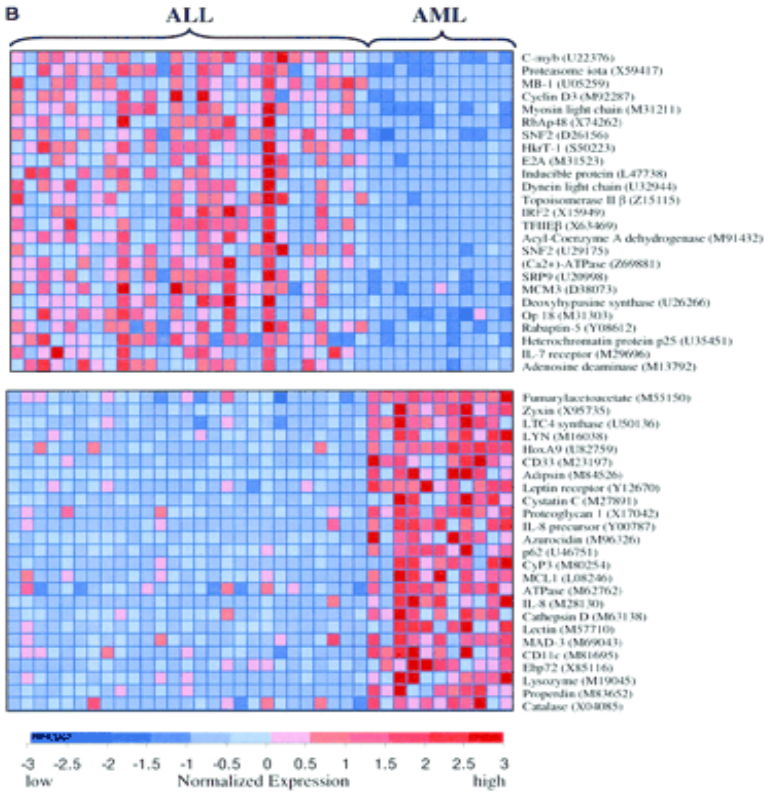
Bioinformatika
Gene expression data analysis

Michael Anděl

Classification task

Challenge:

- samples (10^1) x features (10^3)



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

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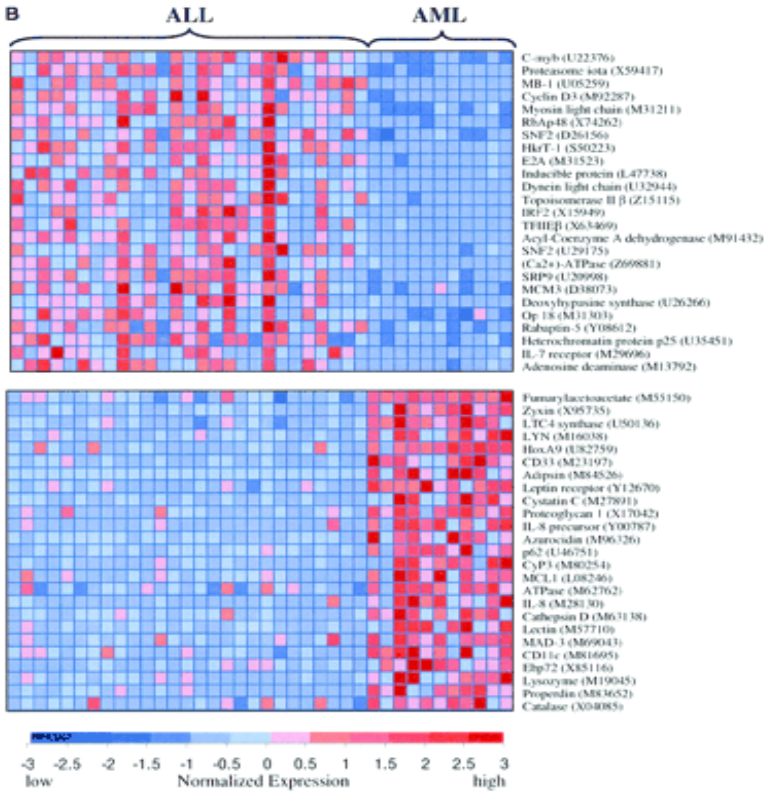
- False hypotheses, overfitting



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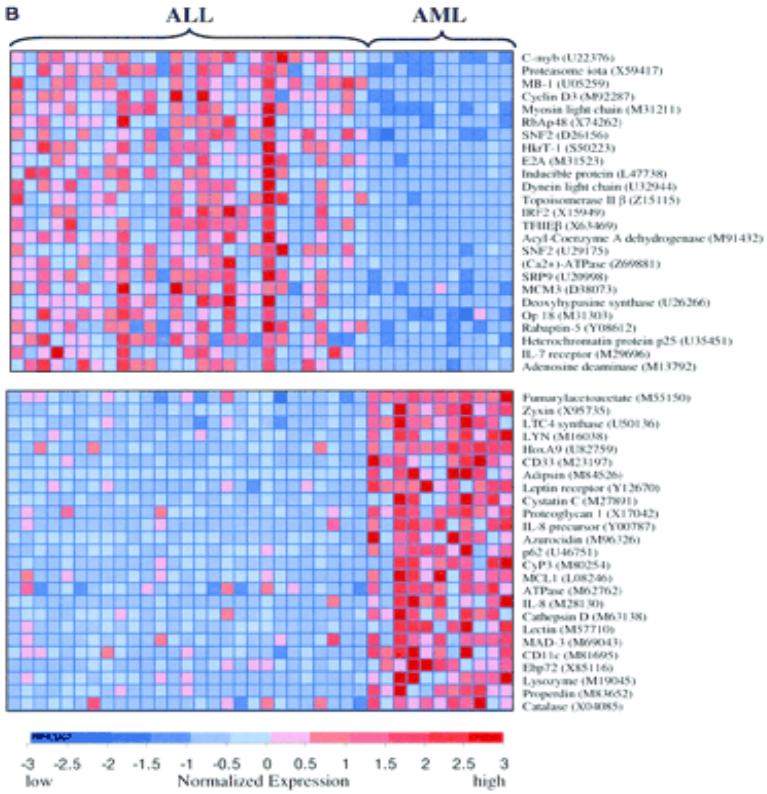
- Interpretability:
  are the expressed genes the causal ones?

What to do?



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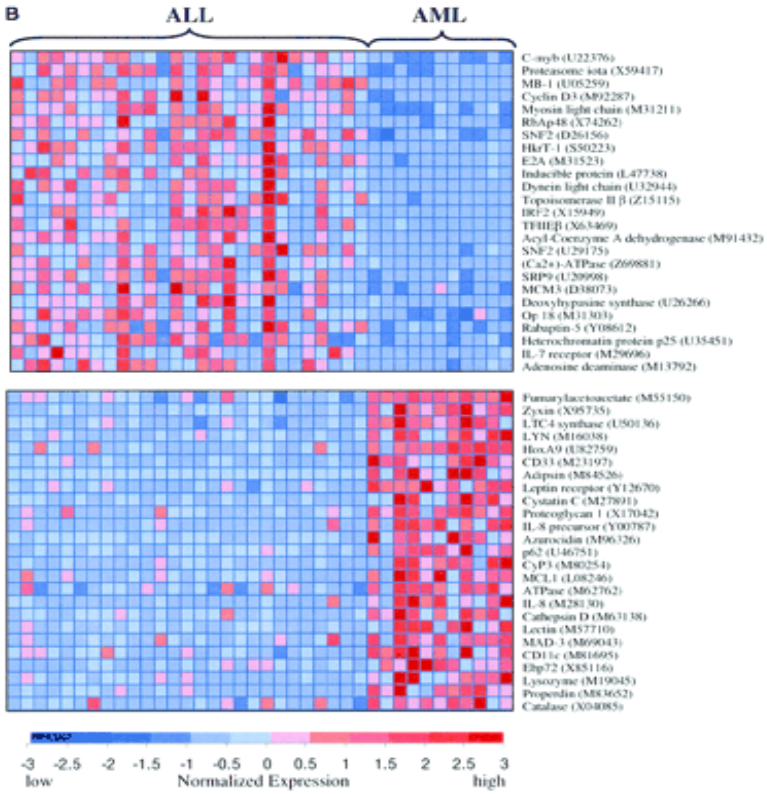
What to do?

- Decrease number of hypotheses



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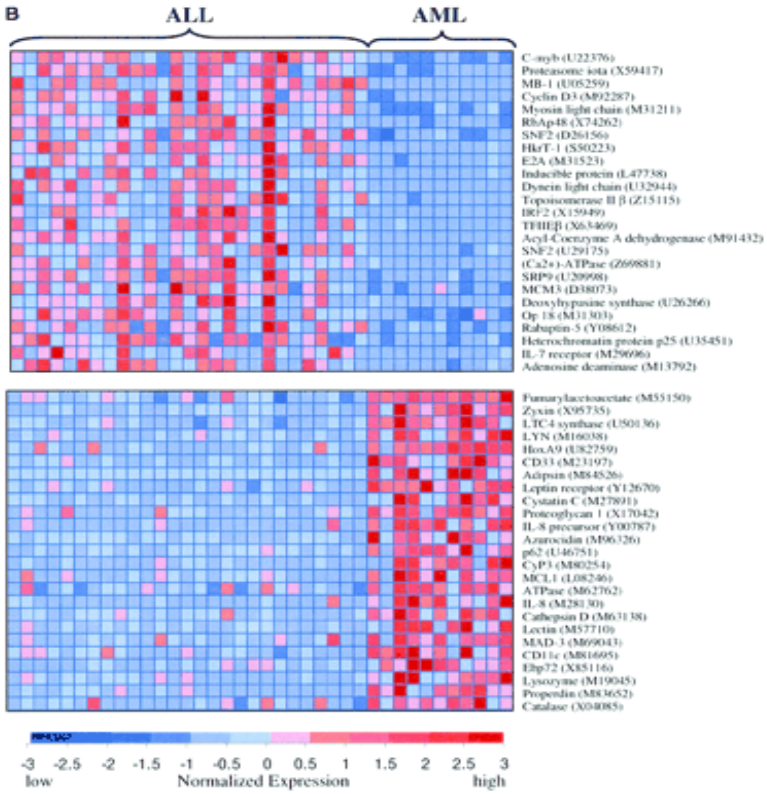
What to do?

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



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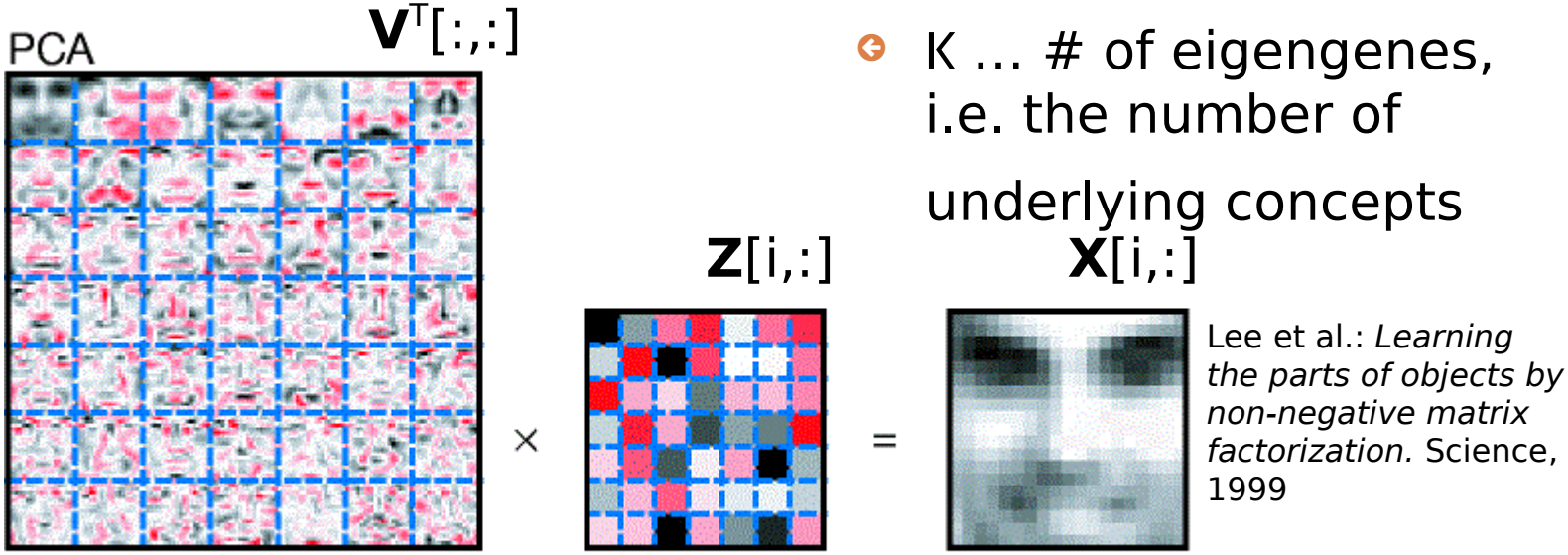
PCA – motivation

- 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



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

Assignment

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.**

Assignment

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.

Assignment

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: $Z = XV^T_{1:K,1:}$
   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 ;-)

Assignment

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 insperd e.g. here ;-)