by Δ=1: reduce length by 1



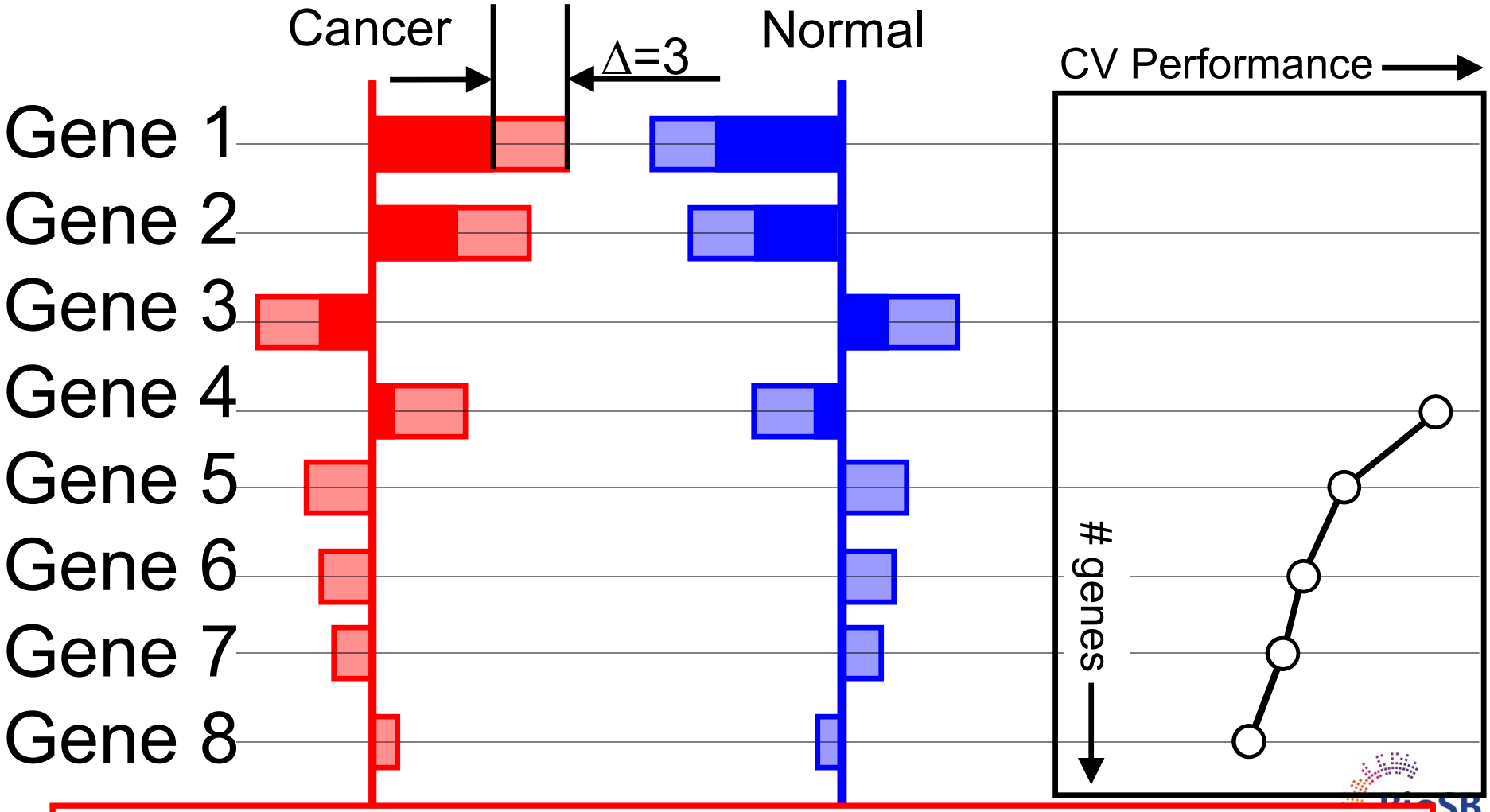
Train classifier on 7 genes (D>0); estimate CV performance

Shrink all D by Δ=2: reduce length by 2



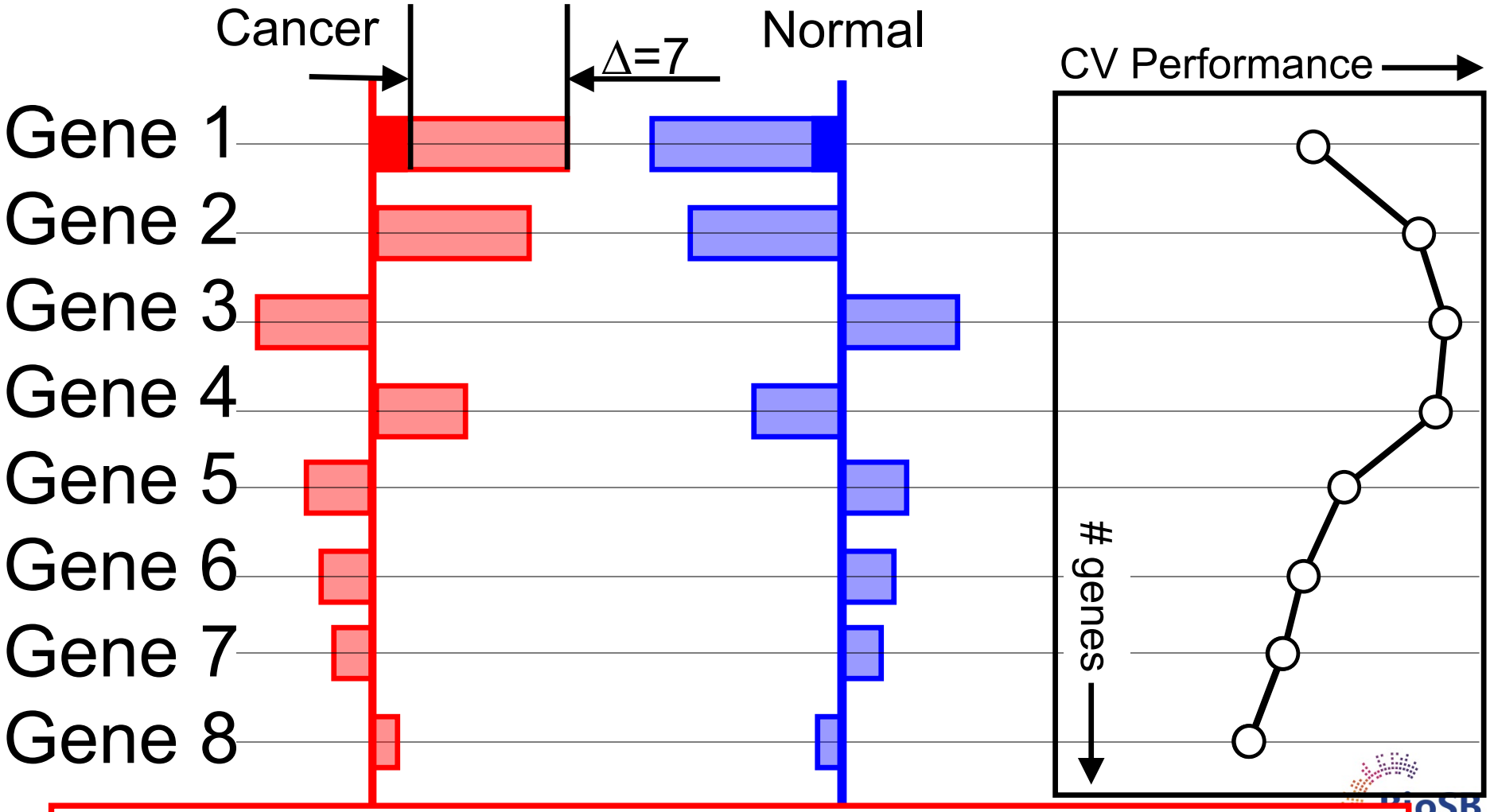
Train classifier on 5 genes (D>0); estimate CV performance

Shrink all D by Δ=3: reduce length by 3



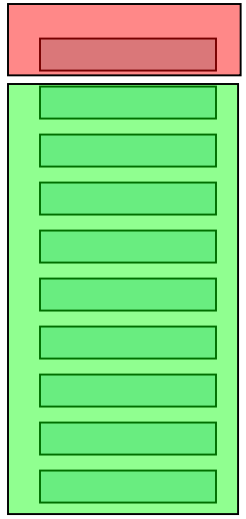
Train classifier on 4 genes (D>0); estimate CV performance

Shrink all D by Δ=7: reduce length by 7

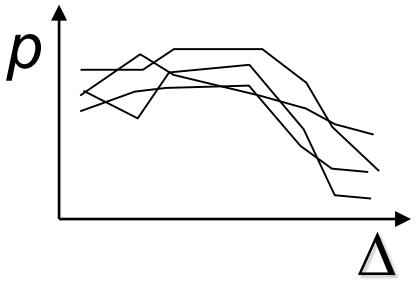


Train classifier on 1 gene (D>0); estimate CV performance

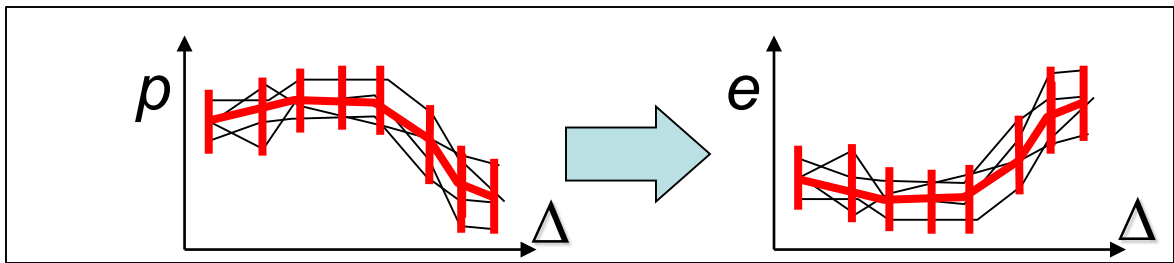
Determining the optimal Δ



1. Split the data (X) in 10 equal parts (x_1,…x_{10})
2. For each of the 10 folds (i=1,2,…,10)
3. On the training set ($X \backslash x_i$)
   1. Compute the class and overall centroids
   2. For a range of Δ (Δ = [0,0.5,…,7])
      i. Shrink D for all genes
      ii. Compute 'shrunken centroids' on training set
      iii. Test the resulting classifier on the test set (x_i)
   3. Result: 10 Curves of performance vs. Δ

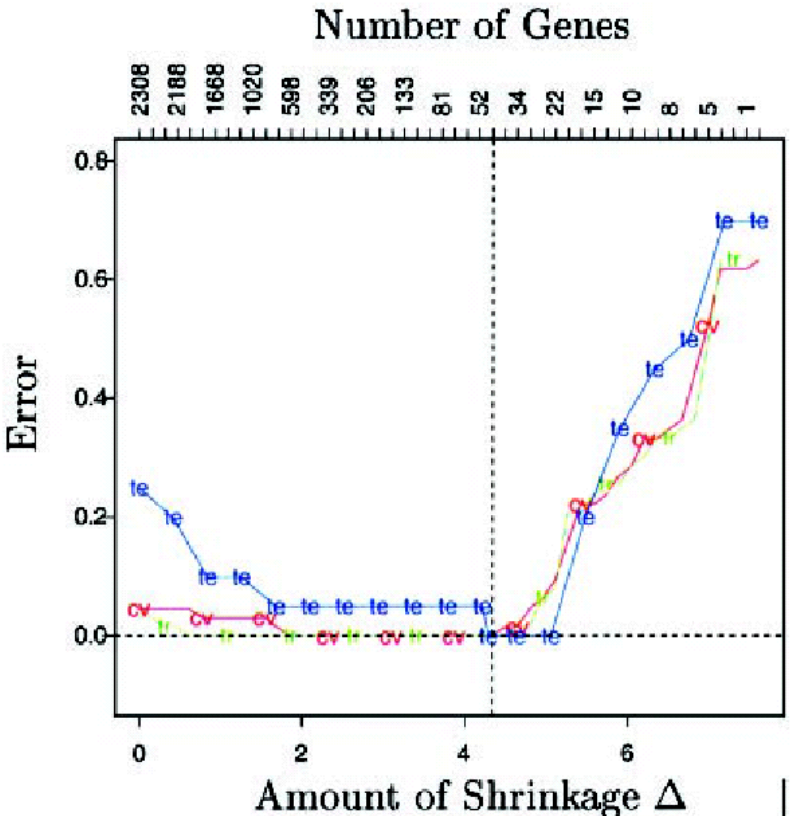


4. Average all 10 curves and compute std. dev. at each Δ
5. Pick the Δ where the performance is maximal (error min.)



PAM

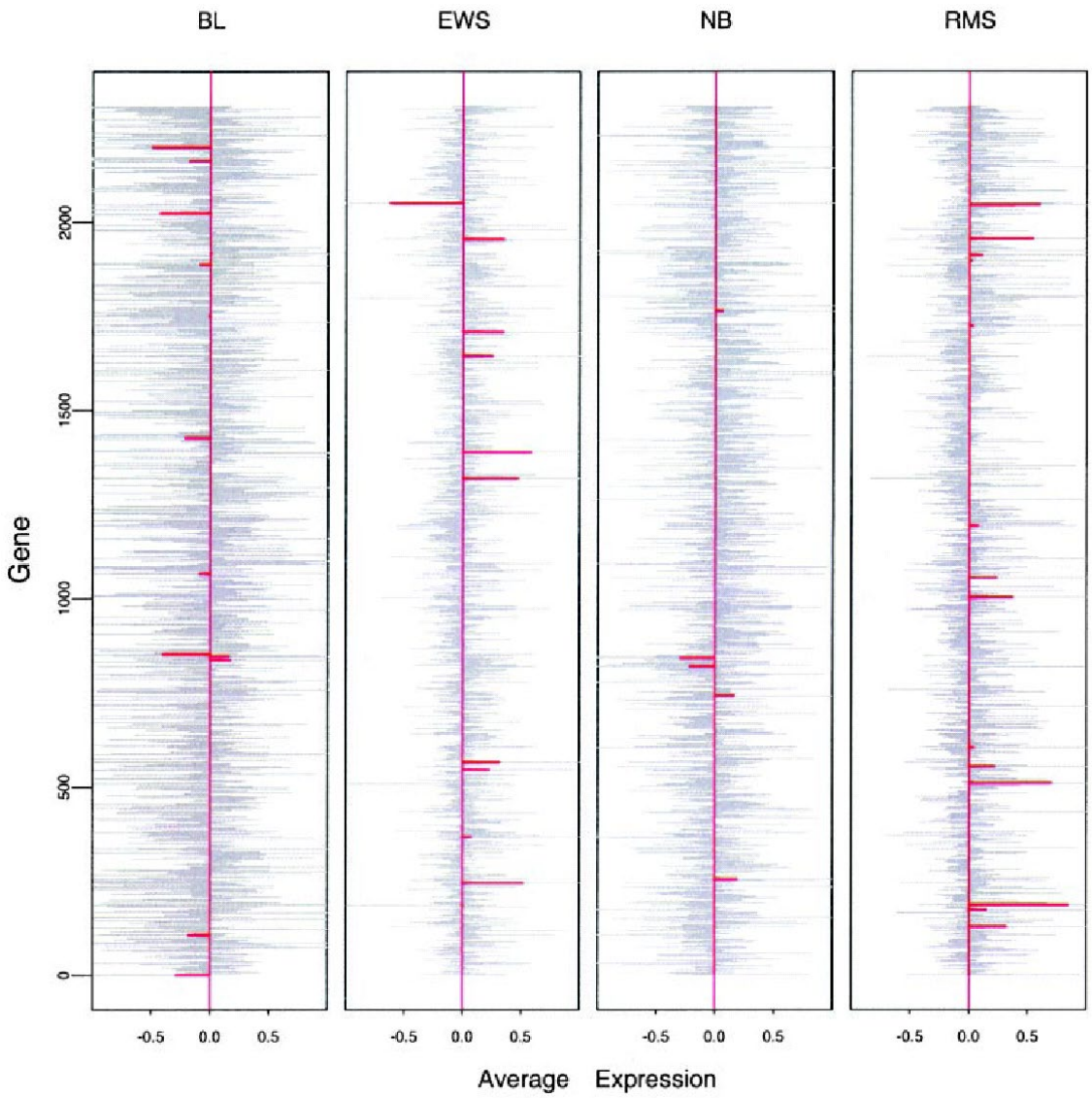
- For the Khan datatset; 4 classes: BL, EWS, NB, RMS
- At optimal Δ : 43 genes *not* shrunk away



Neuroblastoma (NB)
Rhabdomyosarcoma (RMS)
Burkitt lymphoma (BL)
Ewing family of tumors (EWS),

R. Tibshirani *et al.* (2002) PNAS 99(10):6567-6572, 2002.

PAM (2)



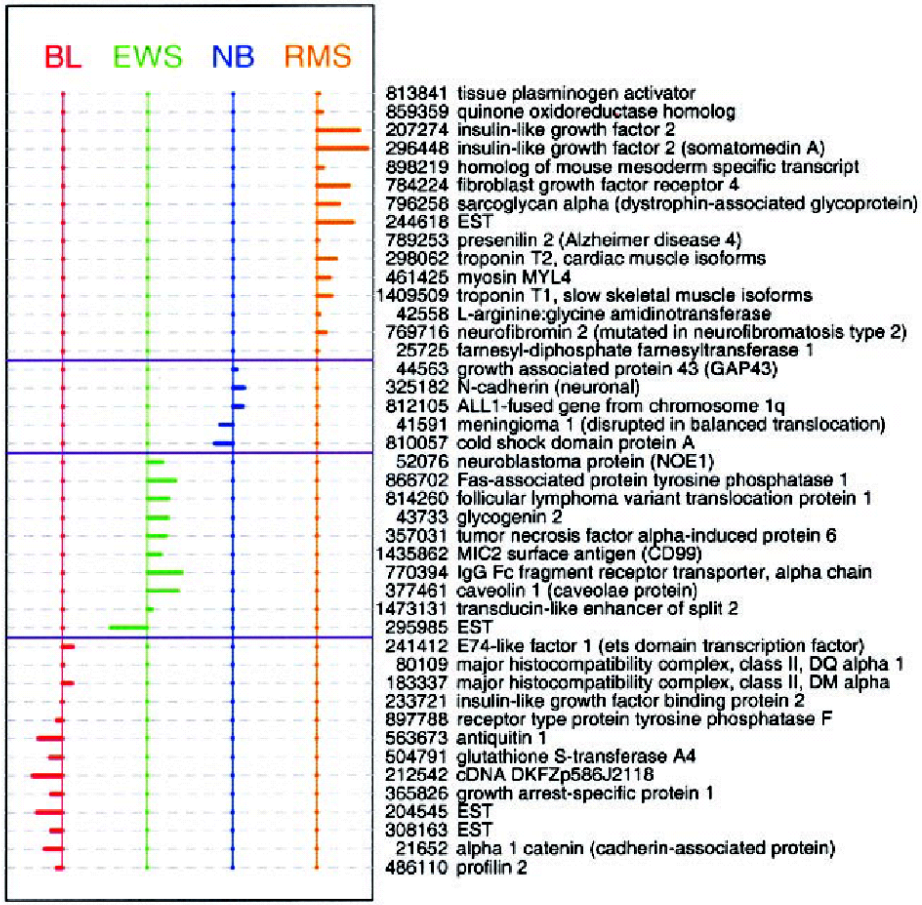
shrunk

unshrunk

BioSB

PAM (3)

At optimal Δ : 43 genes *not* shrunk away



- Neuroblastoma (NB)
- Rhabdomyosarcoma (RMS)
- Burkitt lymphoma (BL)
- Ewing family of tumors (EWS),

R. Tibshirani *et al*. (2002) PNAS 99(10):6567-6572, 2002.

BioSB

PAM (4)

- For a new sample x* (assuming normal class conditionals and applying Bayes' rule):

$$C(l^*) = l, \text{where } \delta_l(x^*) = \min_k(\delta_k(x^*))$$

$$\delta_k(x^*) = \sum_{i=1}^{p} \frac{(x_i^* - \overline{x}'_{ik})^2}{(s_i + s_0)^2} - 2\log(\pi_k)$$

Discriminant for class *k*

PAM (4)

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$$C(l^*) = l, \text{where } \delta_l(x^*) = \min_k(\delta_k(x^*))$$

$$\delta_k(x^*) = \sum_{i=1}^{p} \frac{(x_i^* - \overline{x}'_{ik})^2}{(s_i + s_0)^2} - 2\log(\pi_k) \qquad \left[\sum_{k=1}^{K} \pi_k = 1 \right]$$

Compensate for prior prob.

Discriminant for class *k*

BioSB

PAM (4)

- For a new sample x* (assuming normal class conditionals and applying Bayes' rule):

$$C(l^*) = l, \text{where } \delta_l(x^*) = \min_k(\delta_k(x^*))$$

$$\delta_k(x^*) = \sum_{i=1}^{p} \frac{(x_i^* - \overline{x}'_{ik})^2}{(s_i + s_0)^2} - 2\log(\pi_k) \qquad \left[\sum_{k=1}^{K} \pi_k = 1 \right]$$

Discriminant for class *k*

Squared distances to (shrunken) Centroid of class *k*

Compensate for prior prob.

PAM (4)

- For a new sample x* (assuming normal class conditionals and applying Bayes' rule):

$$C(l^*) = l, \text{where } \delta_l(x^*) = \min_k(\delta_k(x^*))$$

$$\delta_k(x^*) = \sum_{i=1}^{p} \frac{(x_i^* - \overline{x}'_{ik})^2}{(s_i + s_0)^2} - 2\log(\pi_k) \qquad \left[\sum_{k=1}^{K} \pi_k = 1 \right]$$

Discriminant for class *k*

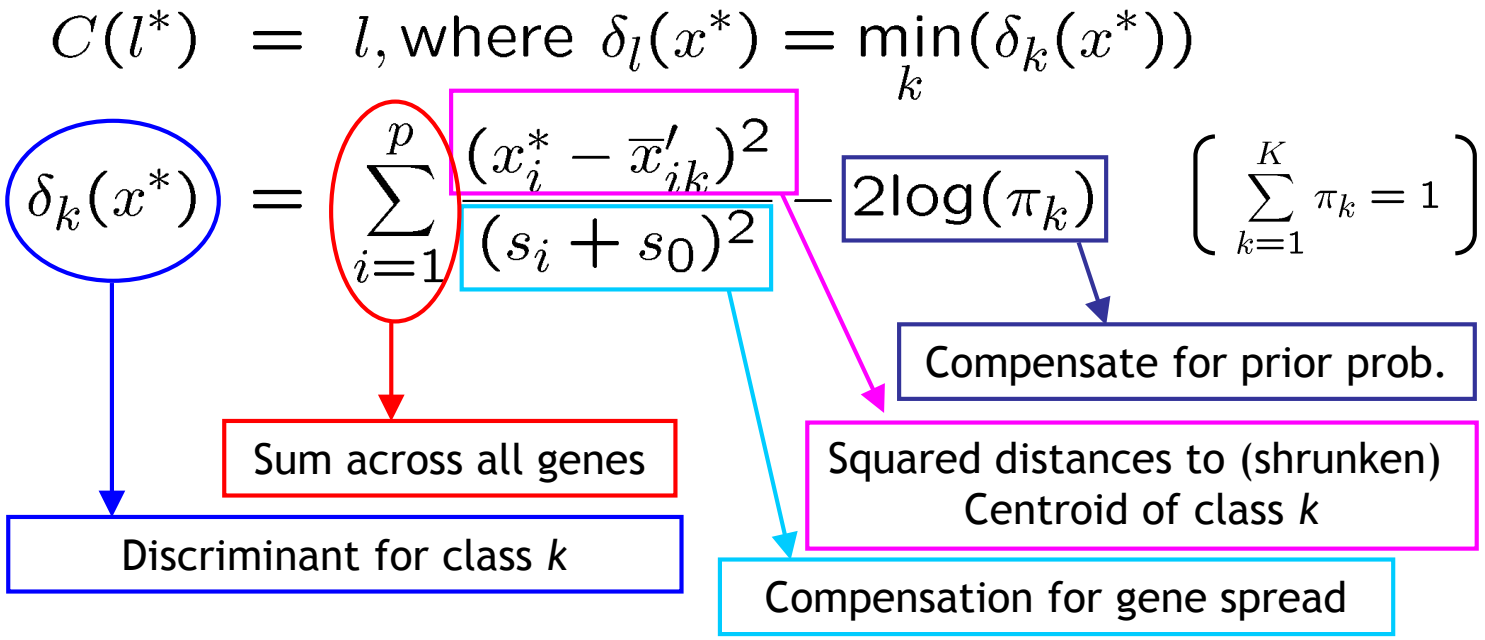
Compensate for prior prob.

Squared distances to (shrunken) Centroid of class *k*

Compensation for gene spread

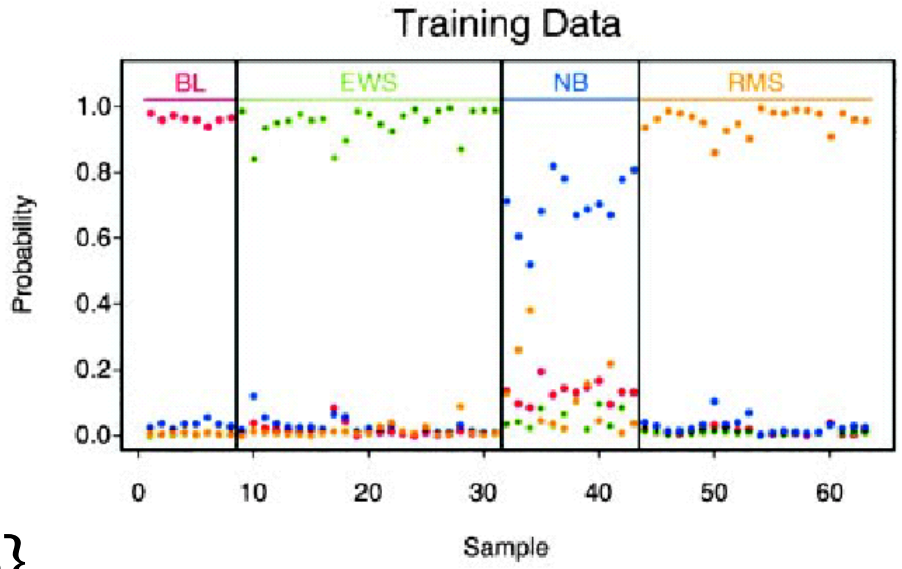
PAM (4)

- For a new sample x* (assuming normal class conditionals and applying Bayes' rule):



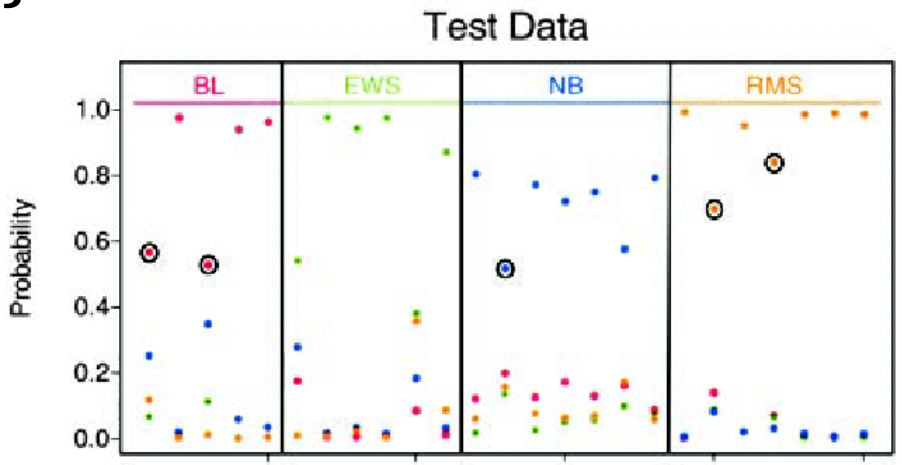
Scoring samples by posterior prob's

$$\hat{p}(k|x^*)$$



k = {BL,EWS,NB,RMS}

$$\hat{p}(k|x^*)$$



BioSB

Shrinkage

- PAM determines a weight for every gene based on the predictive capacity of the gene (type of t-statistic)
- This weight determines role of the gene in a DLDA classifier (weights can be zero, i.e. no participation)
- Weights of all genes are shrunk by the same amount (Δ)
- PAM computes effect of shrinkage on error rate, and chooses shrinkage (=number of genes) with lowest error
- PAM: implicit simultaneous error and complexity minimisation
- Other approach: regularisation, combine error and penalty for number of genes explicitly

BioSB

Shrinkage (2)

- Model: $y = \beta_0 + \sum_{i=1}^{p} \beta_i x_i + \varepsilon$

- Penalised (*aka* regularised) least squares:
  - Ridge regression:

$$\hat{\boldsymbol{\beta}} = \arg\min_{\boldsymbol{\beta}} \left[\sum_{j=1}^{n} \left(y_j - \beta_0 - \sum_{i=1}^{p} \beta_i x_{j,i} \right)^2 + \lambda \sum_{i=1}^{p} \beta_i^2 \right]$$

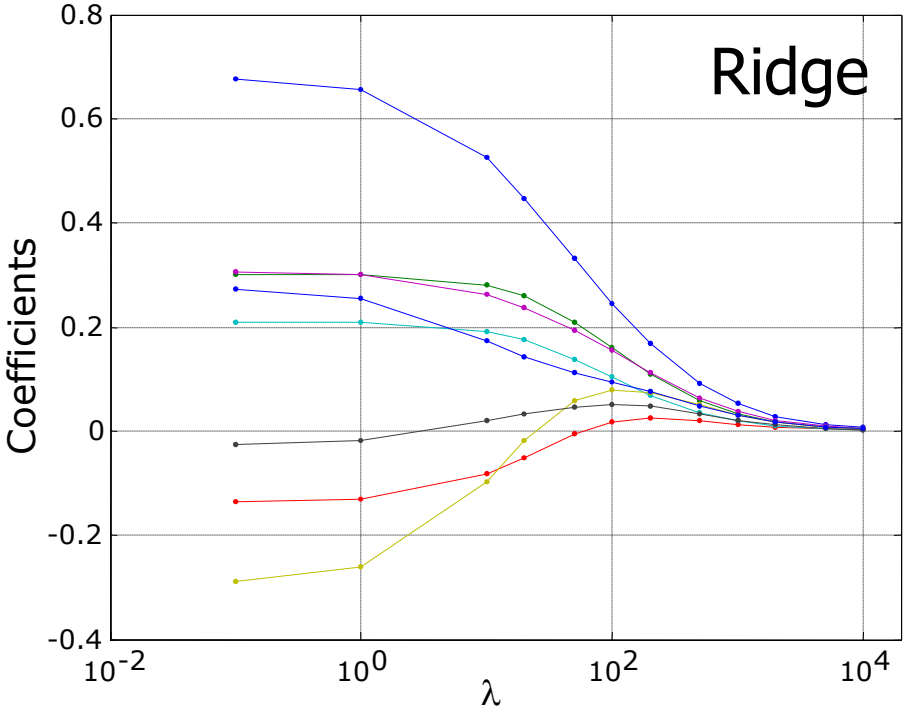
  - LASSO: minimise

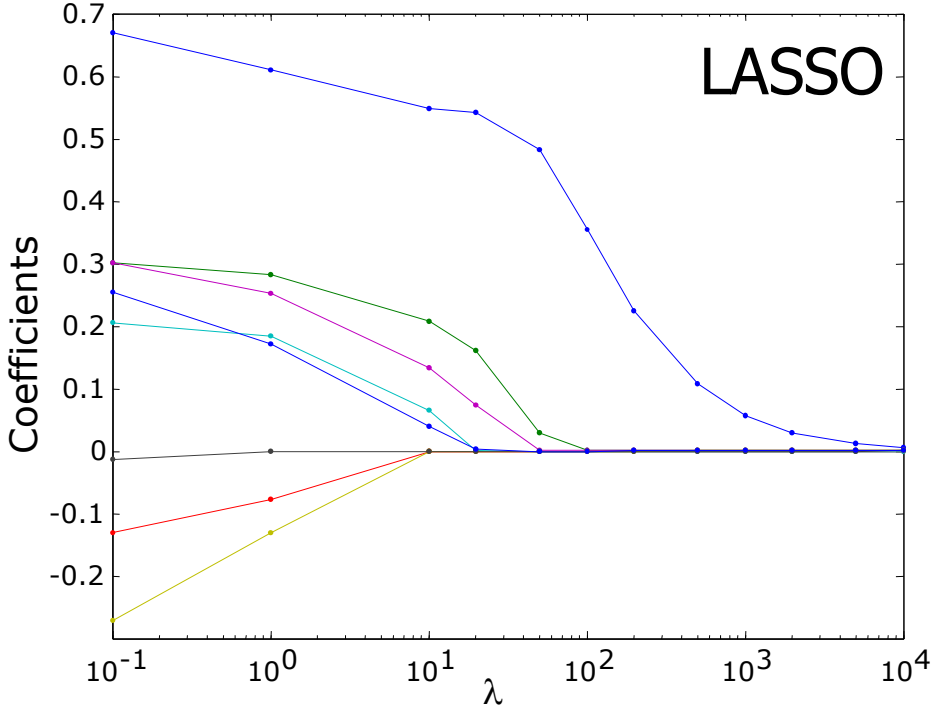
$$\hat{\boldsymbol{\beta}} = \arg\min_{\boldsymbol{\beta}} \left[\sum_{j=1}^{n} \left(y_j - \beta_0 - \sum_{i=1}^{p} \beta_i x_{j,i} \right)^2 + \lambda \sum_{i=1}^{p} |\beta_i| \right]$$

BioSB

LASSO

- Difference seems small, but effect of LASSO is that genes are no longer used (like in PAM!)

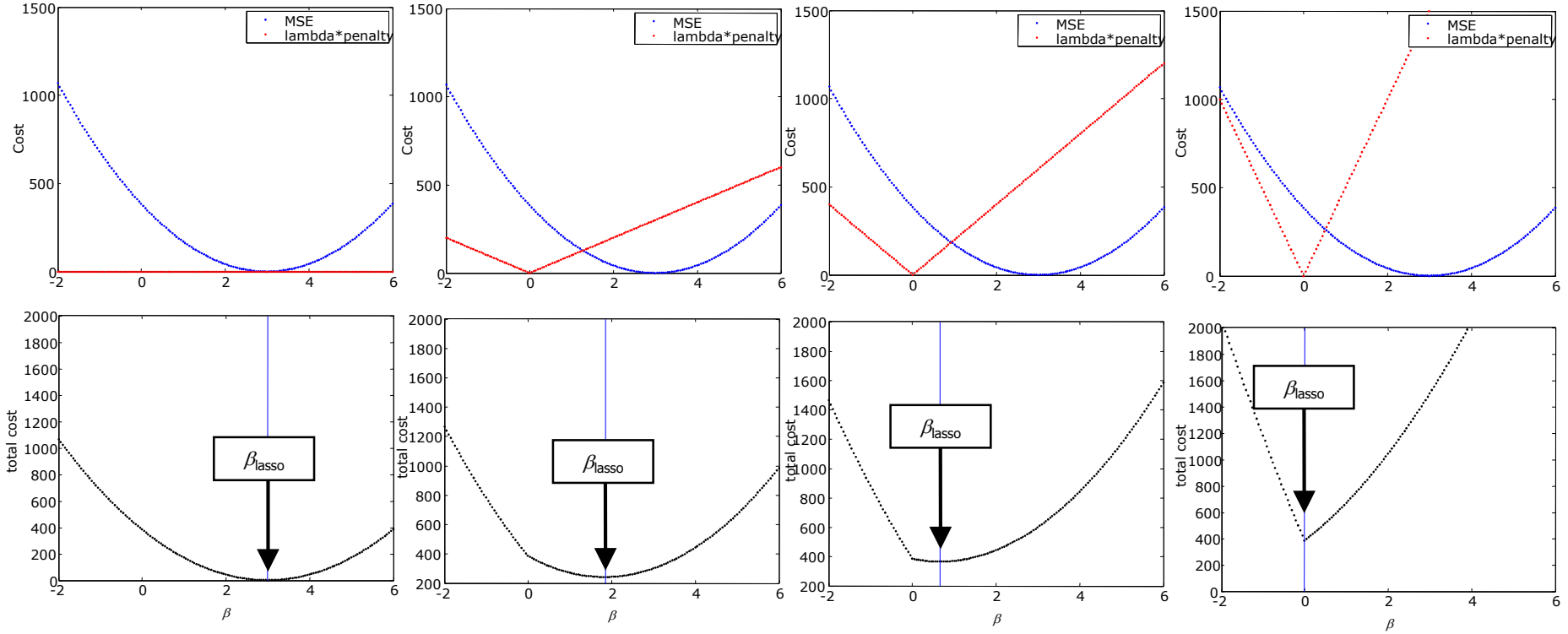




BioSB

LASSO (2)

- Example: true function y = 3x

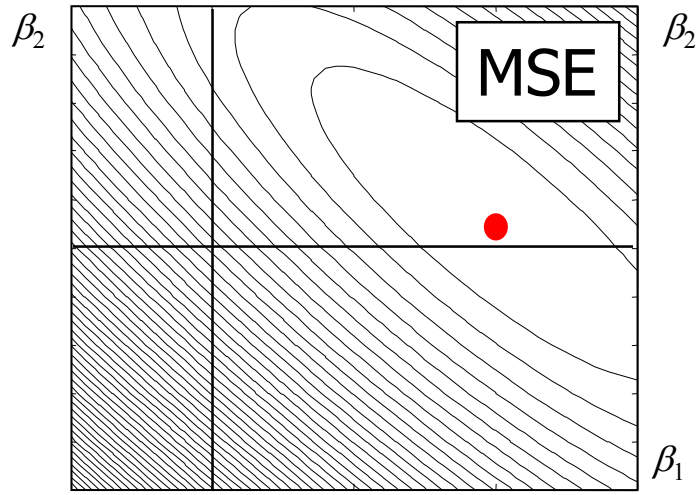


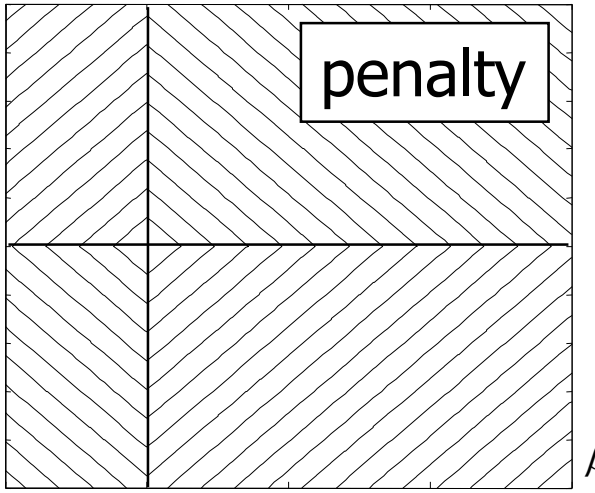
λ = 0 λ = 100 λ = 200 λ = 500

LASSO (3)

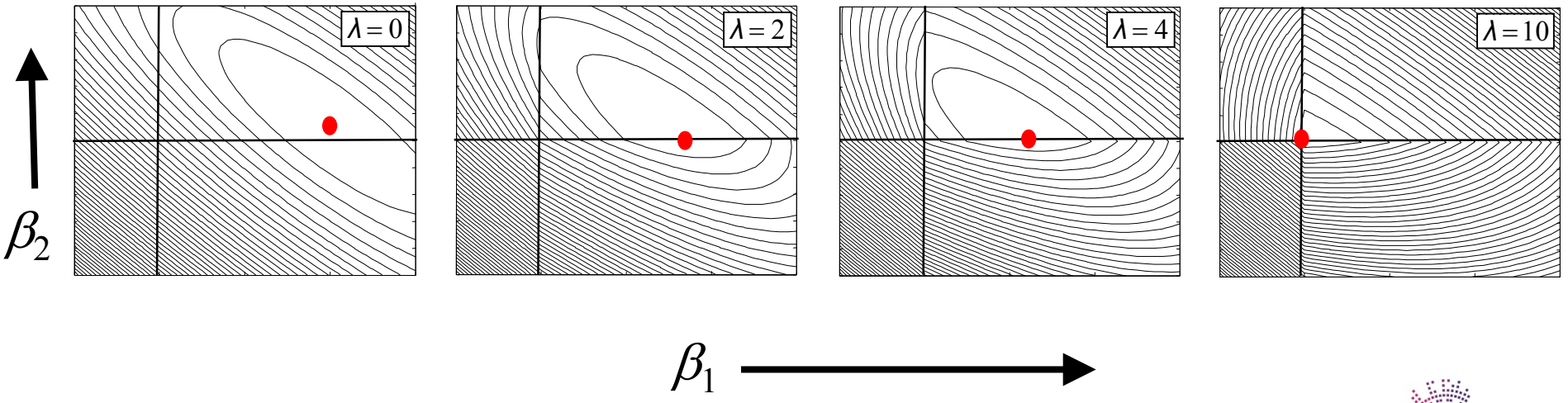
Example:

$y = 0.1x_1 + 0.01x_2$





Optimum



Final summary

- Feature extraction:
  - Linear:
    - PCA,
    - Fisher
  - Non-linear
    - MDS
- Feature selection:
  - Criteria
  - search algorithms
    - forward,
    - backward,
    - branch & bound.
- Sparse classifiers:
  - Ridge,
  - LASSO

BioSB