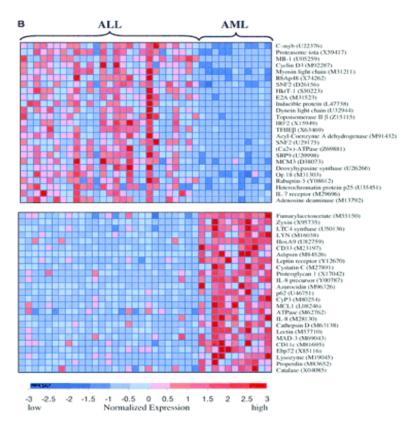
Bioinformatika **Gene expression data analysis**

Michael Anděl

Challenge:

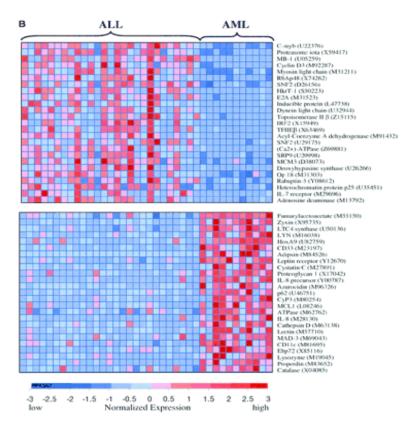
 \circ samples (10¹) x features (10³)



Golub et al.: Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring. Science, 1999

Challenge:

- \circ samples (10¹) x features (10³)
- False hypotheses, overfitting

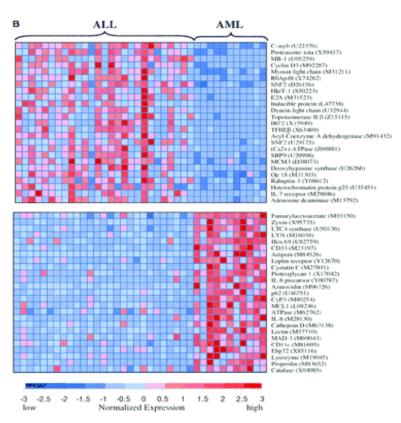


Golub et al.: Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring. Science, 1999

Challenge:

- \circ samples (10¹) x features (10³)
- False hypotheses, overfitting
- Interpretability: are the expressed genes the causal ones?

What to do?



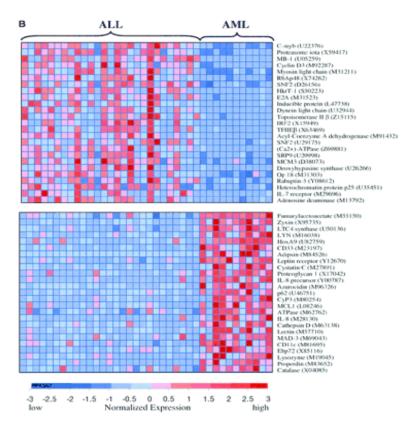
Golub et al.: Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring. Science, 1999

Challenge:

- \circ samples (10^1) x features (10^3)
- False hypotheses, overfitting
- Interpretability: are the expressed genes the causal ones?

What to do?

Decrease number of hypotheses



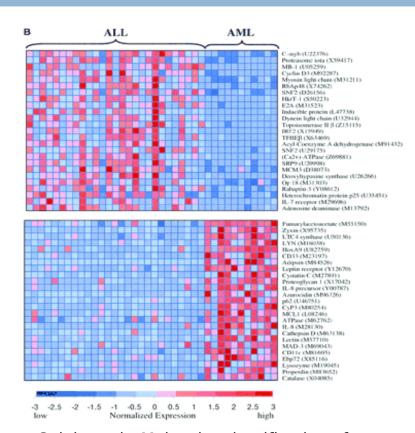
Golub et al.: Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring. Science, 1999

Challenge:

- \circ samples (10¹) x features (10³)
- False hypotheses, overfitting
- Interpretability: are the expressed genes the causal ones?

What to do?

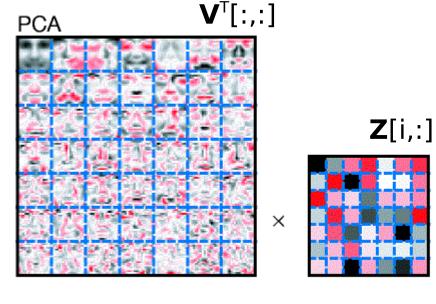
- Decrease number of hypotheses
- Analyze in terms of more abstract entities than genes, e.g. principal components



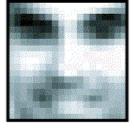
Golub et al.: Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring. Science, 1999

PCA - motivation

- M ... # genes
- N ... # samples
- X (N x M) ... GE data in the space of genes



- V (M x K) ... transformation basis, eigengenes
- Z (N x K) ... transformed GE data in the space of eigengenes
- K ... # of eigengenes,
 i.e. the number of
 underlying concepts
 X[i,:]



Lee et al.: Learning the parts of objects by non-negative matrix factorization. Science, 1999

Data:

- 7,129 GE profiles of 72 patients
- 25 samples: acute myeloid leucaemia (AML)
- 47 samples: acute lymphoblastic leucaemia (ALL)

Golub, T., et al. *Molecular classification of cancer: class discovery and class prediction by gene expression monitoring*. Science 286.5439 (1999): 531-537.

Task:

- Construct decision model to differentiate these types of tumours. Just complete the code in the script attached → ge_cv.m
- Deadline 19.5.

Part I:

- 1. Learn a decision tree on subjected data. Use Matlab class ClassificationTree and its method fit.
- 2. Show the tree (method view) and enumerate its **training** accuracy.
- 3. How would you interpret this model? Which gene is crucial for the decision?
- 4. Is this gene really the one causing the cancer? Look up in the article *Golub et al.*, 1999.
- 5. Estimate **real** accuracy of the tree. Use e.g., cross-validation (alternatively, you can split the data).
- 6. Compare it with the **training** accuracy.

Part II:

- 1. Learn a basis-matrix V of the data. Use the **attached** function pca.m.
- 2. For for a **range** of component numbers K:
 - a) project the original data X to the top K components of V. The result are data Z with reduced dimensionality: $Z = XV_{1:K,1:}^T$
 - b) Create a tree out of these reduced data. Show it and enumerate its **training** accuracy.
- 3. Compare **all** the trees resulting from the reduced data and pick the "best" according to its accuracy and structure. Follow the Occam razor ;-)

Part II:

- 4. Estimate the **real** accuracy of the "best" chosen tree. Again, by e.g. crossvalidation.
- 5. Extract the genes active in the discriminative components. The discriminative components are those vectors of basis-matrix V, which refer to the features your tree consists of. To extract the active genes from a component use the function mineGenes.
- 6. Resulting gene-sets related to each of the discriminative component shall hopefully refer to some abstract biological processes. Use Gorilla to enrich these gene sets in Gene-ontology terms.
- 7. Make a story! Get inspired e.g. here ;-)