Assessment of dimensionality reduction methods for the detection of intermediate cancer phenotypes from ‘omic data

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International Agency for Research on Cancer

World Health Organization

Context : Cancer classification

Cancer classification

Proper diagnostic

Adapted therapeutics

Dimension reduction

Expression matrix

	geneA	geneB	geneC	geneD	...
cancer1_a	42	58	12	47	...
cancer1_b	25	69	87	42	...
cancer2_a	35	91	25	81	...
cancer2_b	9	71	44	7	...

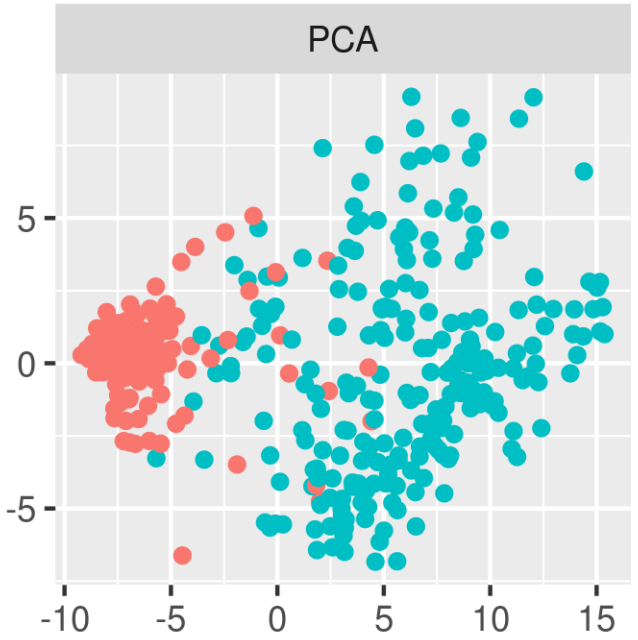
Dimension reduction

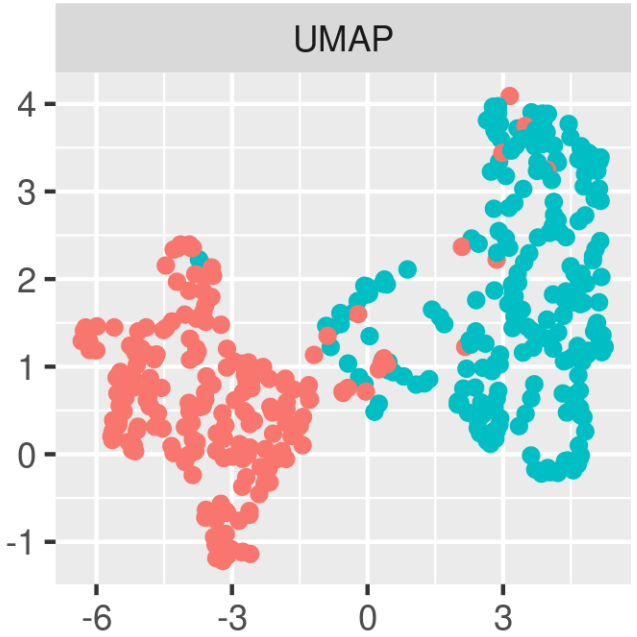
Expression matrix

	geneA	geneB	geneC	geneD	...
cancer1_a	42	58	12	47	...
cancer1_b	25	69	87	42	...
cancer2_a	35	91	25	81	...
cancer2_b	9	71	44	7	...

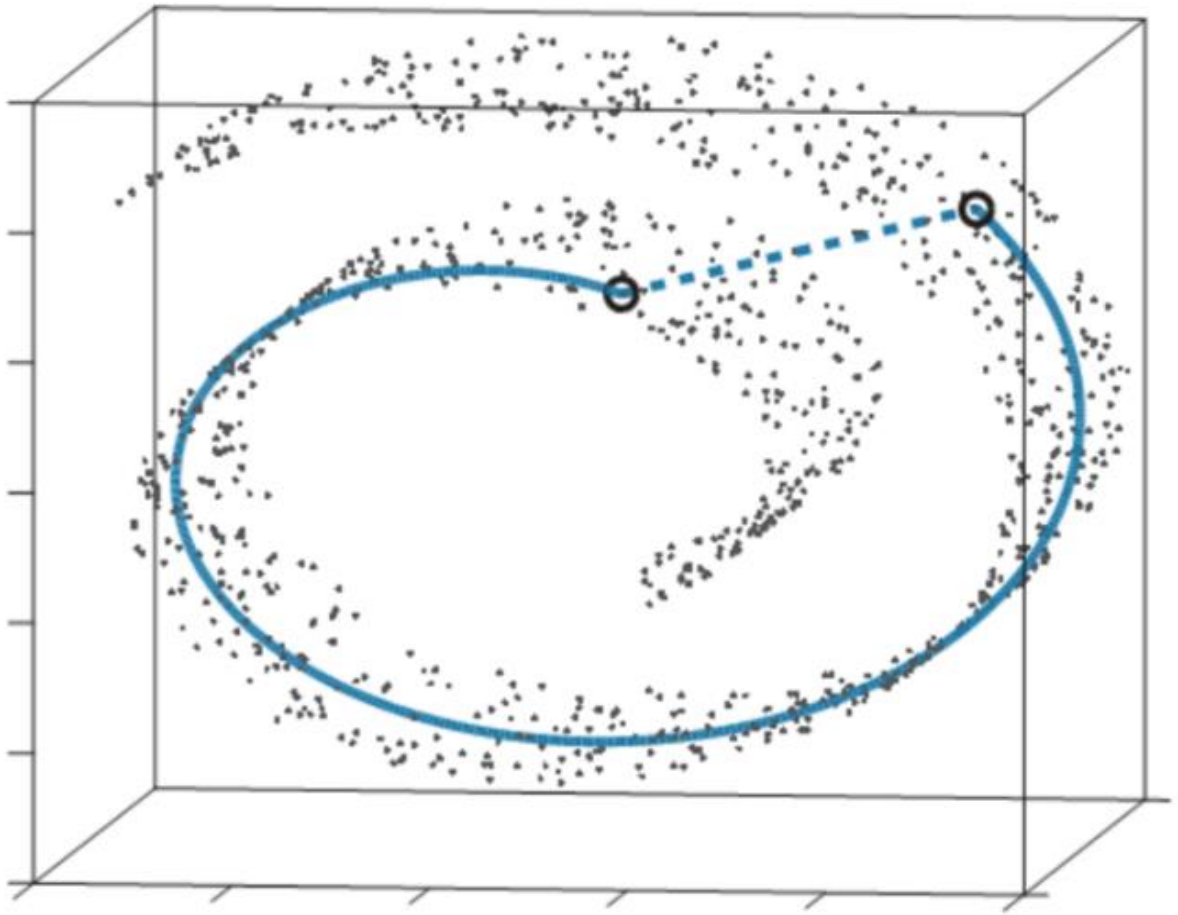
Reduce dimensions to :

- Represent data
- Extract information



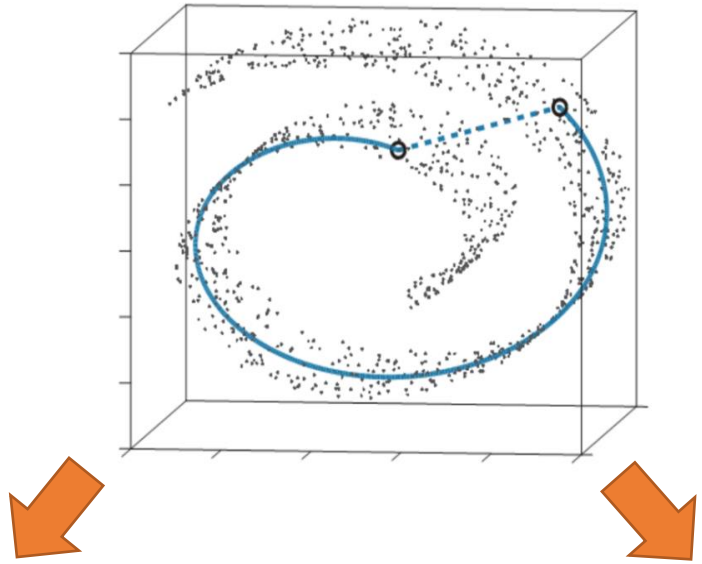


Dimension reduction

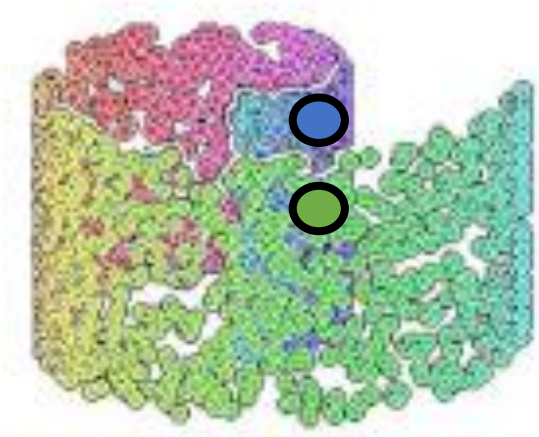


Global and local distances

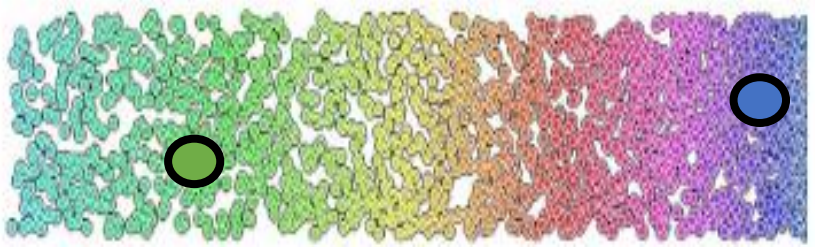
Dimension reduction



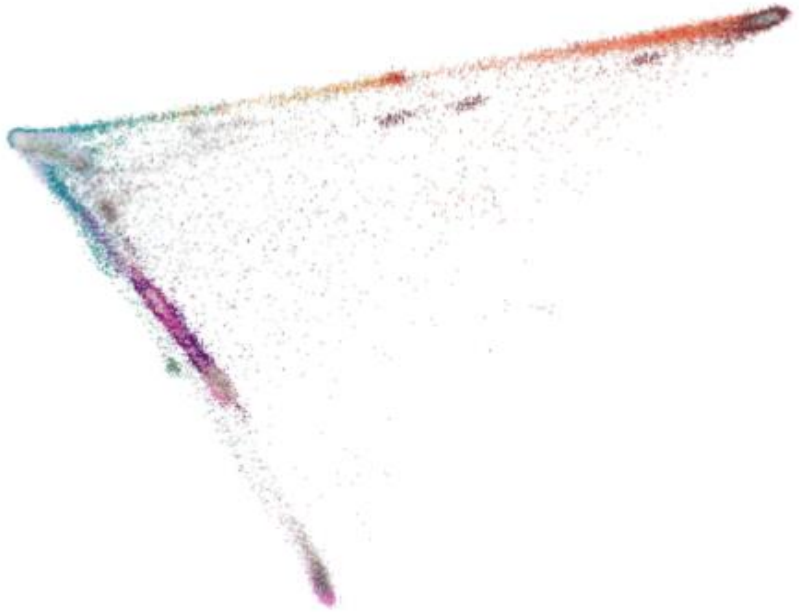
Linear reduction



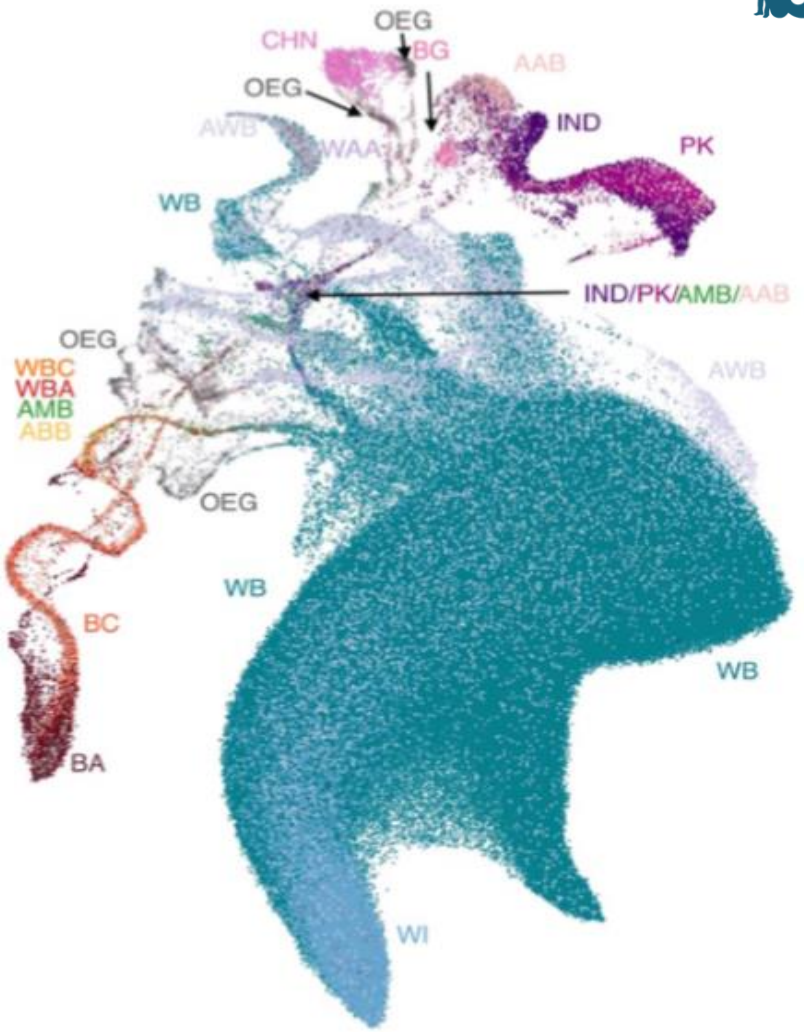
Non-Linear reduction



Dimension reduction



PCA **(a)** Principal components 1 and 2



UMAP **(b)** UMAP on first 10 principal components

Alex Diaz-Papkovich *et al., 2018*

Dimension reduction

Loss of information
Does not deform space

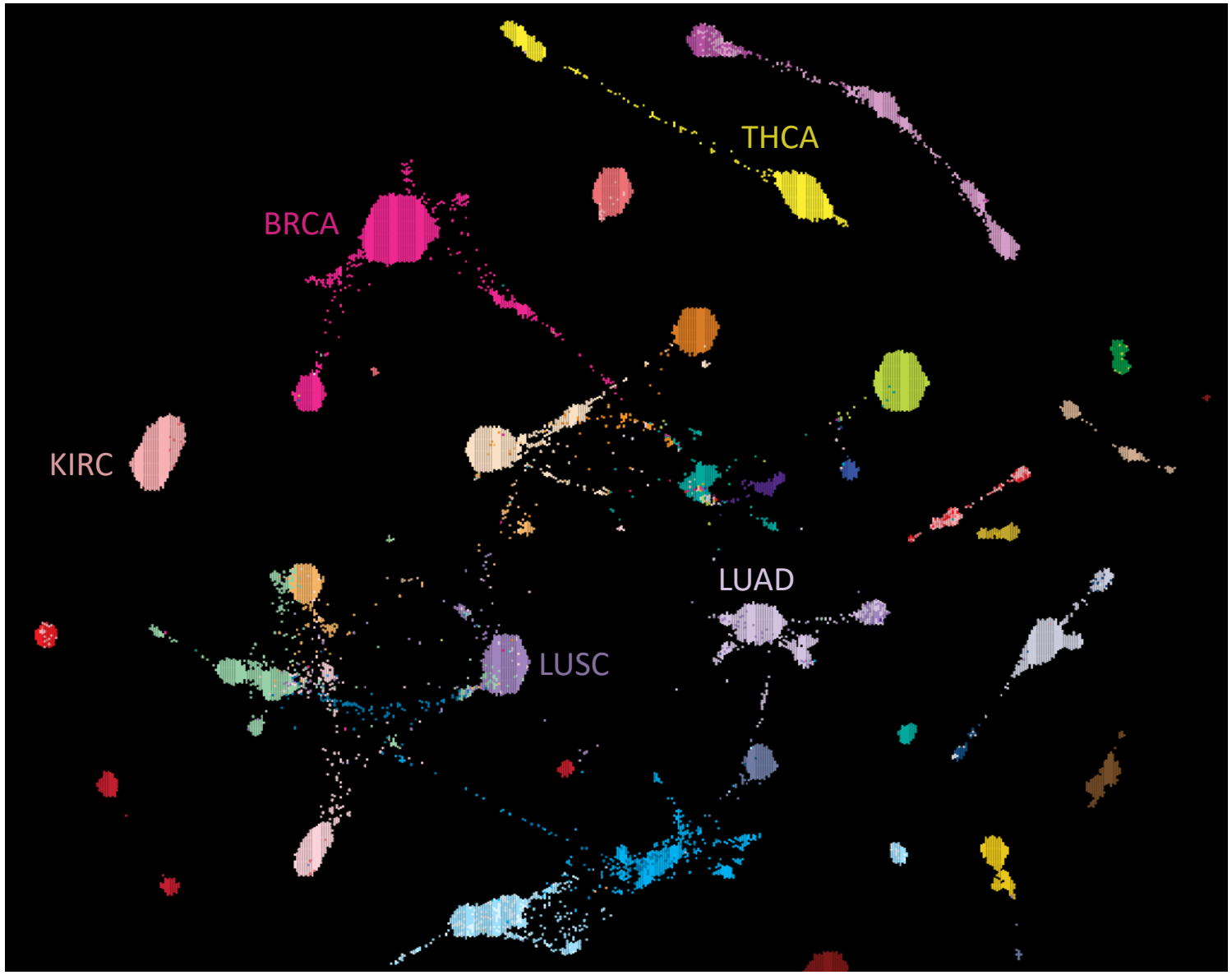
PCA (a) Principal components 1 and 2

Keeps information
Deforms space

UMAP (b) UMAP on first 10 principal components

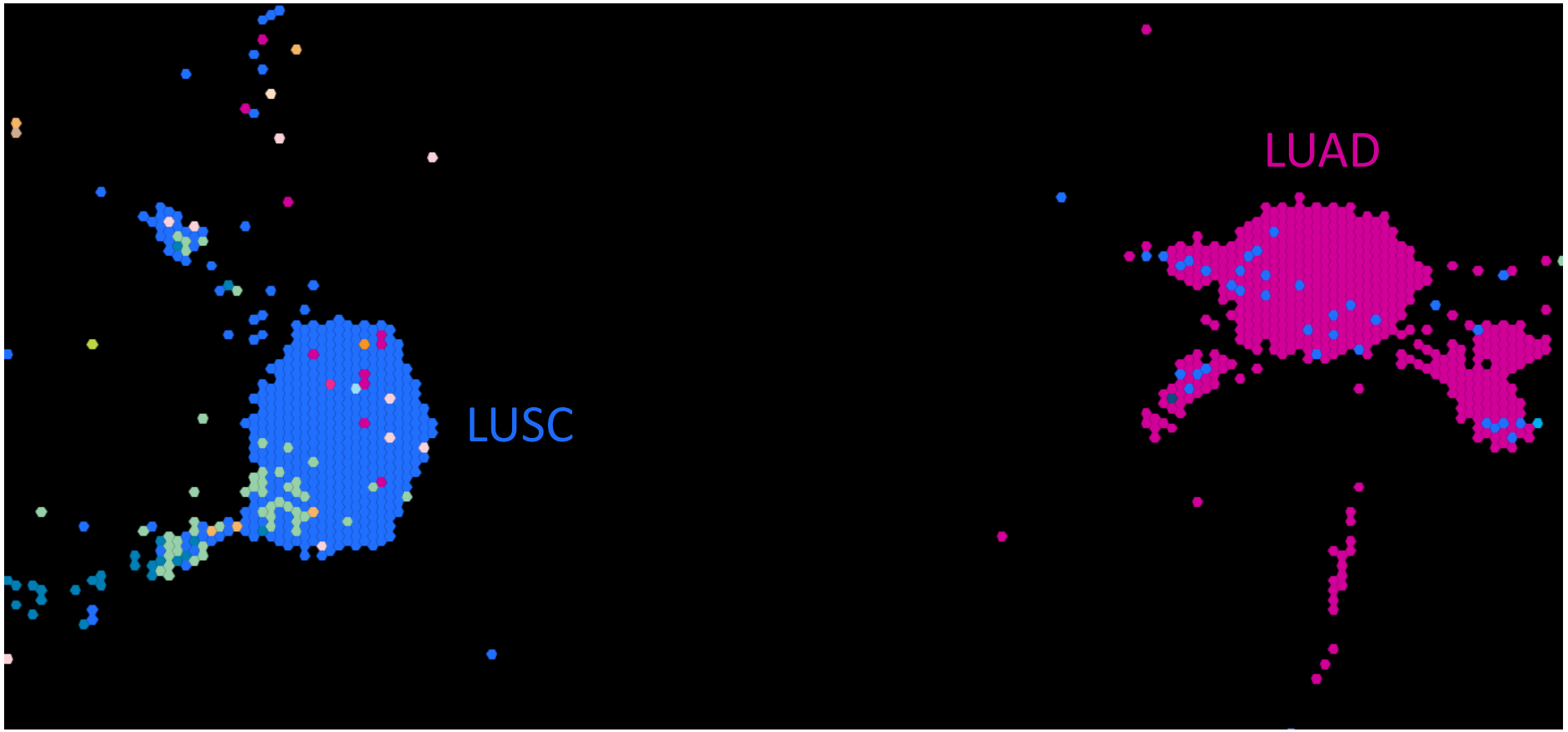
Alex Diaz-Papkovich *et al., 2018*

Dimension reduction

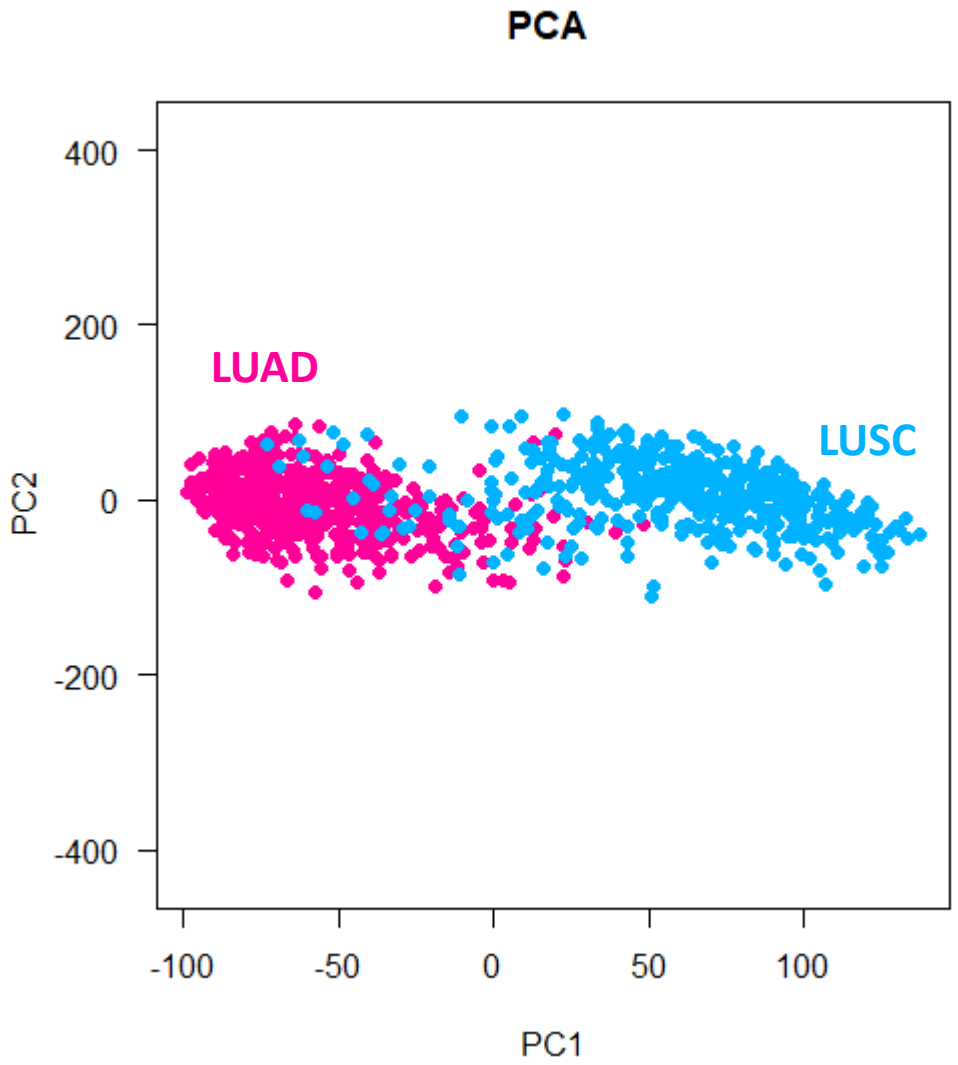


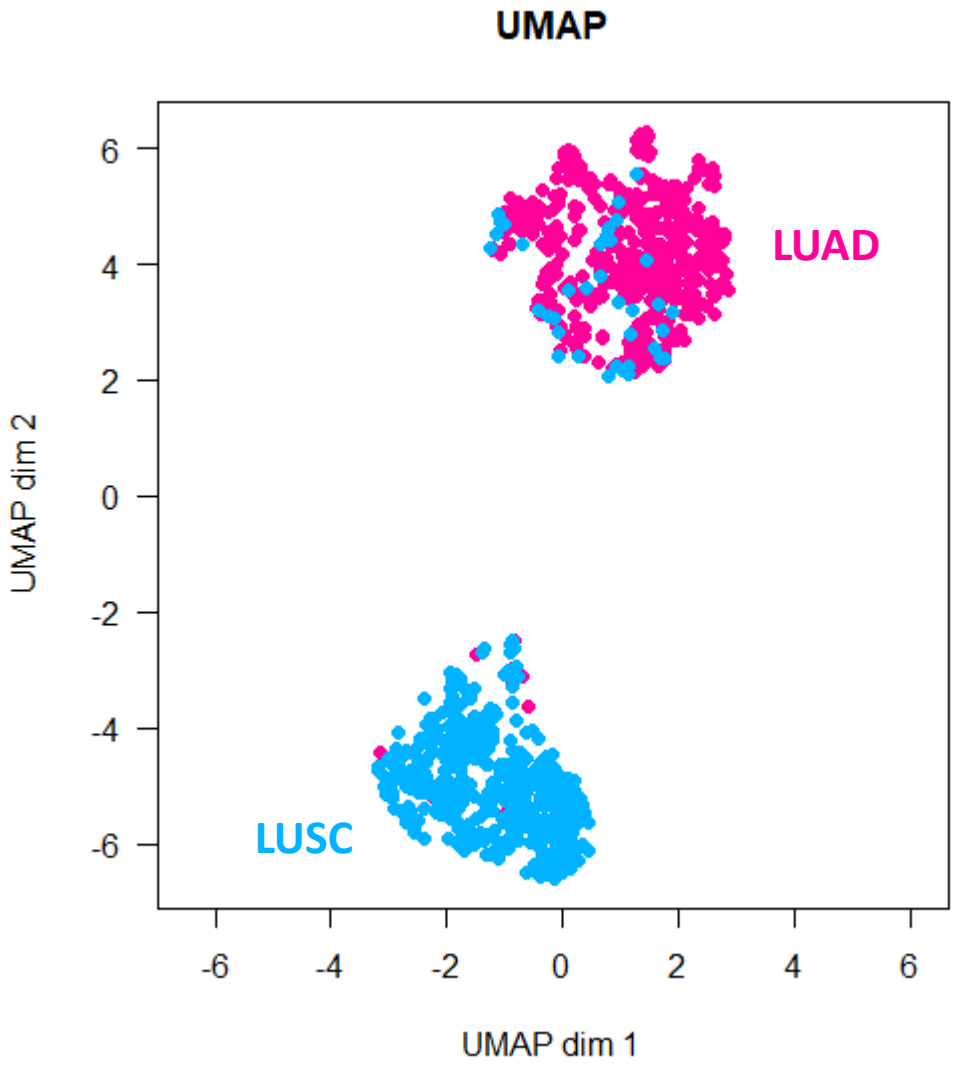
Katherine A. Hoedley *et al.*,2018

Dimension reduction



Dimension reduction

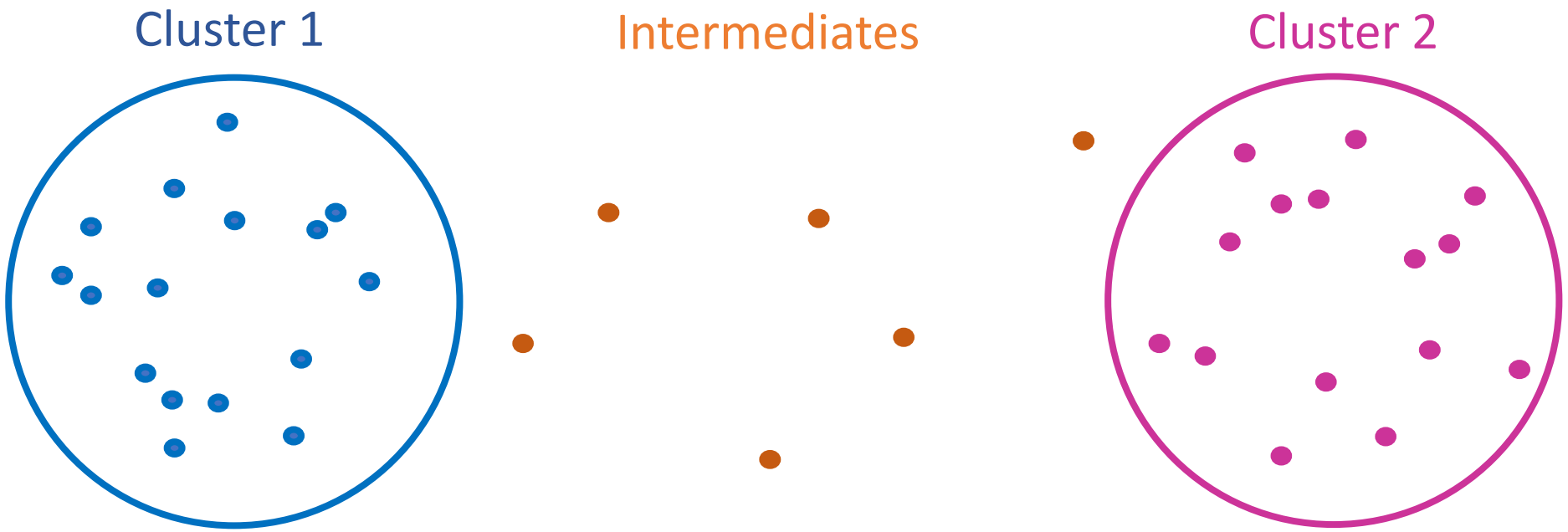




Objective :

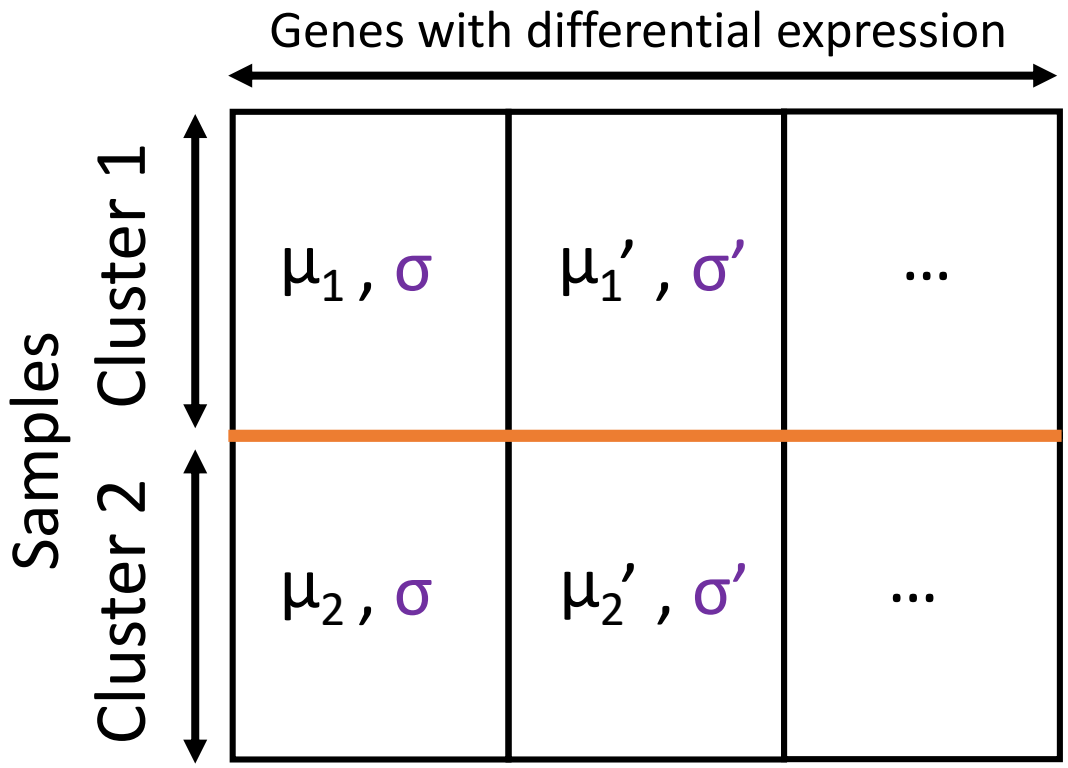
Assess dimensionality reduction (DR) methods for the detection of intermediate cancer phenotypes

Simulation approach

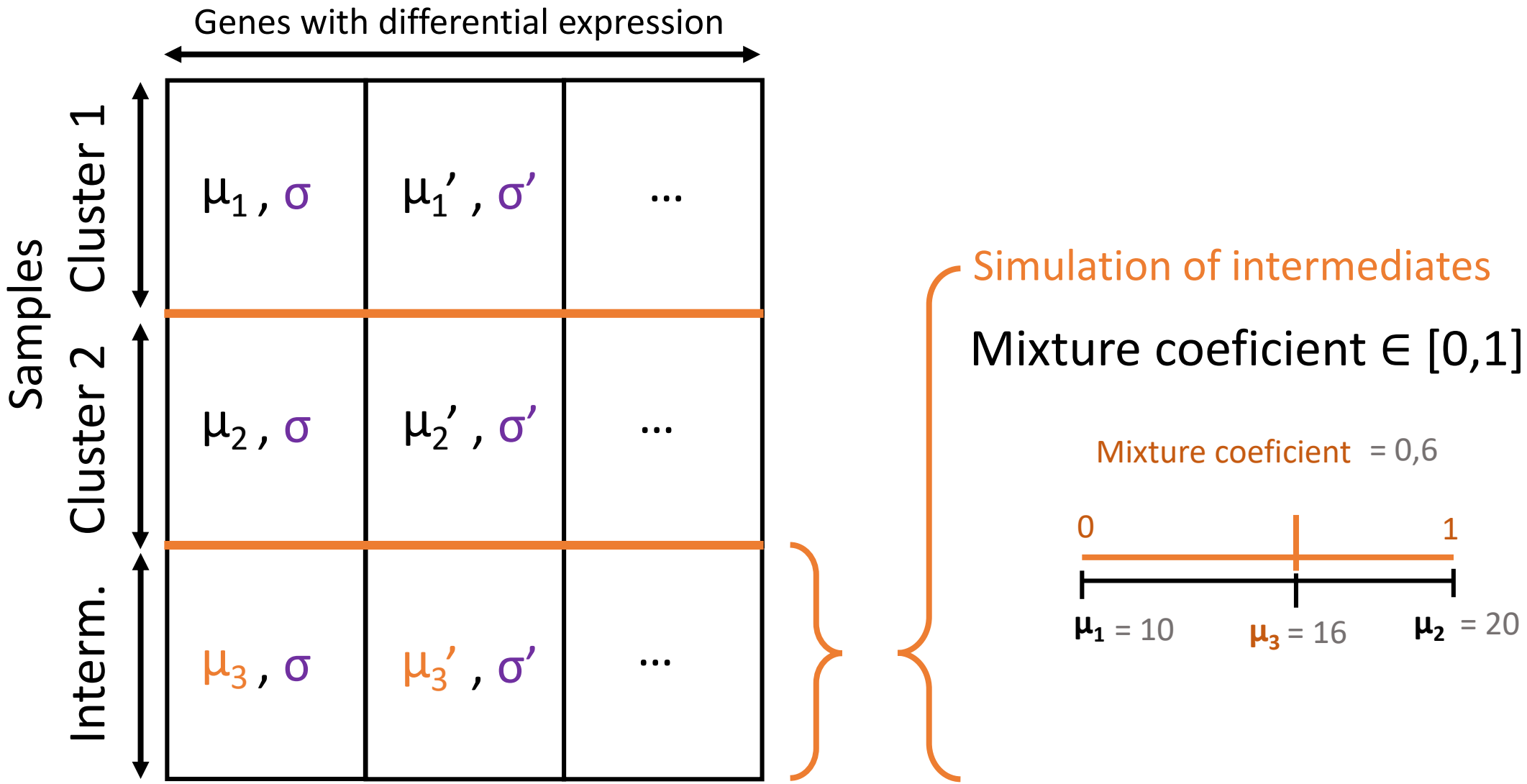


- Know the reality of the data
- Modify data parameters
- No limit in number of replicates

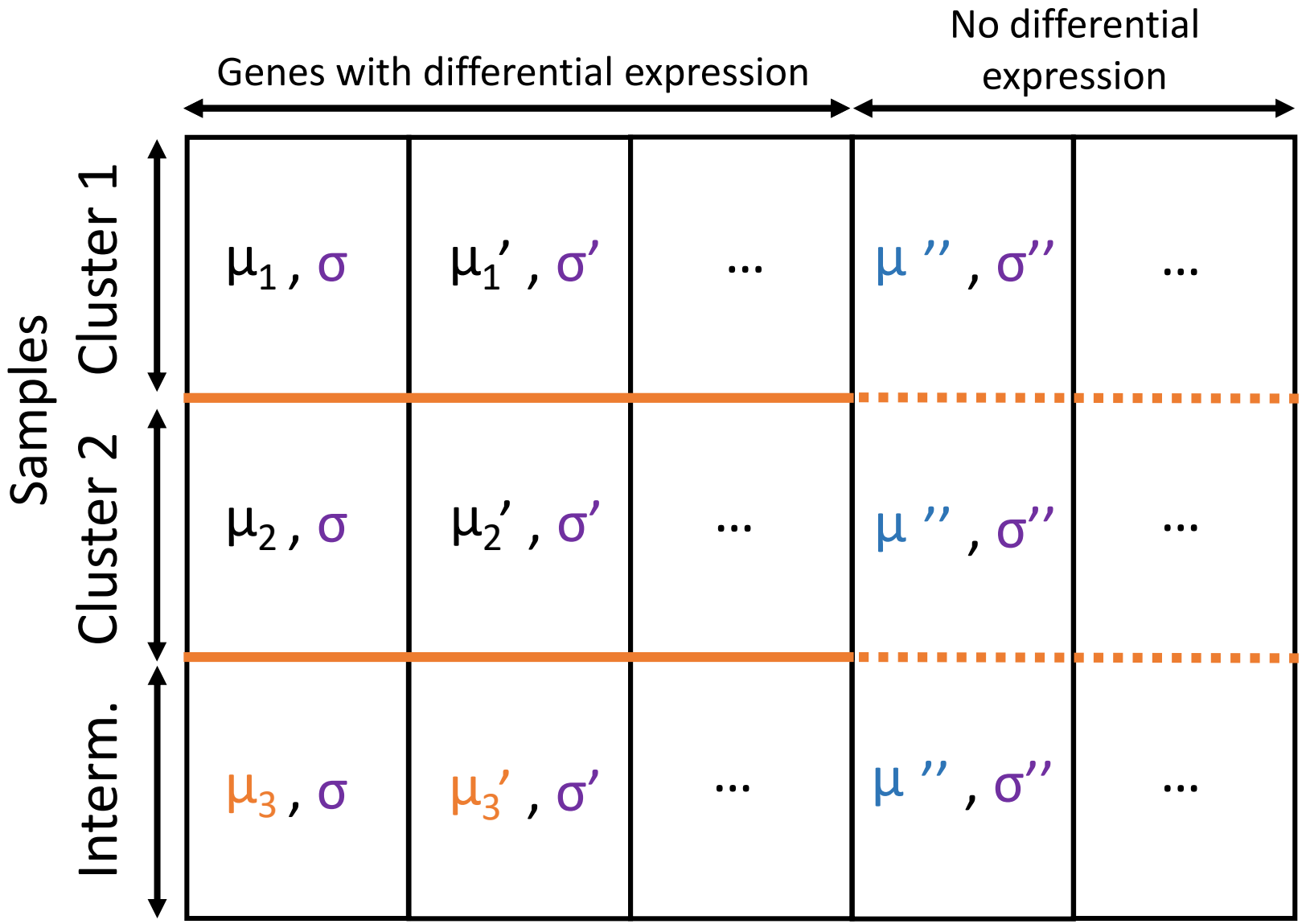
Model : Building an expression matrix



Model : Building an expression matrix

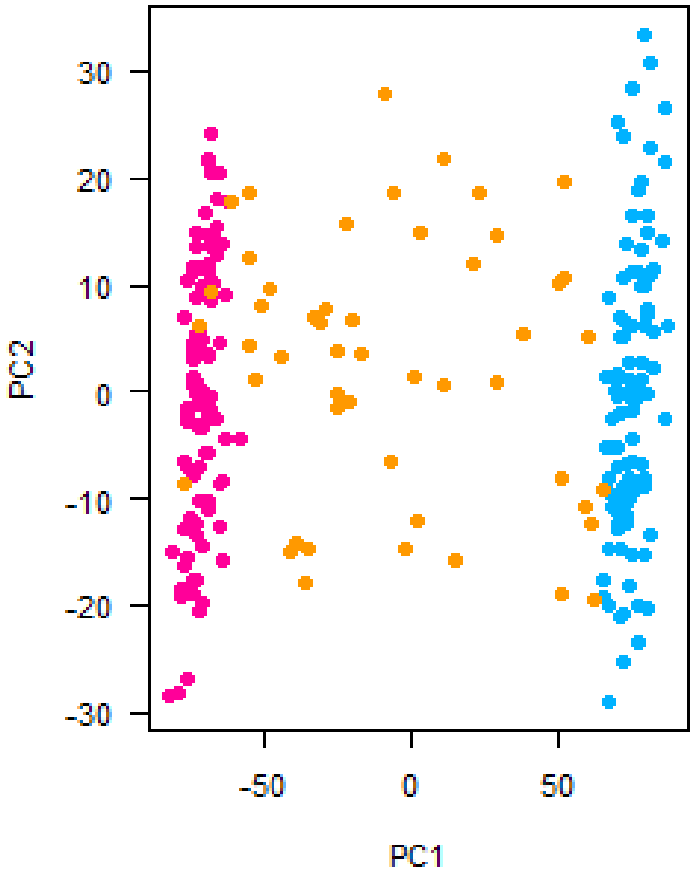


Model : Building an expression matrix

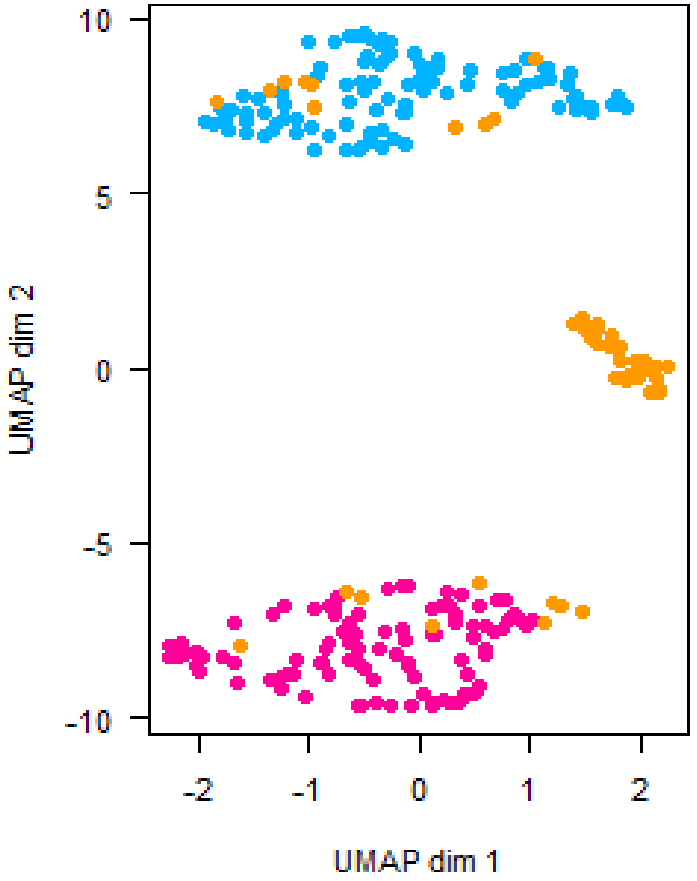


Simulation example

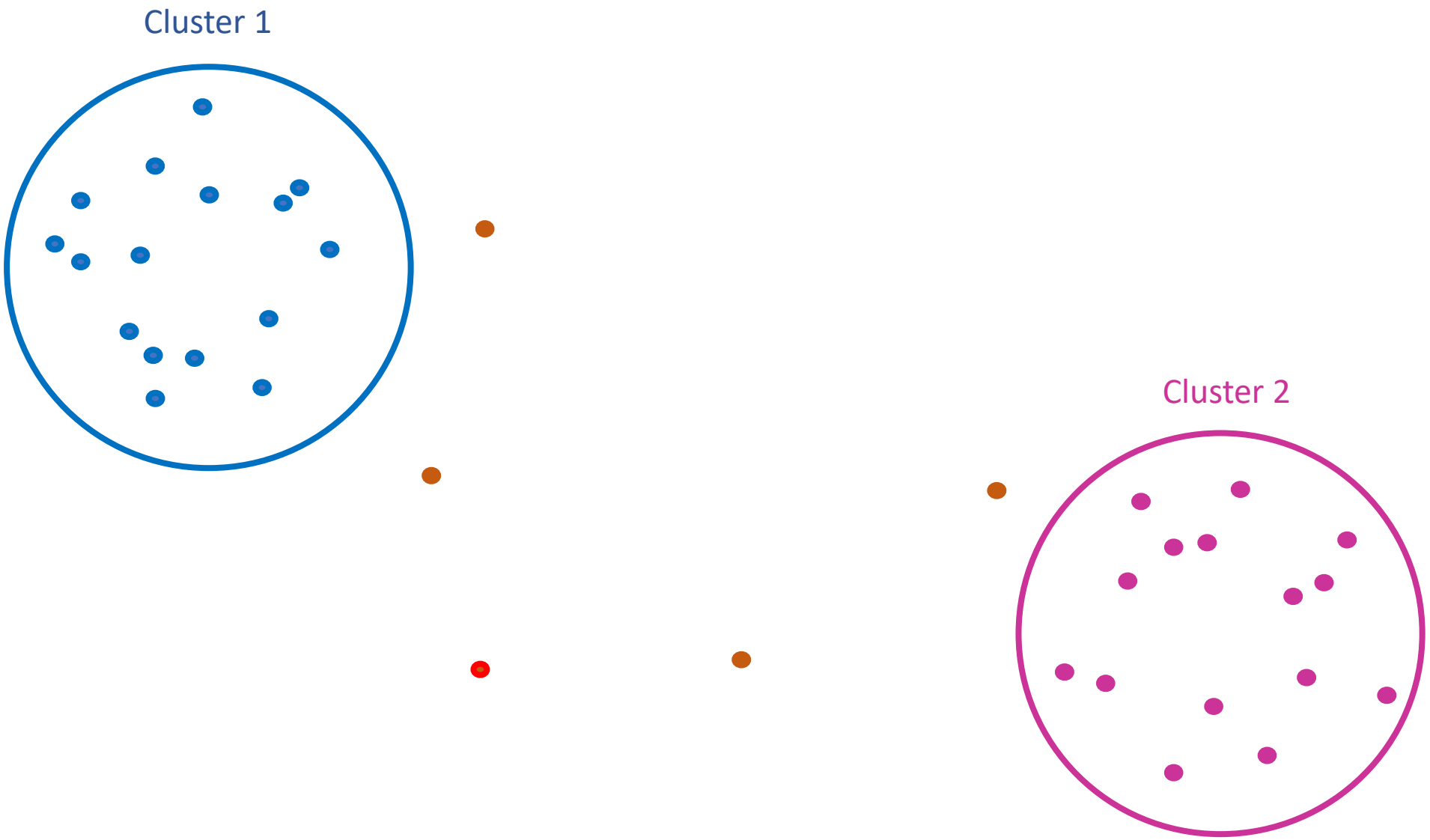
PCA



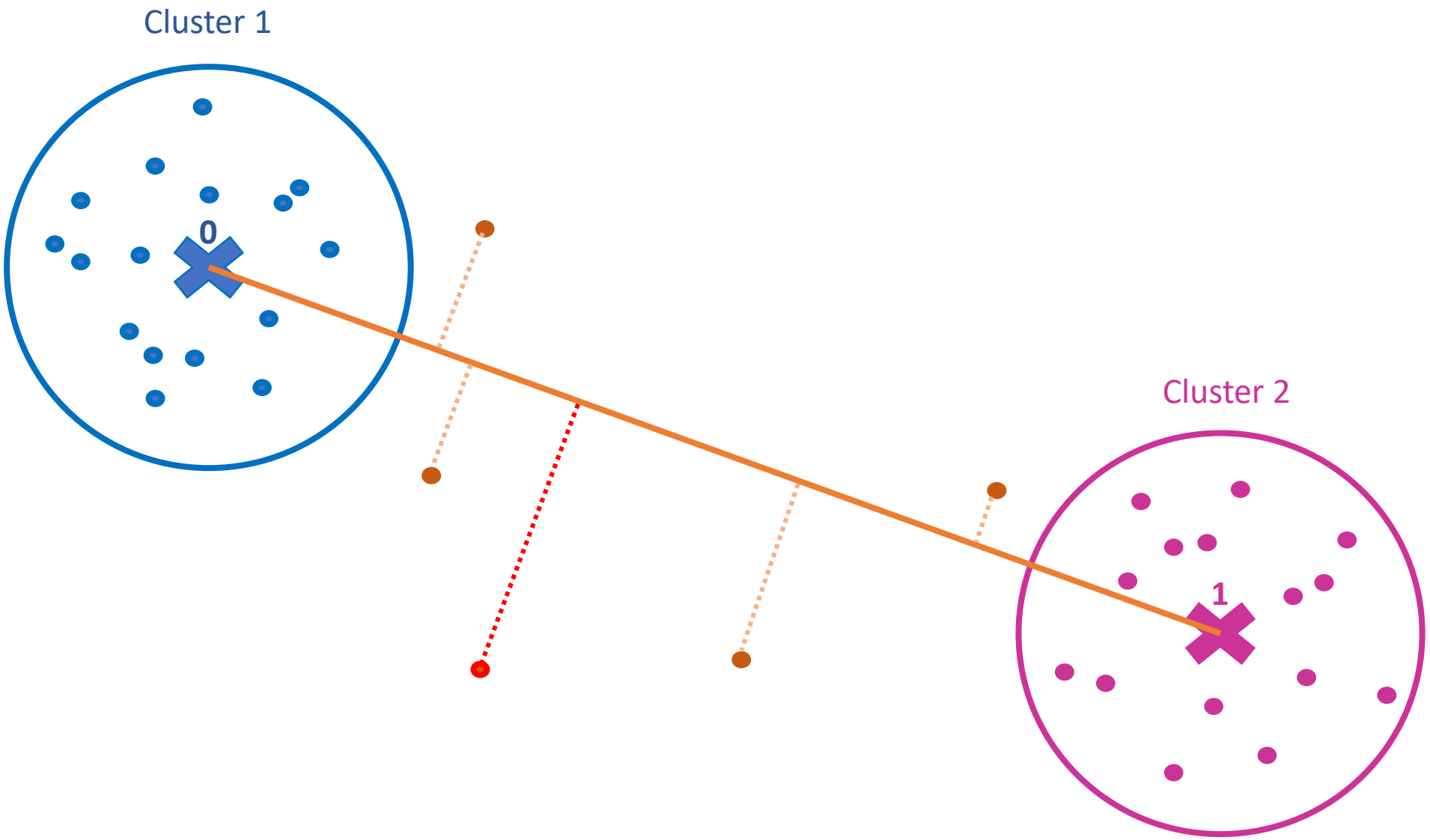
UMAP



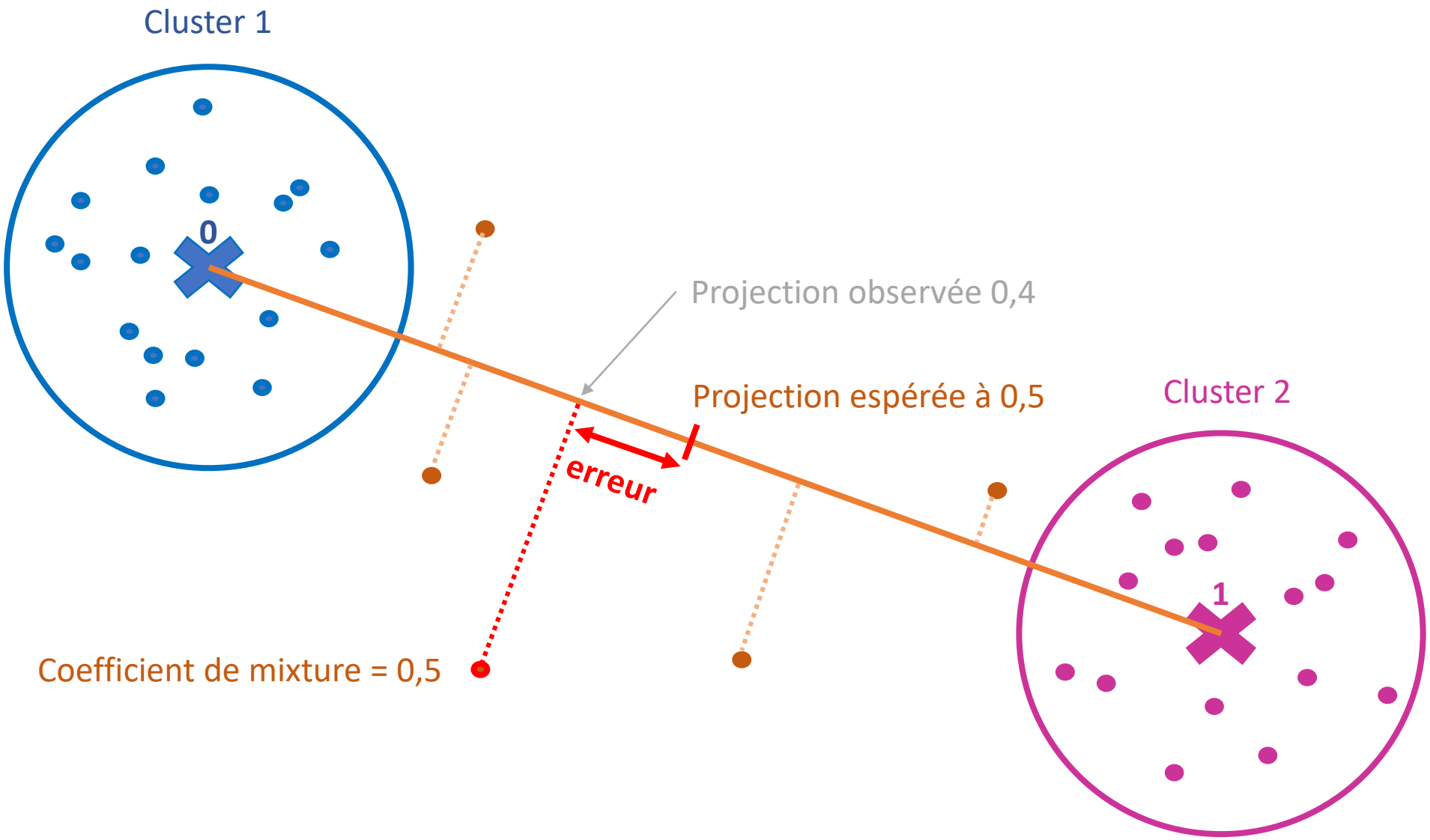
Evaluation : Projection of intermediates



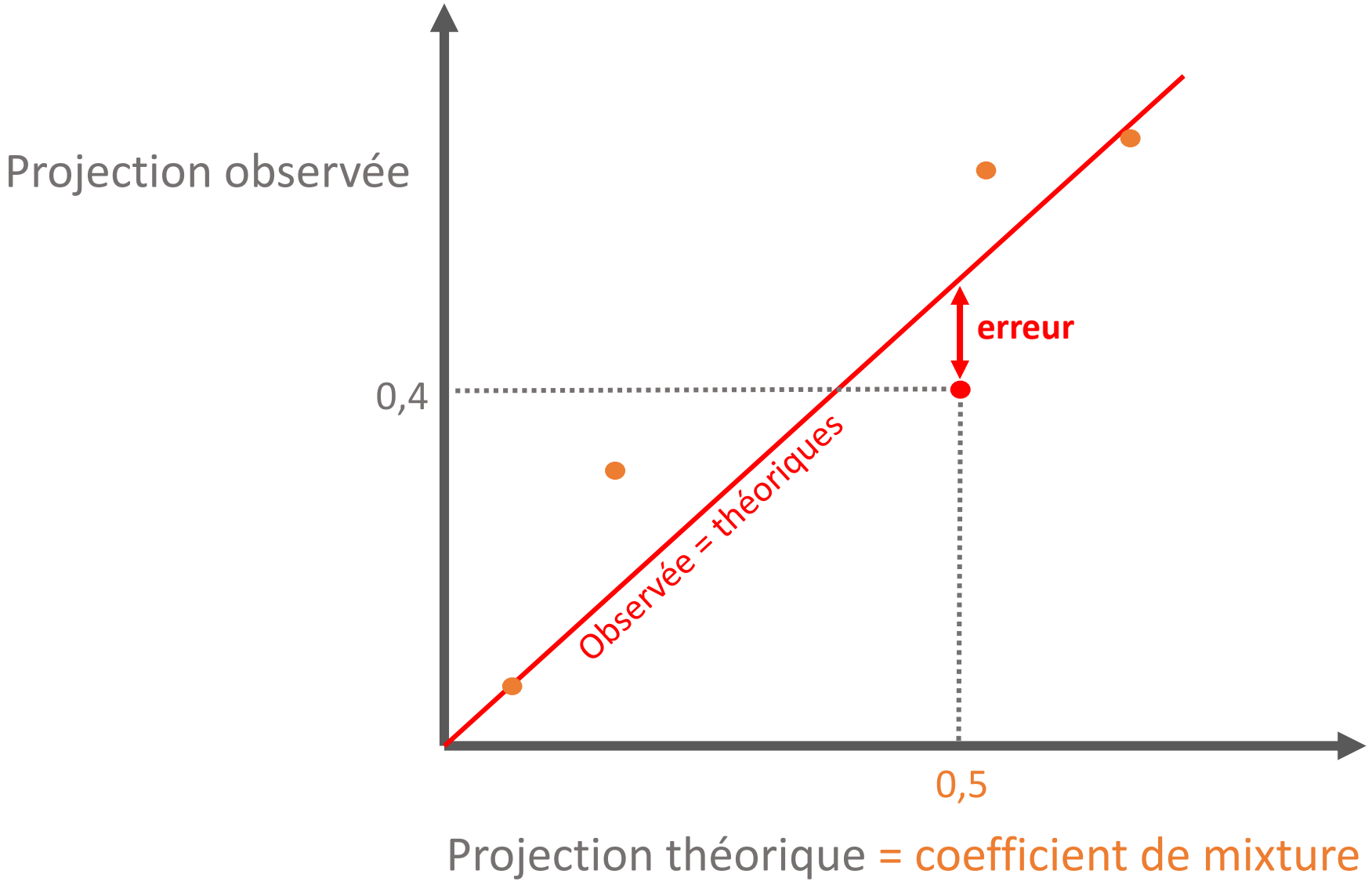
Evaluation : Projection of intermediates



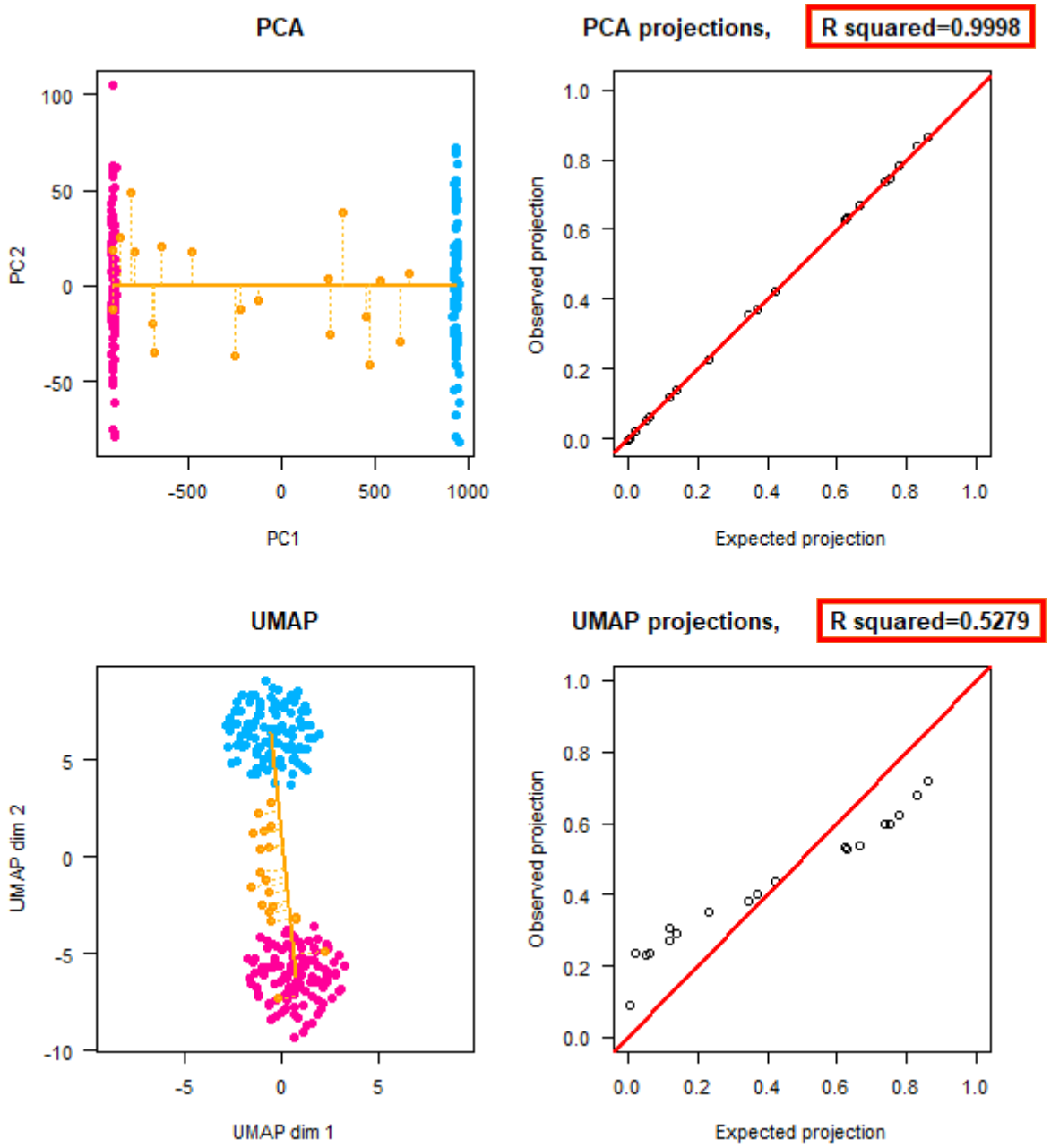
Evaluation : Projection of intermediates



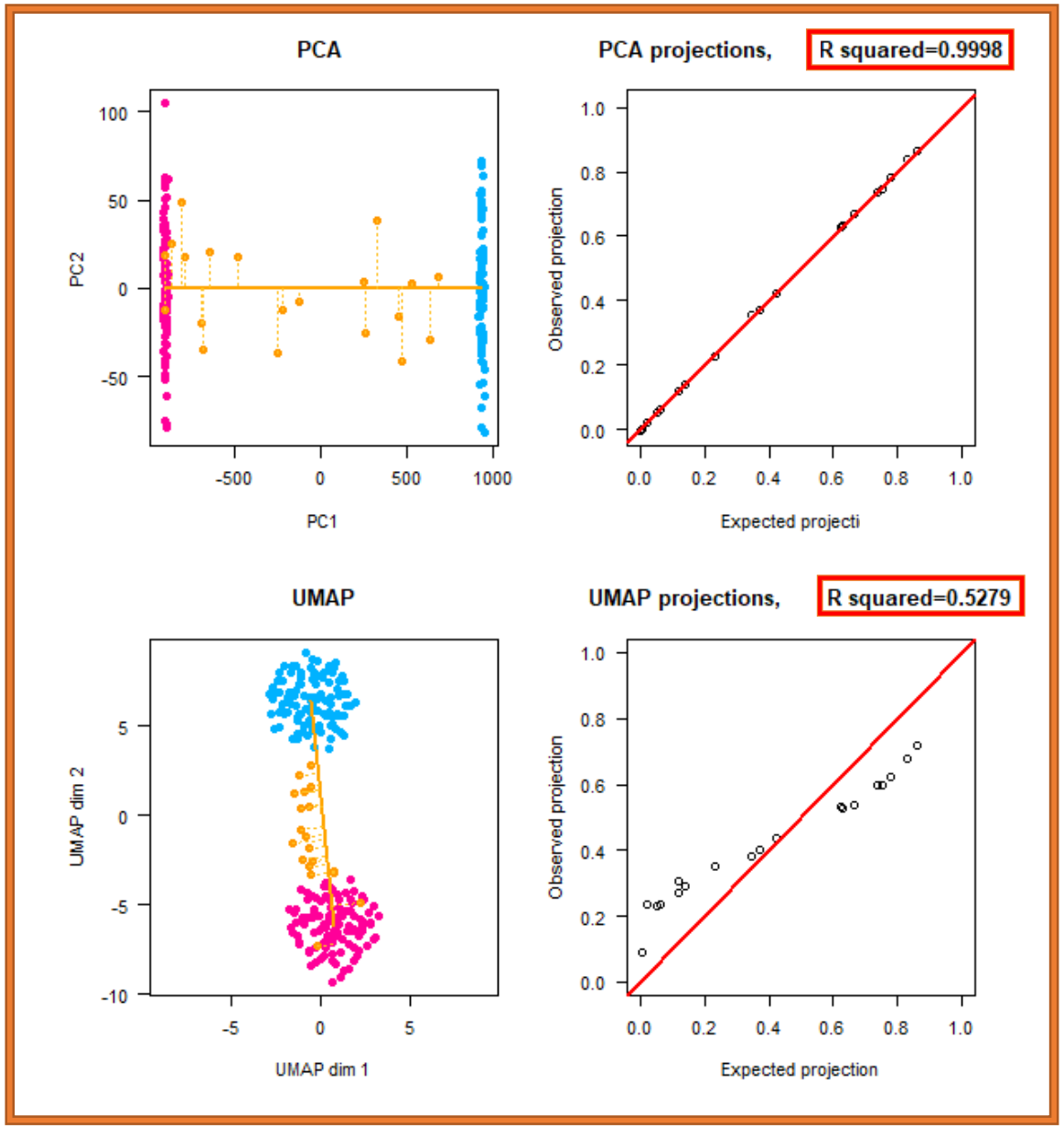
Evaluation : Projection of intermediates



Evaluation of dimension reduction (DR) methods

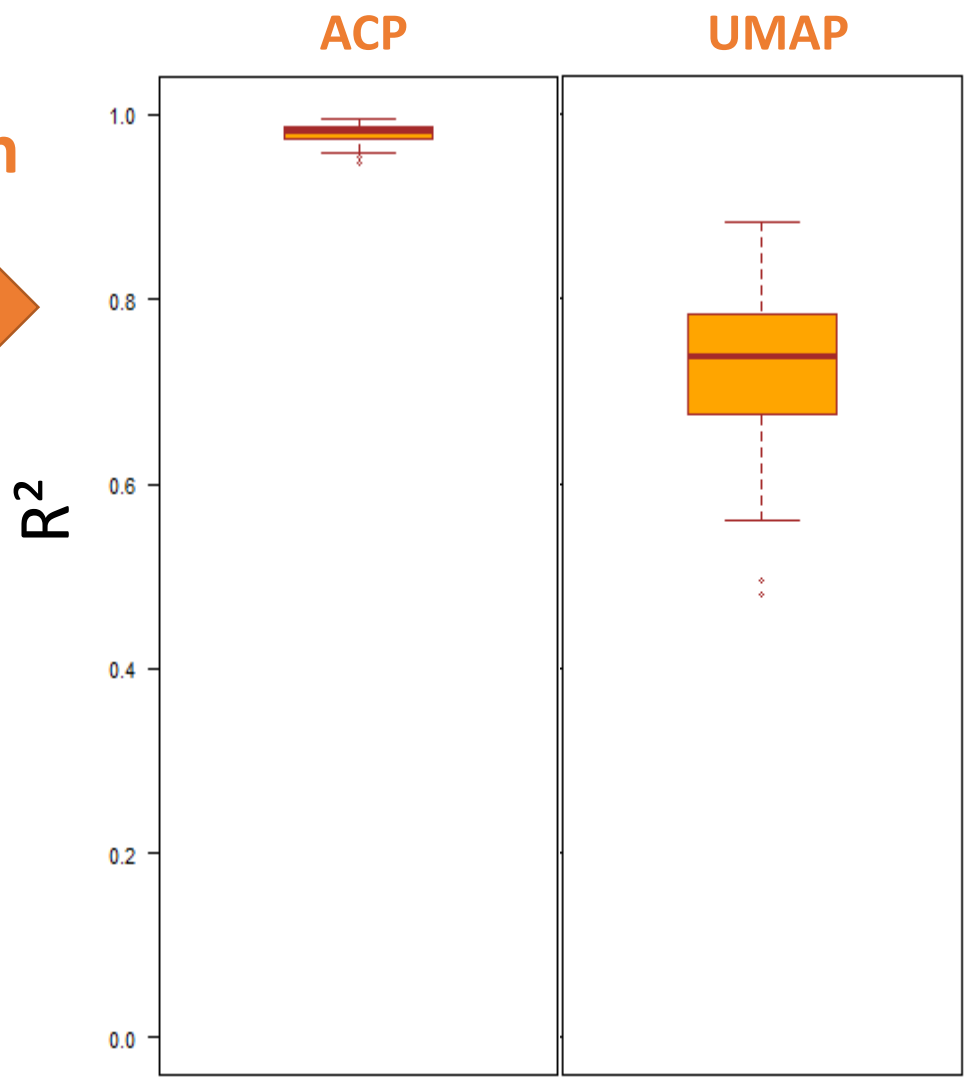


Evaluation of dimension reduction (DR) methods



Simulation

X 100



Exploration of parameters

Data dependent parameters :

- Number of samples (Data size)
- Proportion of intermediates
- Distance between clusters (δ)

DR parameters :

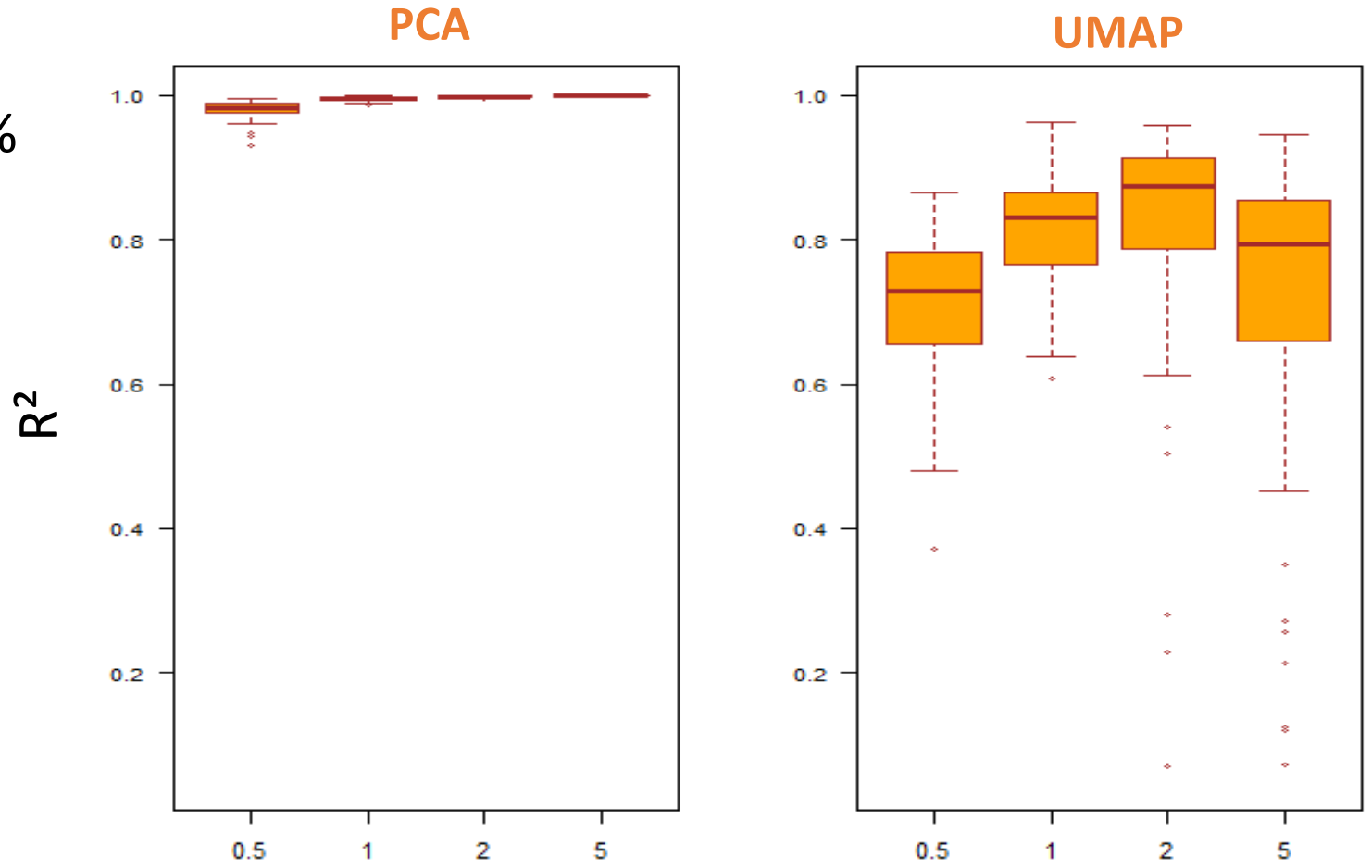
- UMAP Min_dist
- UMAP N_neighbours

Exploration of parameters

Proportion of intermediates : 10%

UMAP min_dist : 0.75

Data size : 200

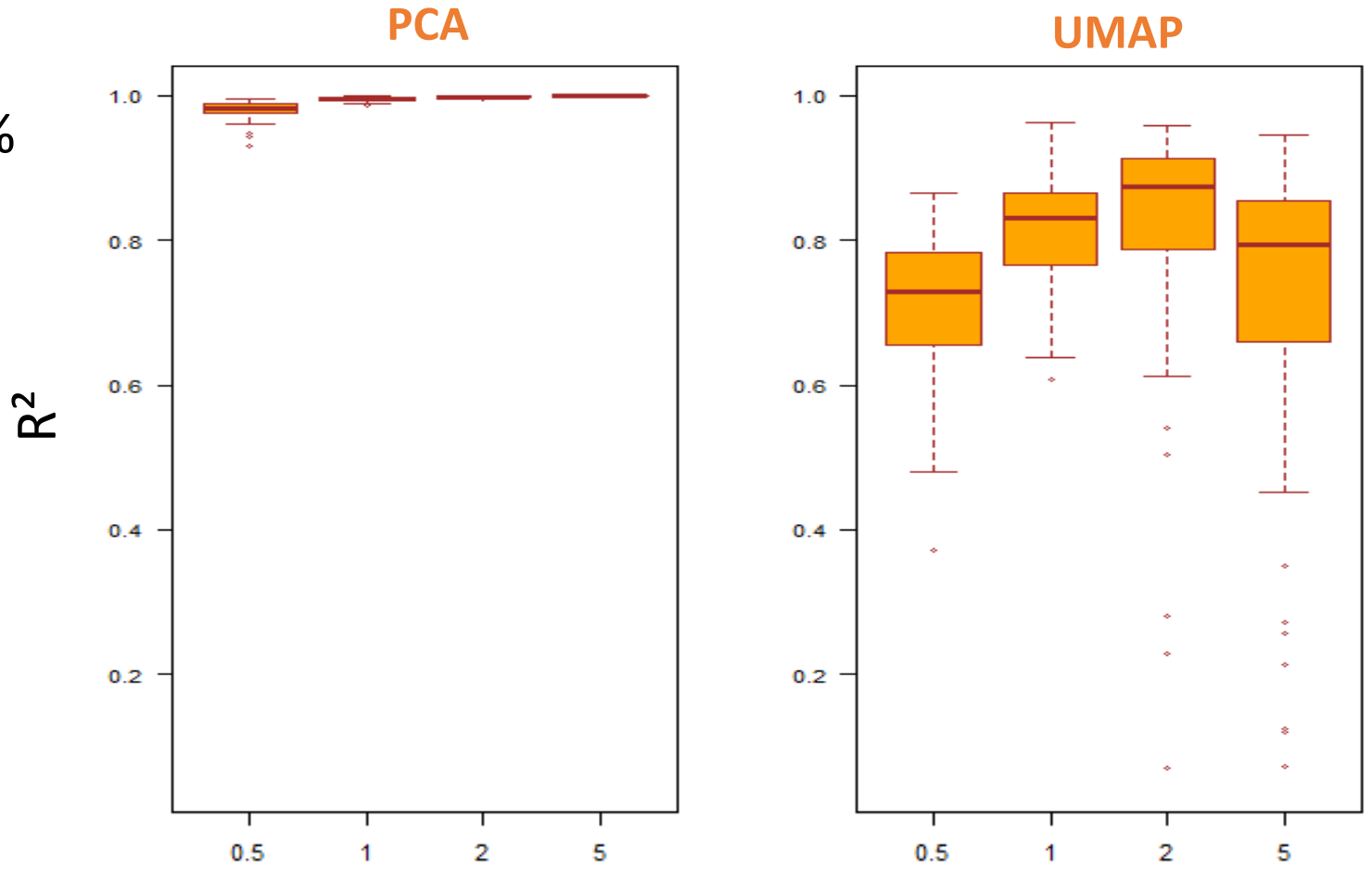


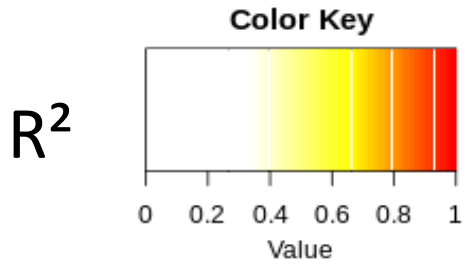
Exploration of parameters

Proportion of intermediates : 10%

UMAP min_dist : 0.75

Data size : 200



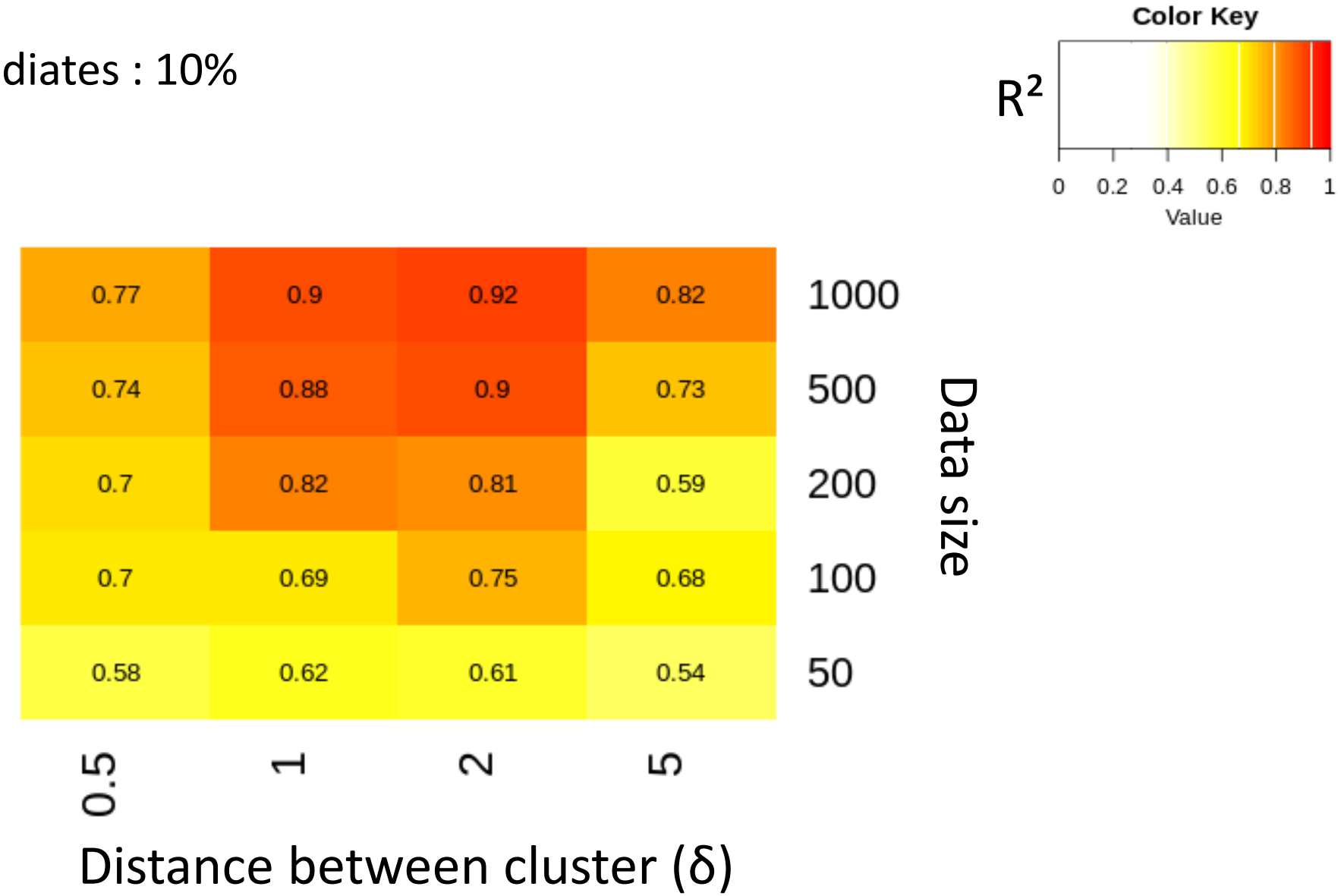


Distance between clusters (δ)

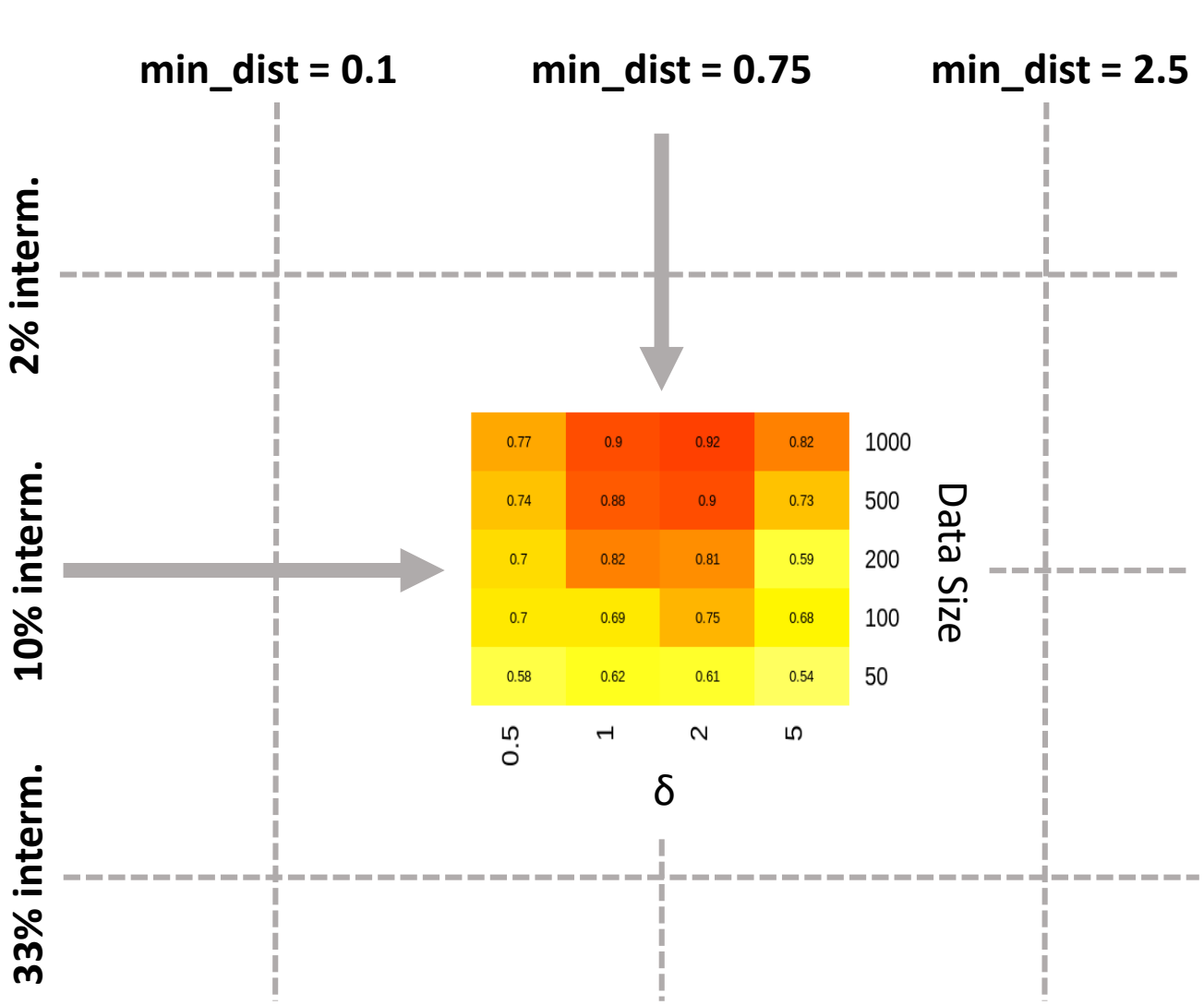
Exploration of parameters

Proportion of intermediates : 10%

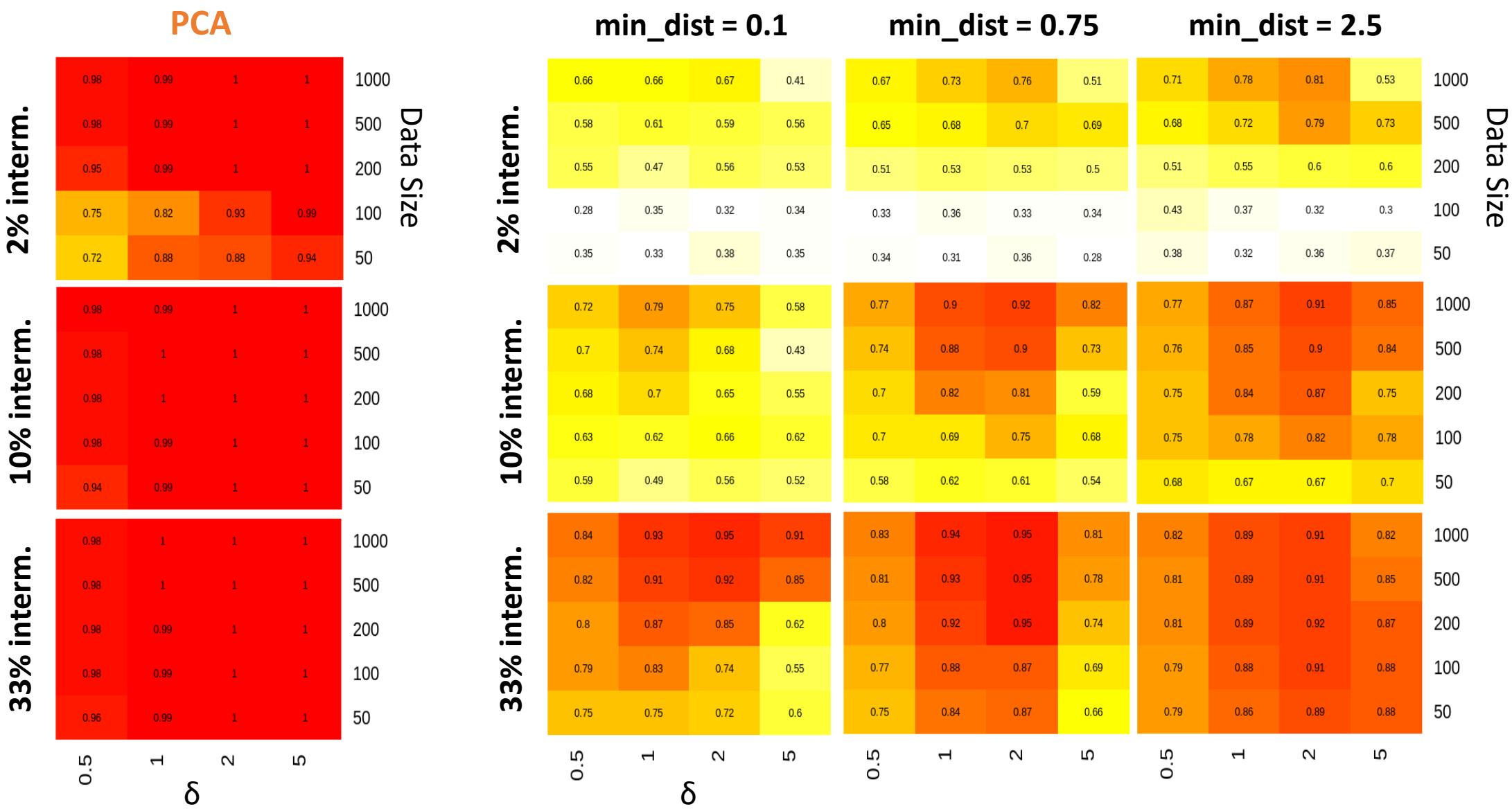
UMAP min_dist : 0,75



Exploration of parameters

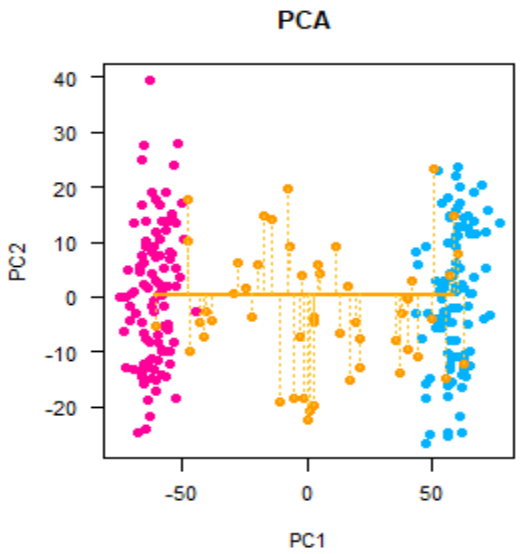


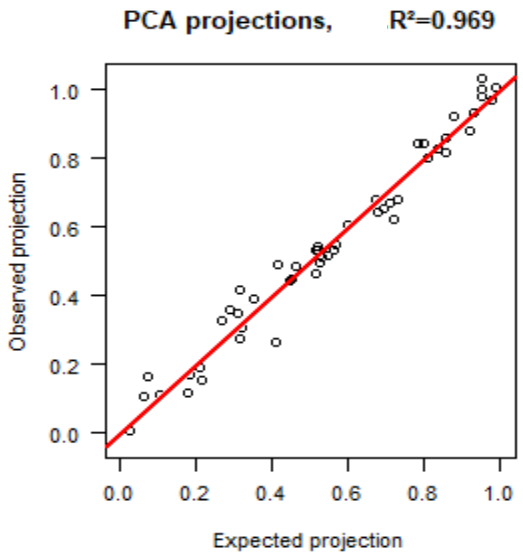
Results:

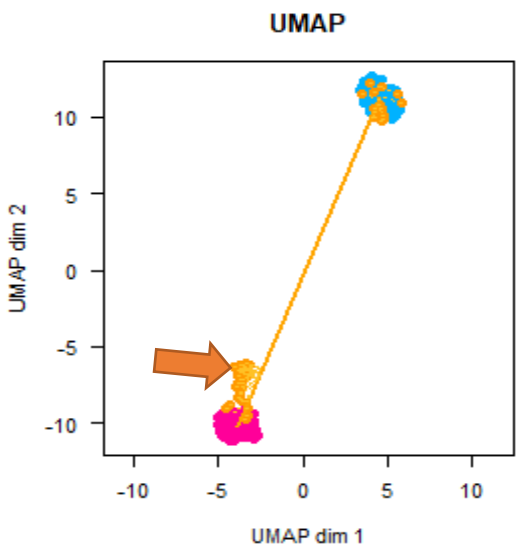


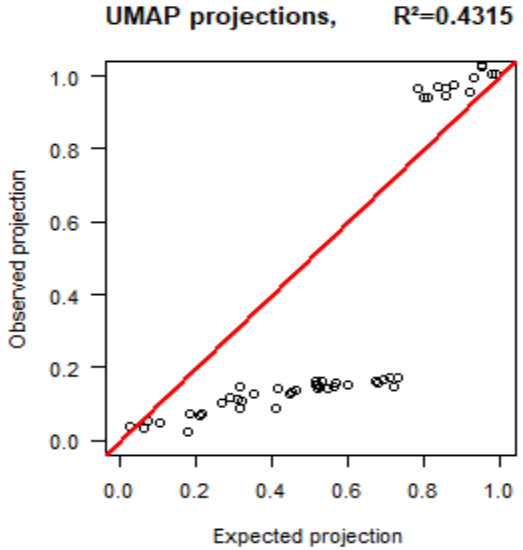
Exploration of parameters and evaluation of DR methods

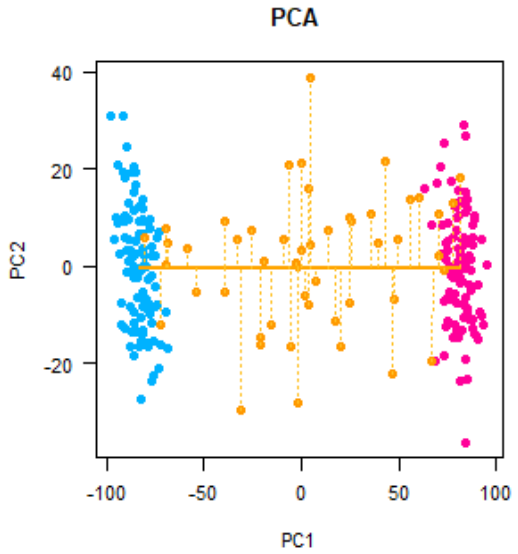
UMAP behavior

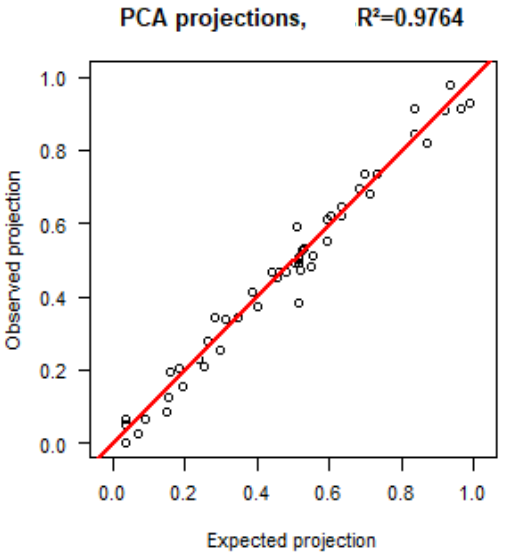


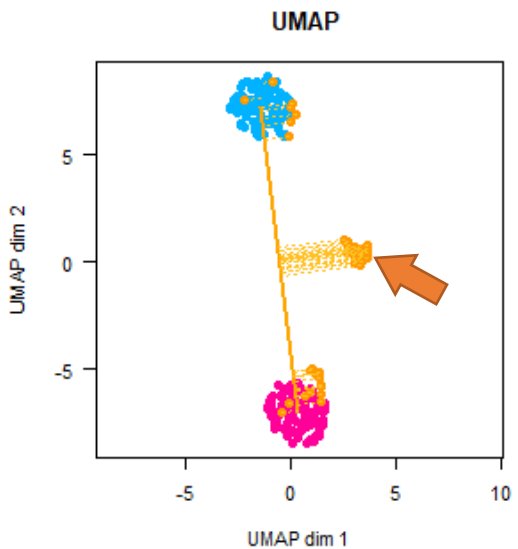


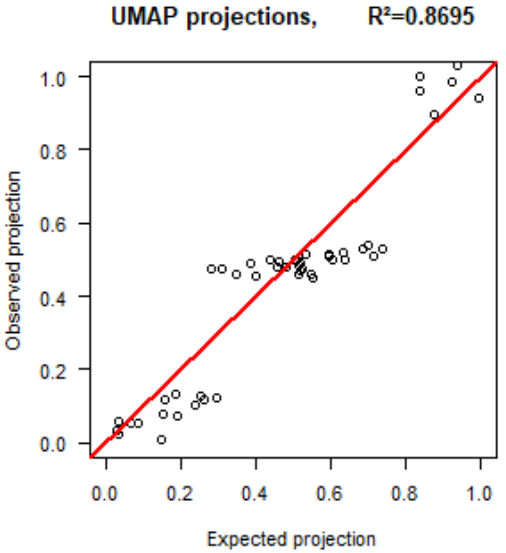






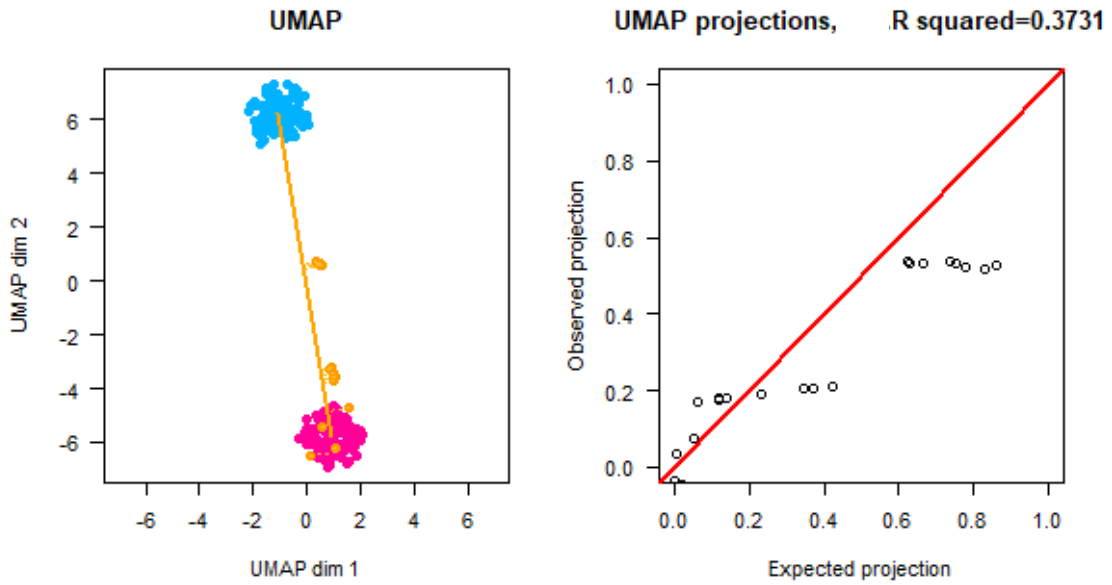




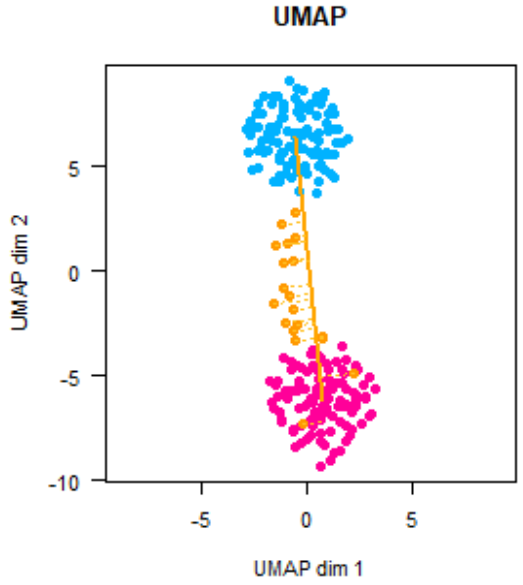


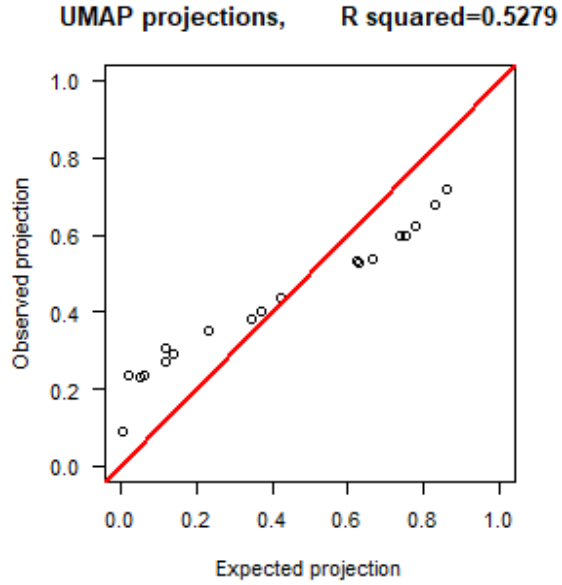
UMAP min_dist

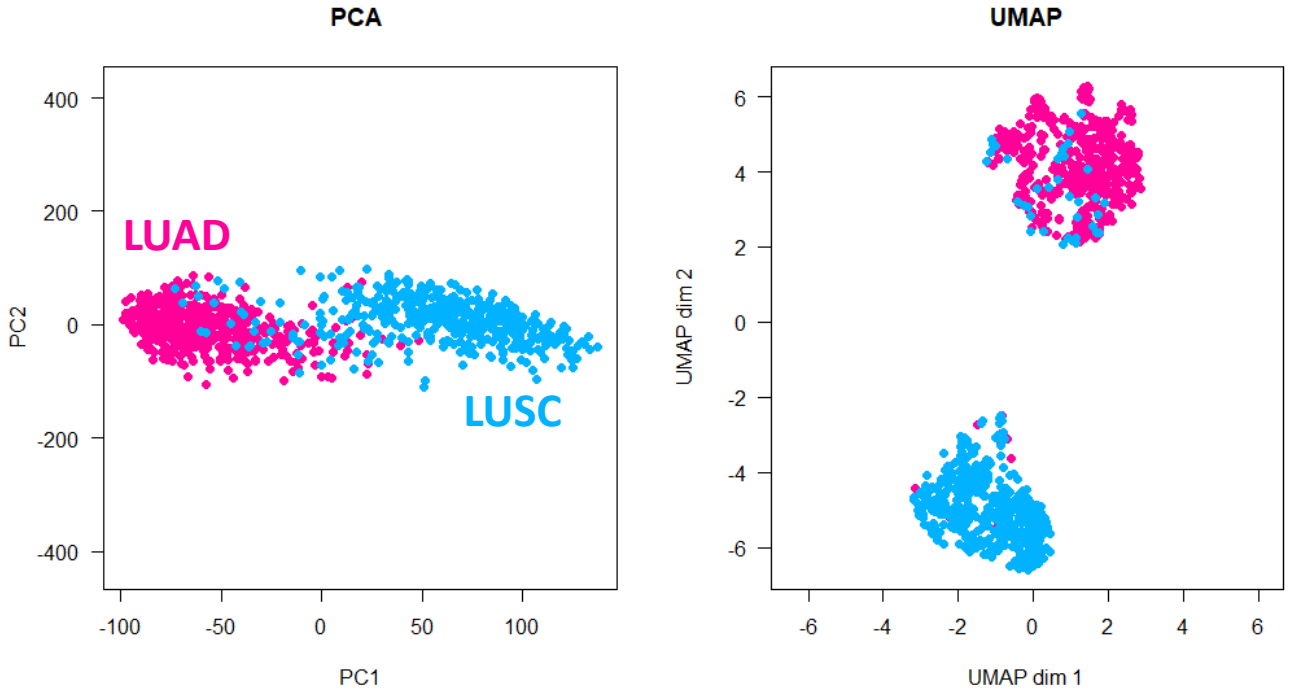
UMAP min_dist = 0



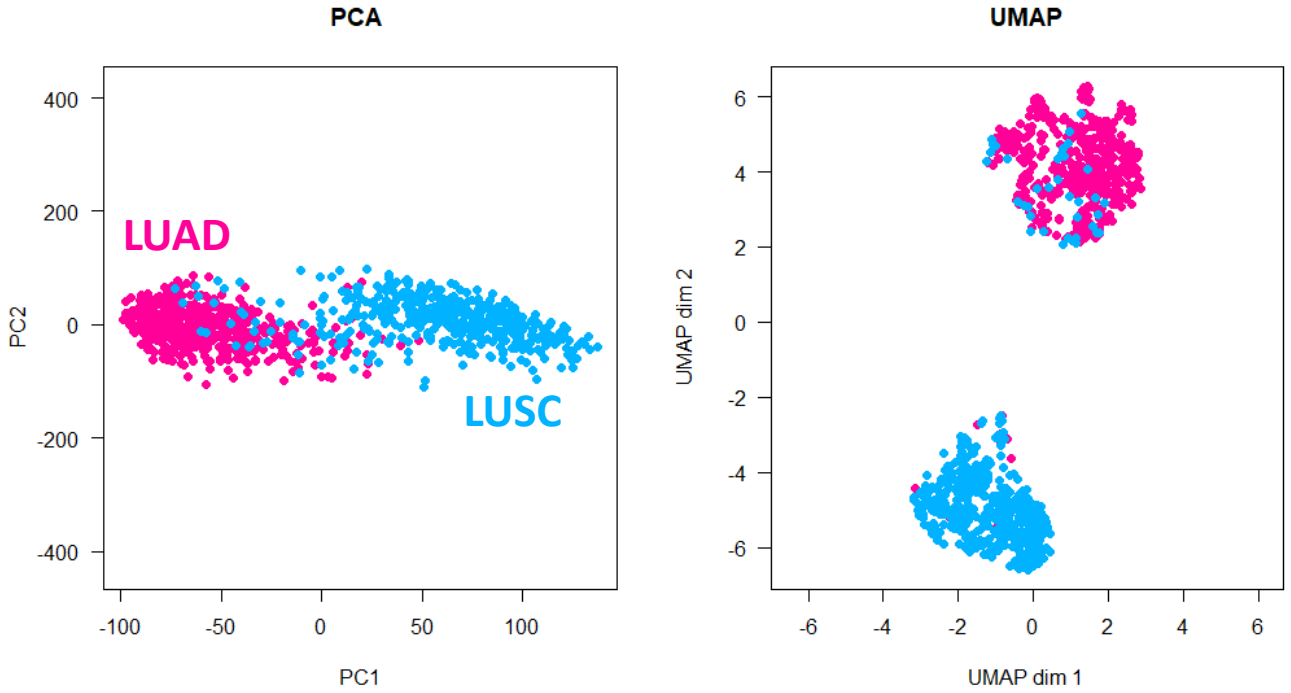
UMAP min_dist = 1



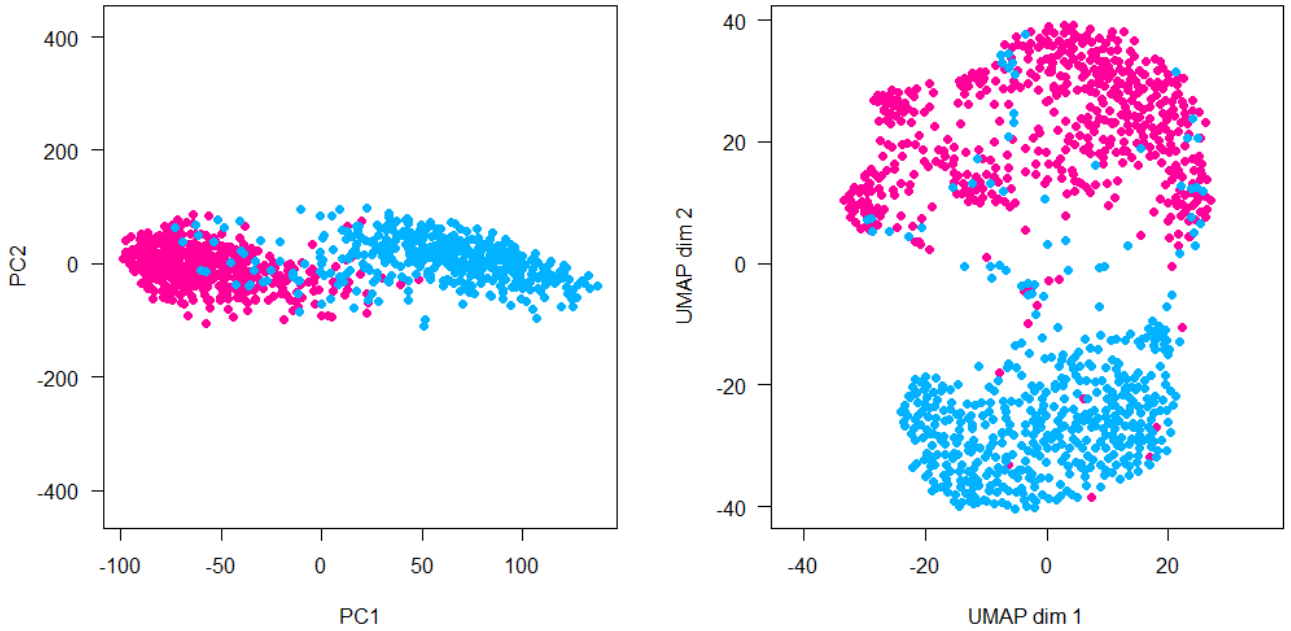




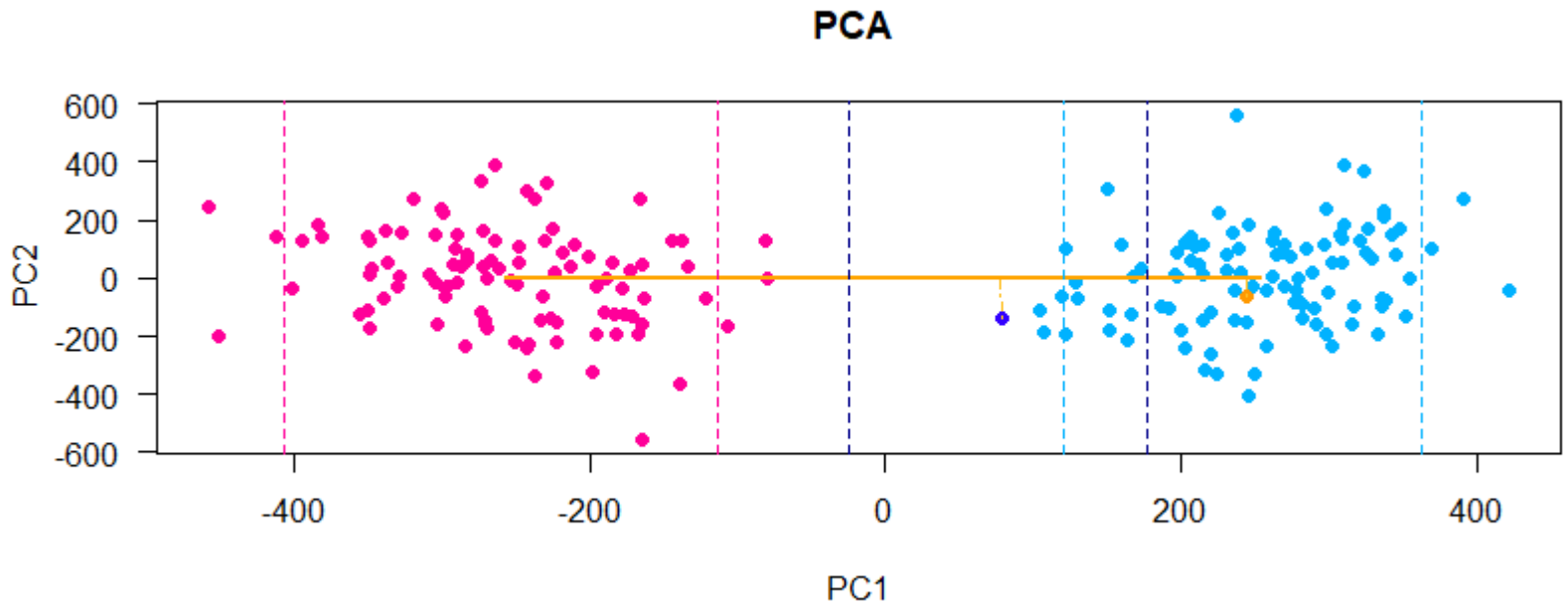
UMAP min_dist = 0

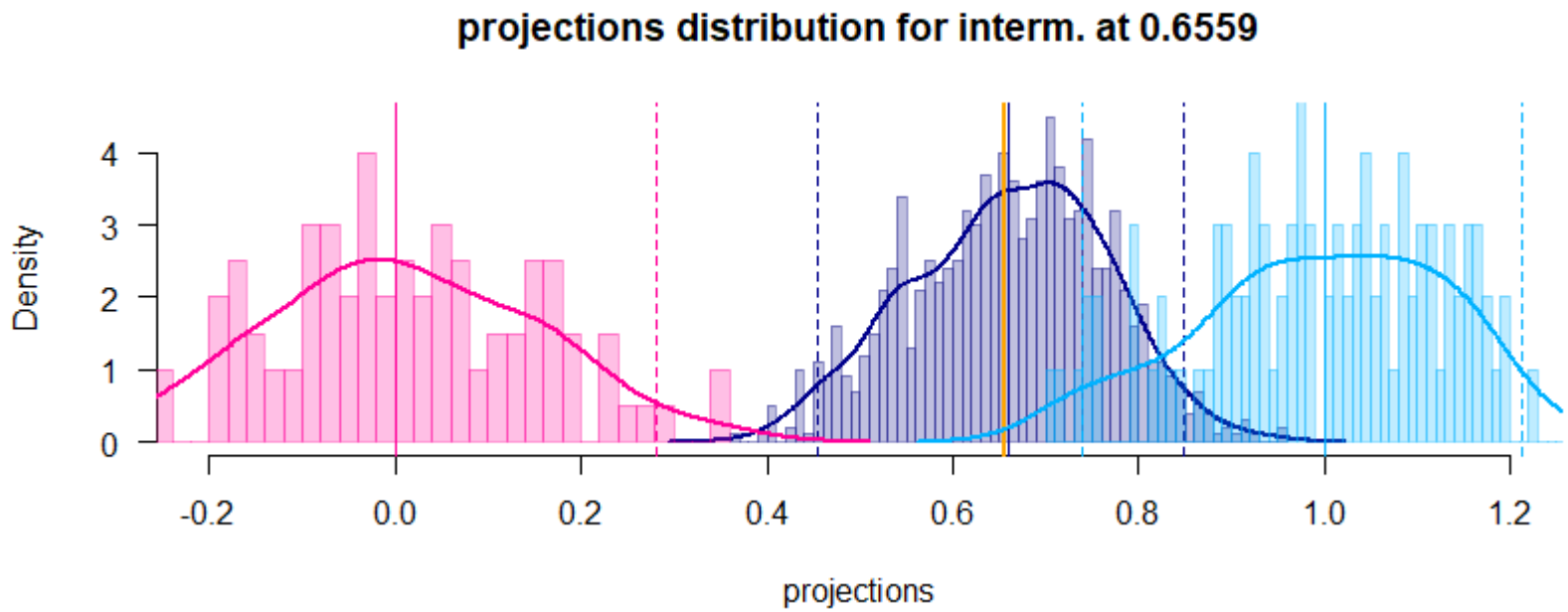


UMAP min_dist = 0

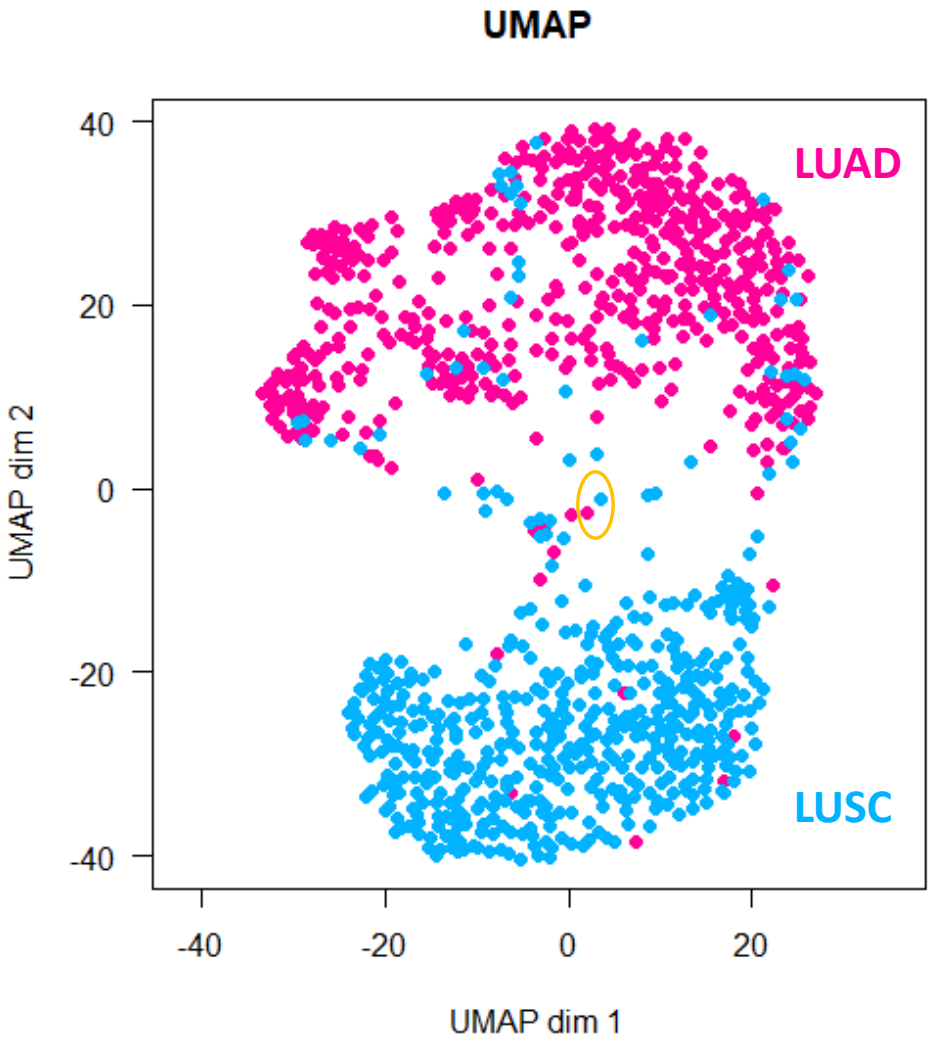


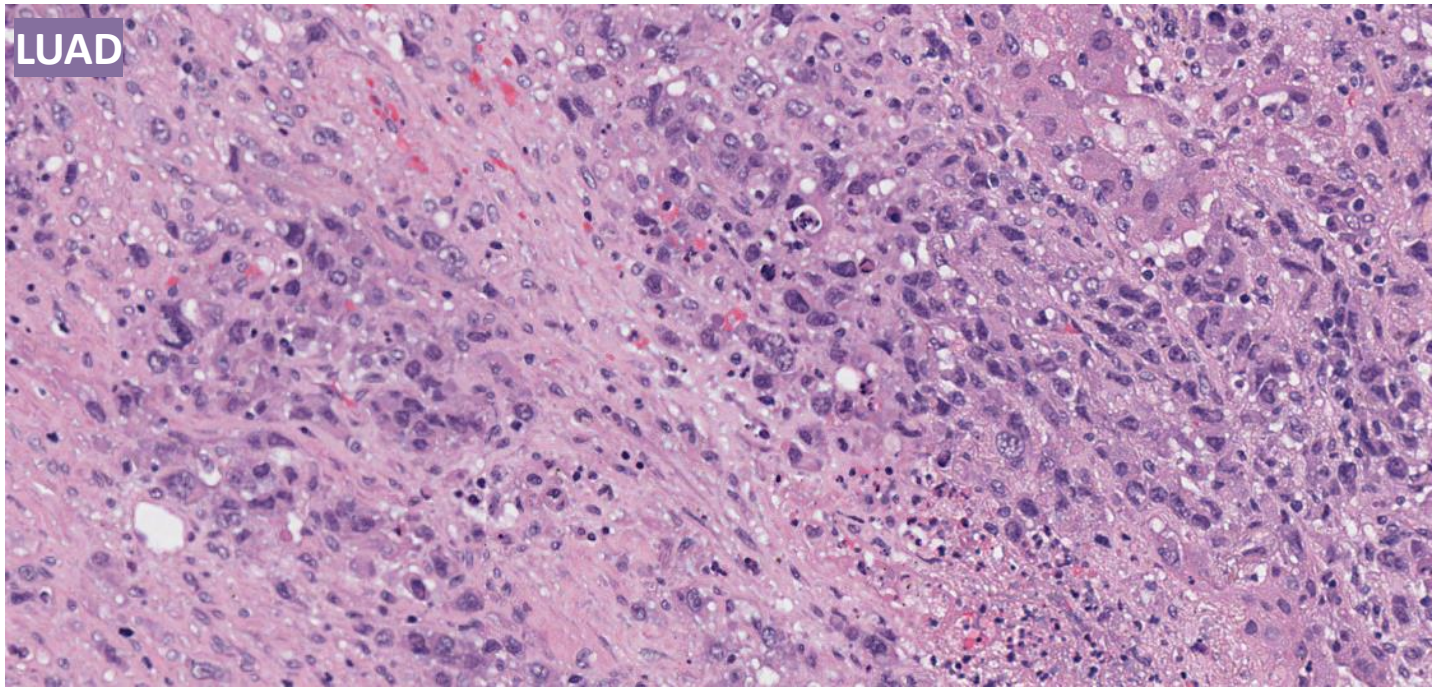
UMAP min_dist = 2.5

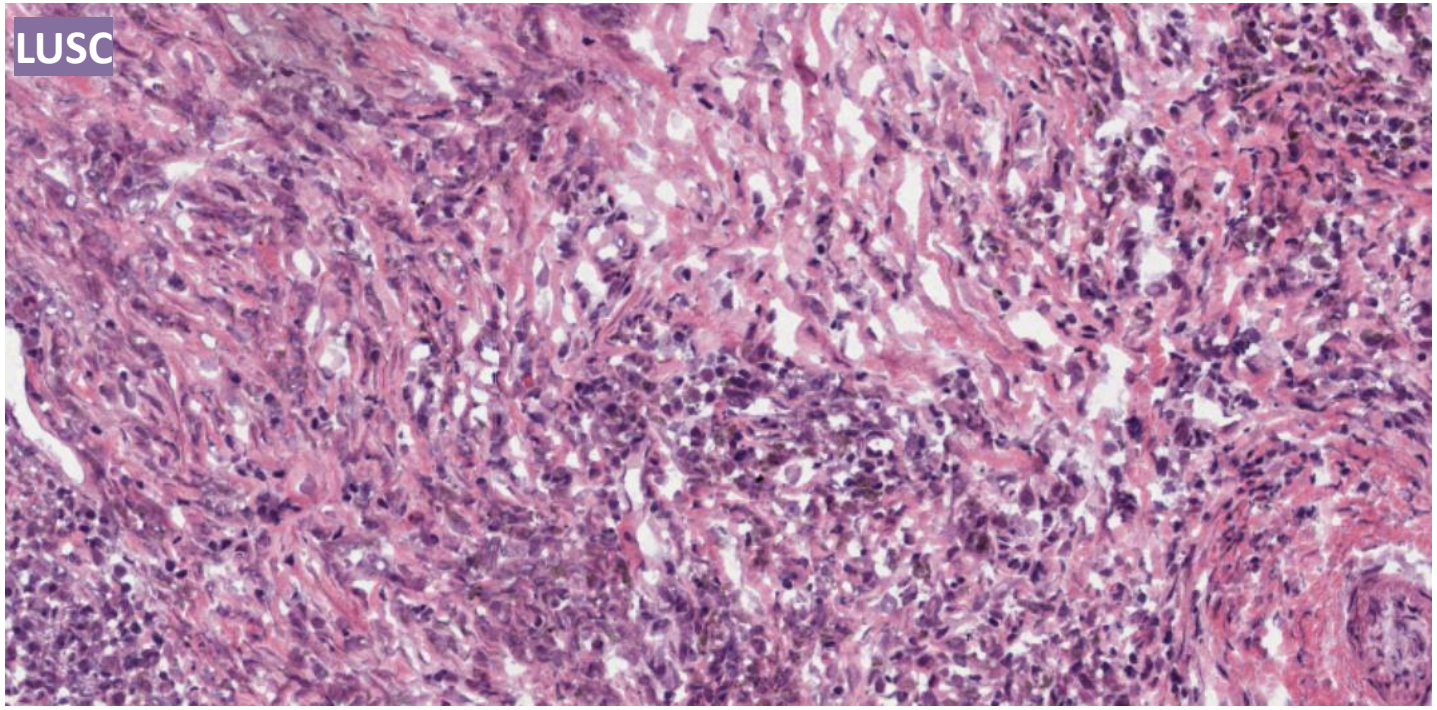

PCA
600
400
200
0
-200
-400
-600
PC2
-400
-200
0
200
400
PC1


projections distribution for interm. at 0.6559
4
3
2
1
0
Density
-0.2
0.0
0.2
0.4
0.6
0.8
1.0
1.2
projections

Conclusion


UMAP
LUAD
LUSC
UMAP dim 2
UMAP dim 1
40
20
0
-20
-40
-40
-20
0
20


LUAD


LUSC

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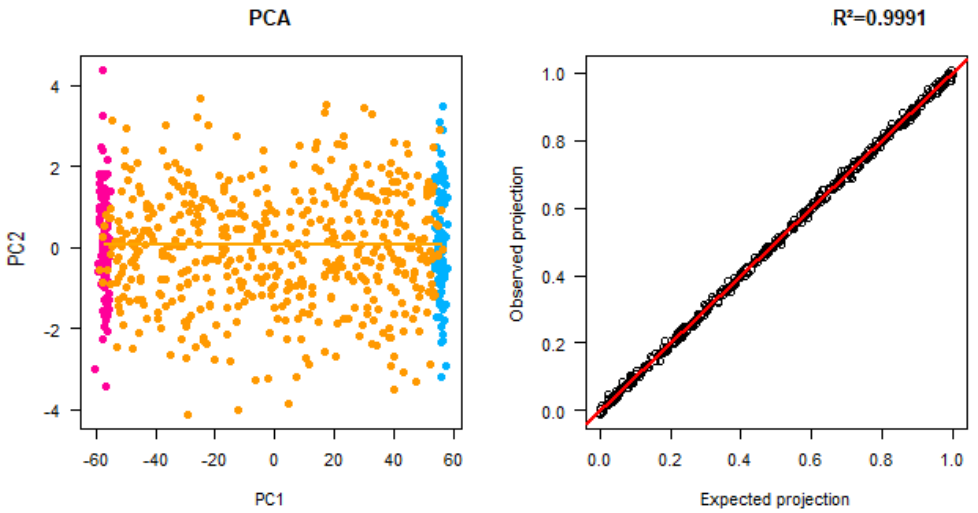
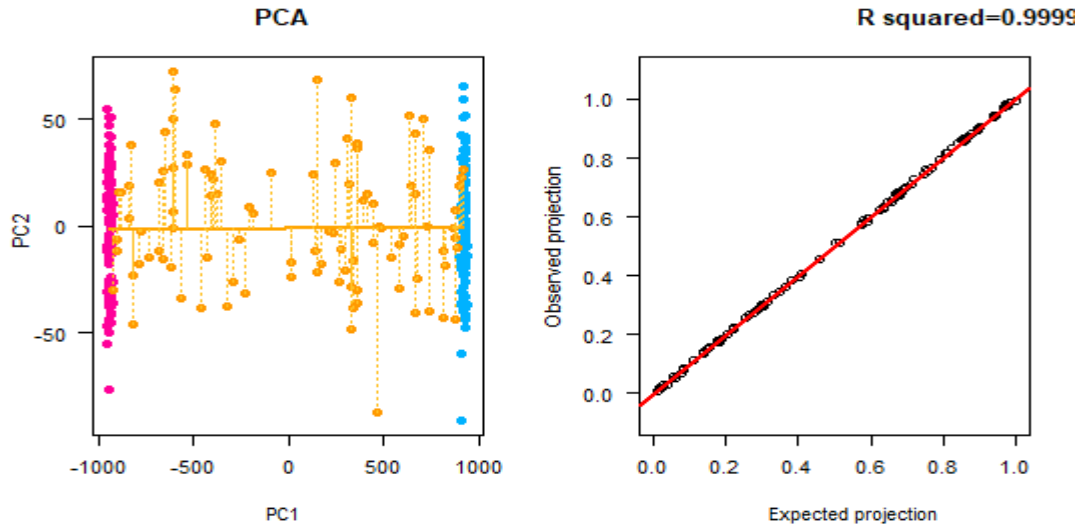
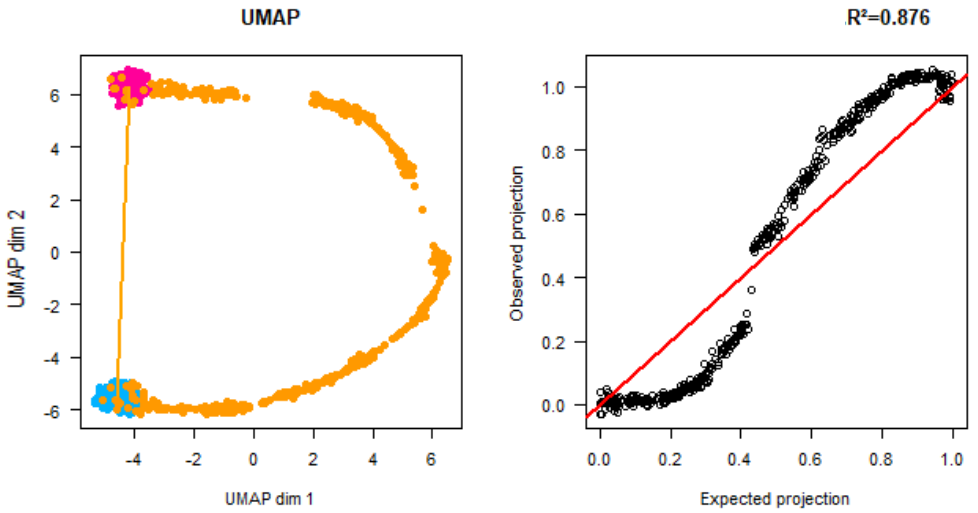
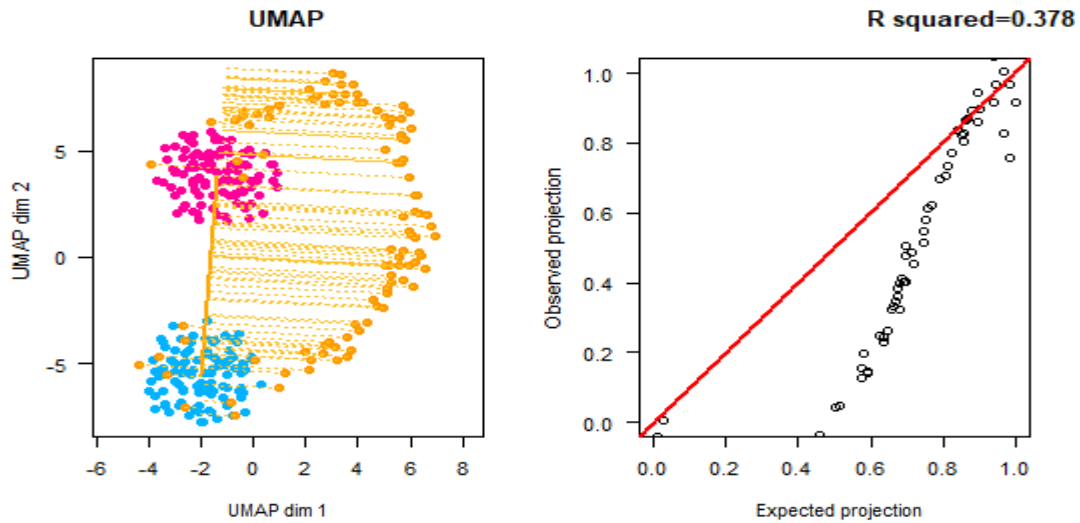
LA LIGUE CONTRE LE CANCER

UMAP


PCA
PC2
PC1
R²=0.9991
Observed projection
Expected projection


PCA
PC2
PC1
R squared=0.9999
Observed projection
Expected projection


UMAP
UMAP dim 2
UMAP dim 1
R²=0.876
Observed projection
Expected projection


UMAP
UMAP dim 2
UMAP dim 1
R squared=0.378
Observed projection
Expected projection