Supervised Graph Inference

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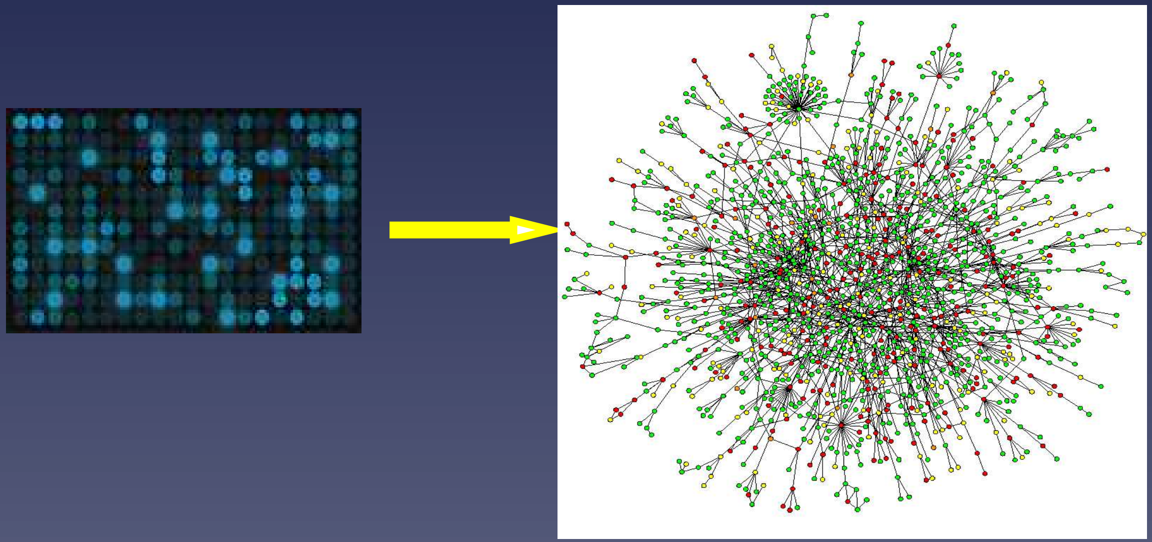
Motivations: systems biology



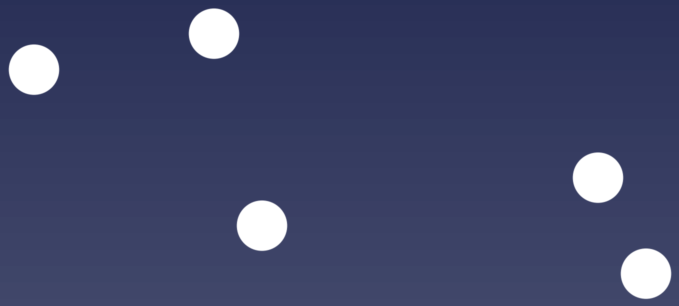
- Gene expression
- Sequence
- Protein structure
- Protein localization, etc...

- Regulatory network
- Signaling pathways
- Metabolic pathways
- Interaction network, etc...

Related approaches

- Bayesian nets for regulatory networks (Friedman et al. 2000)
- Boolean networks (Akutsu, 2000)
- Nearest neighbors method (Marcotte et al, 1999)

Example: nearest neighbors method



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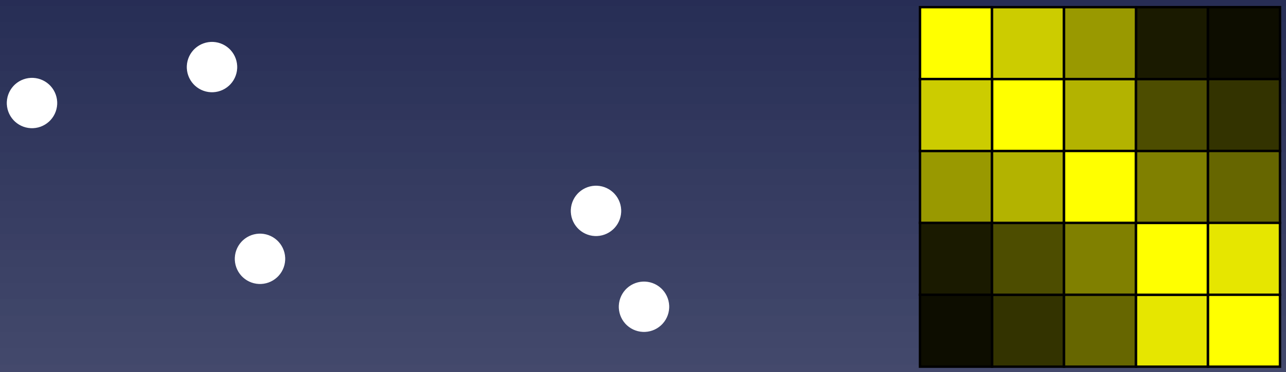

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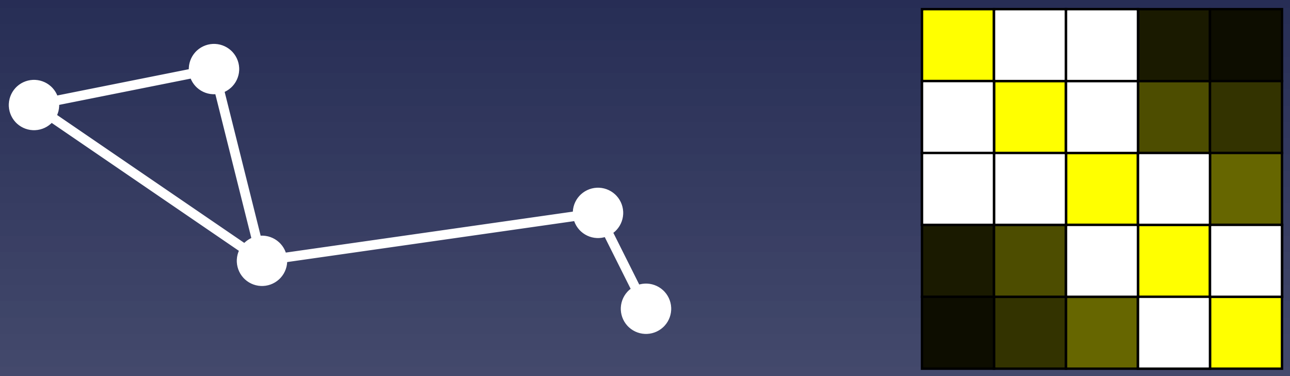

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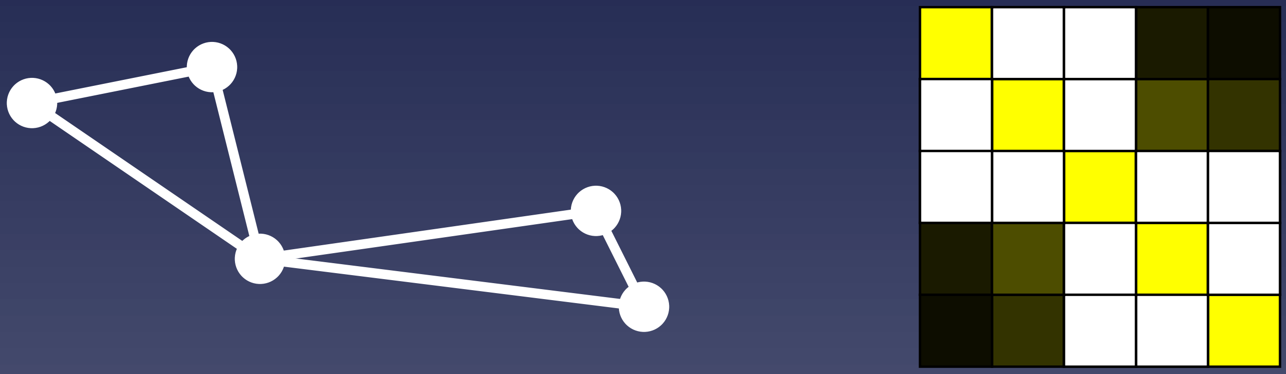

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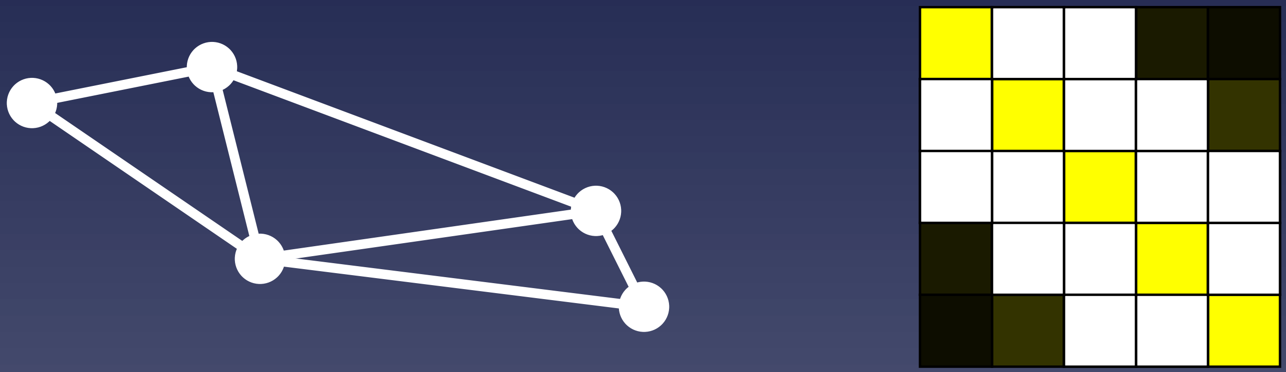

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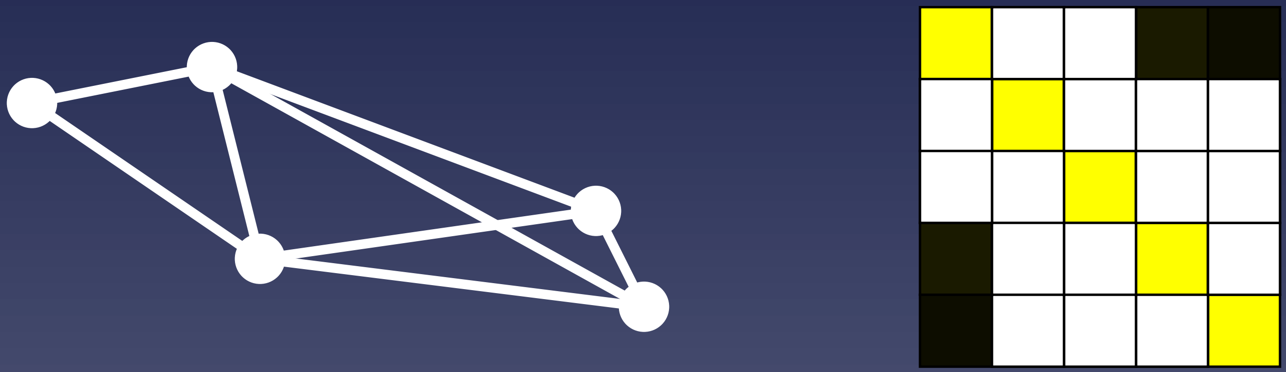

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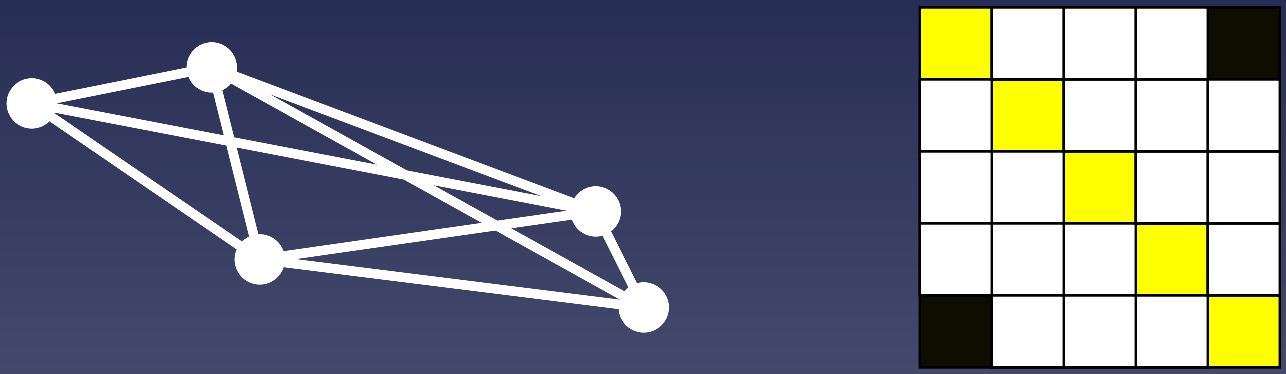

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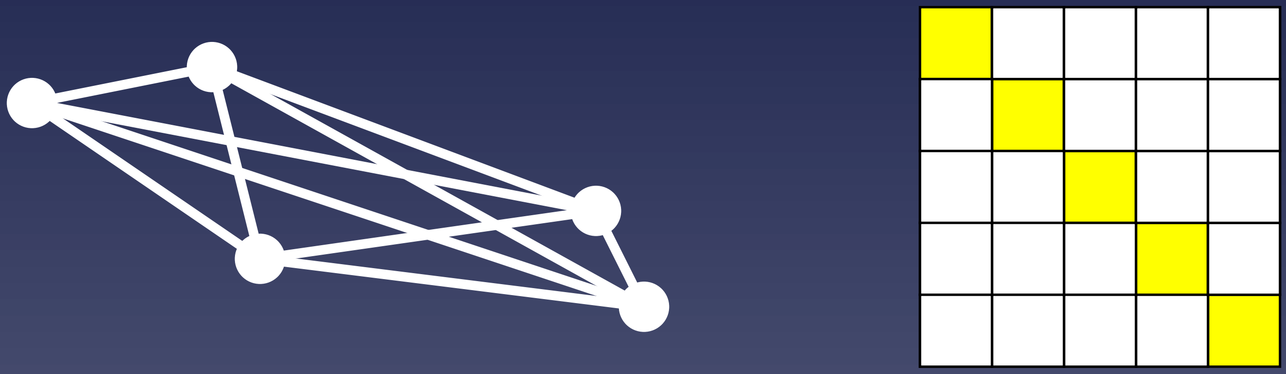

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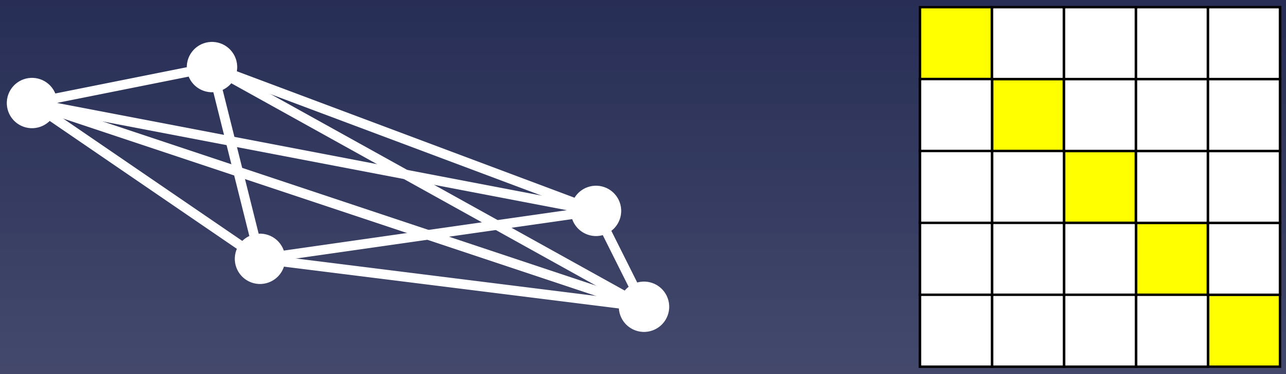
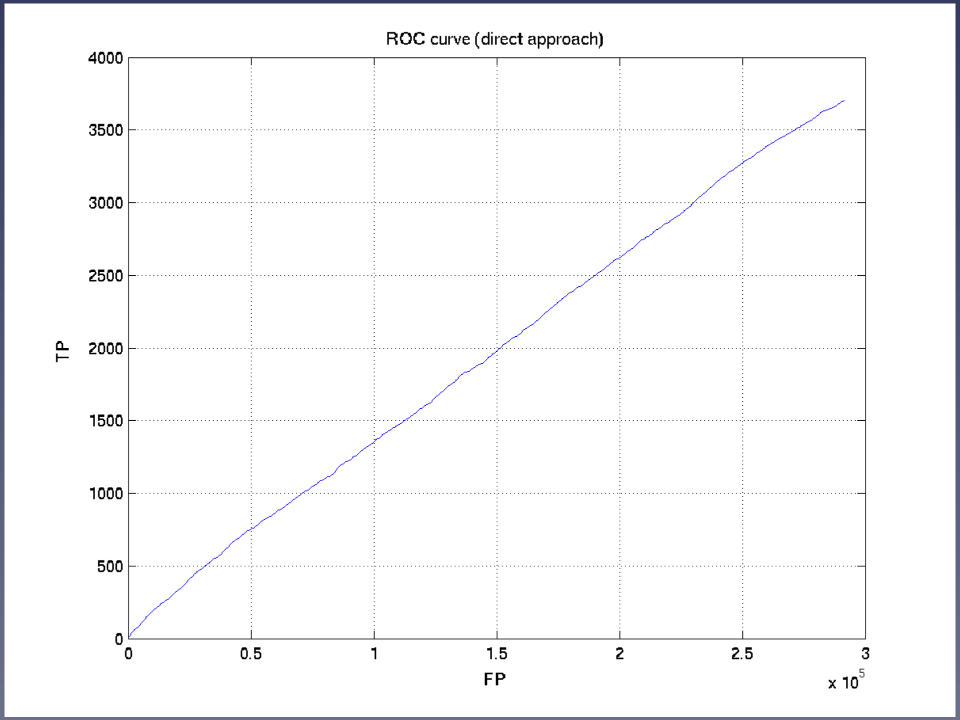


Application: metabolic network reconstruction

The metabolic network of the yeast involves 769 genes. Each gene is represented by 157 expression measurements. (ROC=0.52)



What is wrong?

- What similarity measure between profiles should be use?

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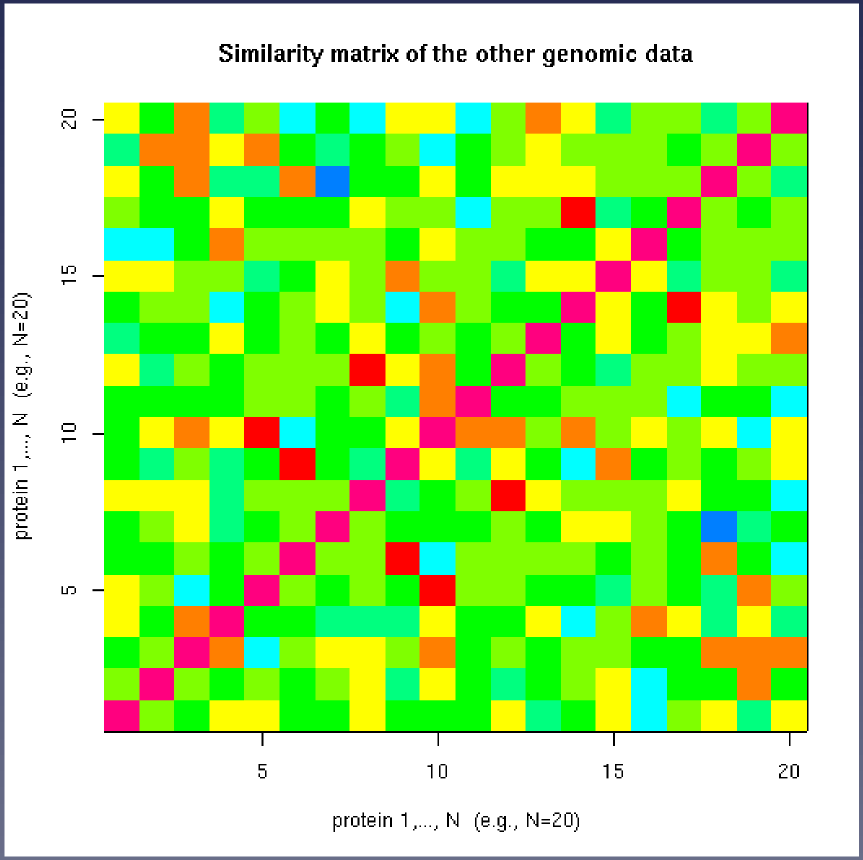
- Which network are we expecting to recover?

The supervised gene inference problem



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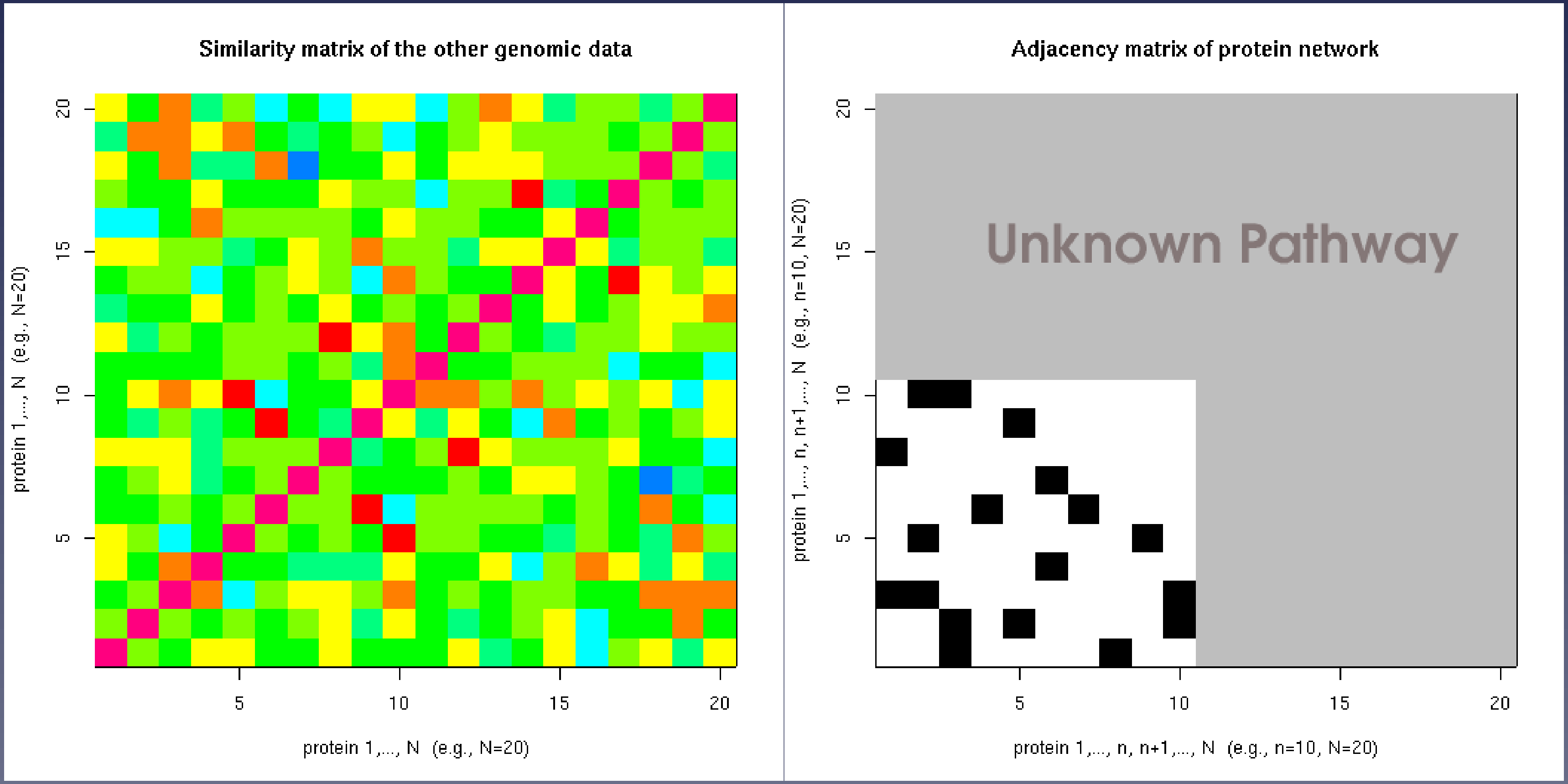
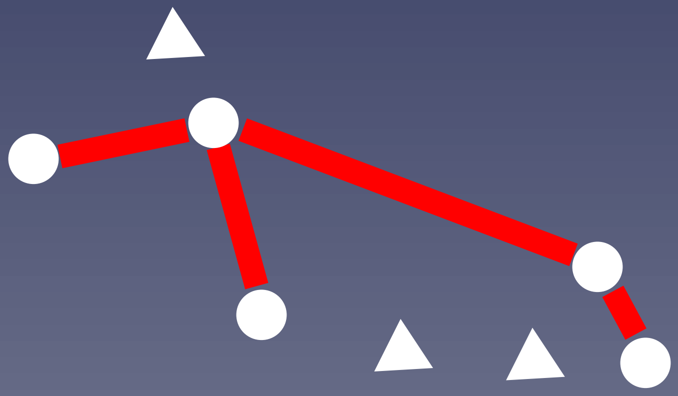


The main idea

Supervised graph inference
through
distance metric learning



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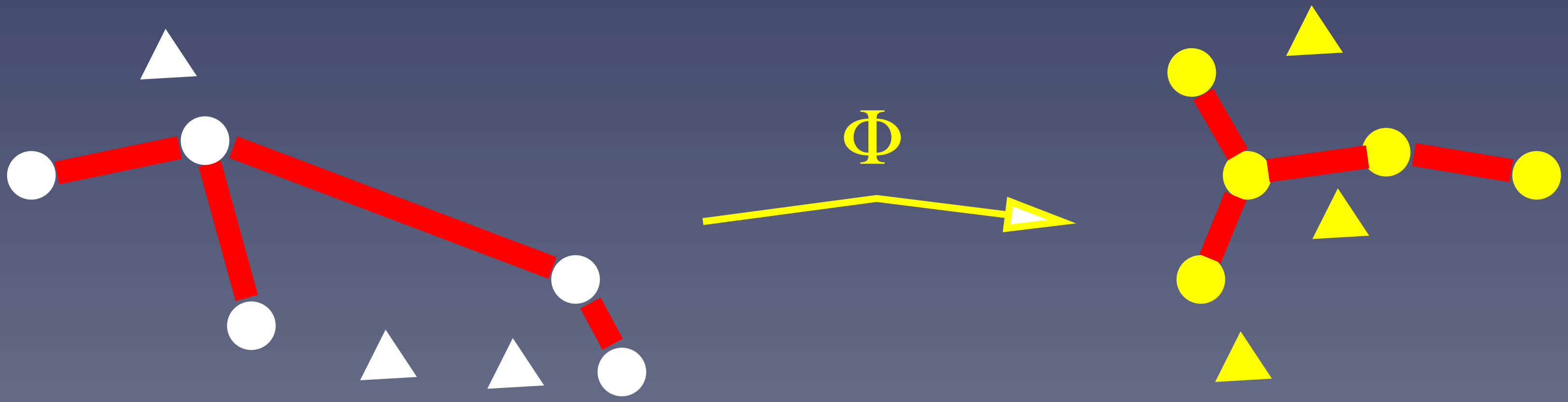

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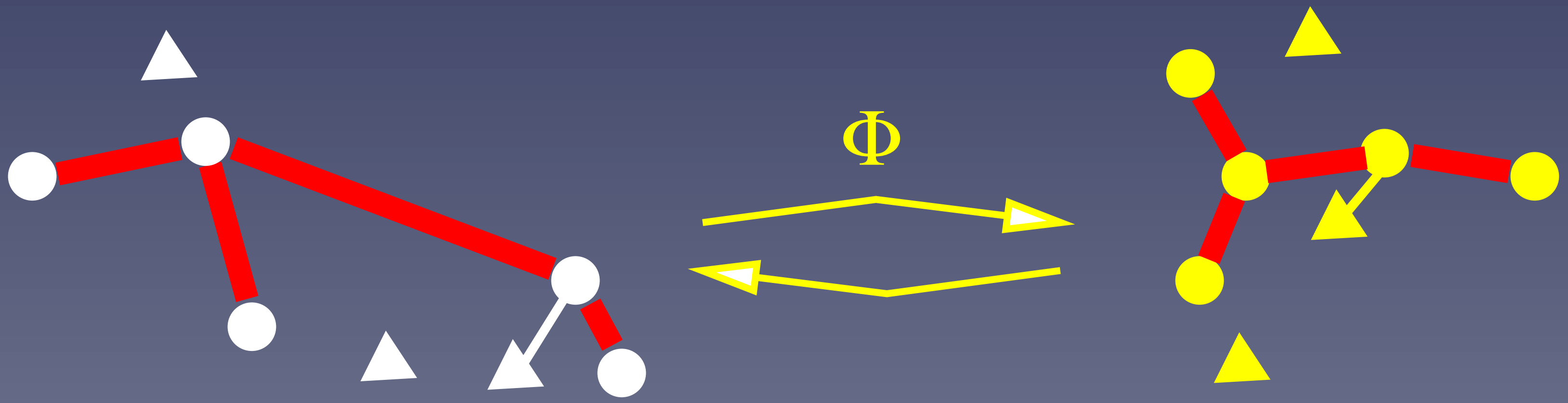

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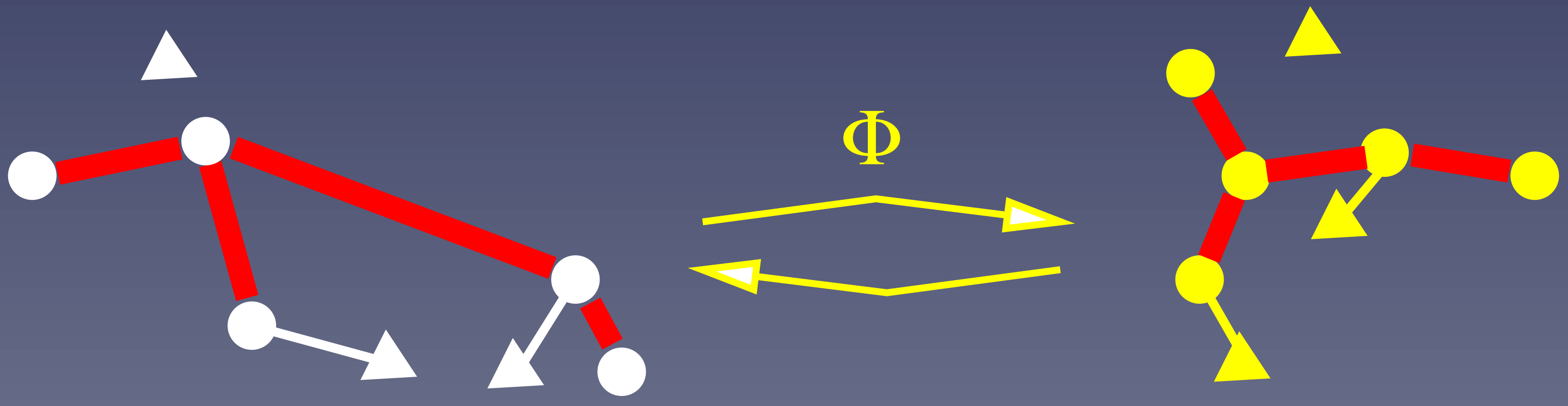

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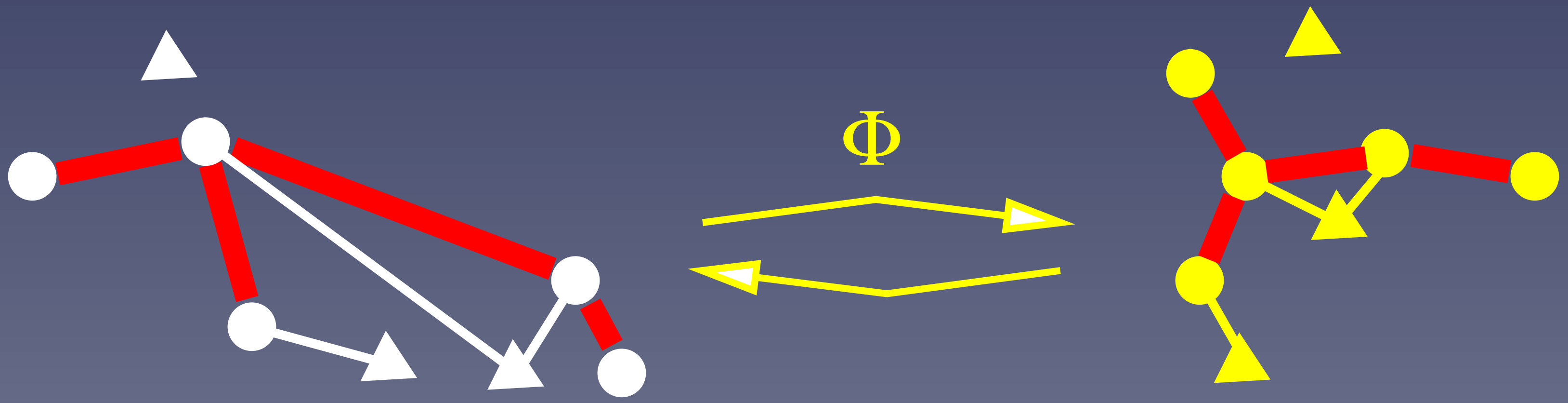

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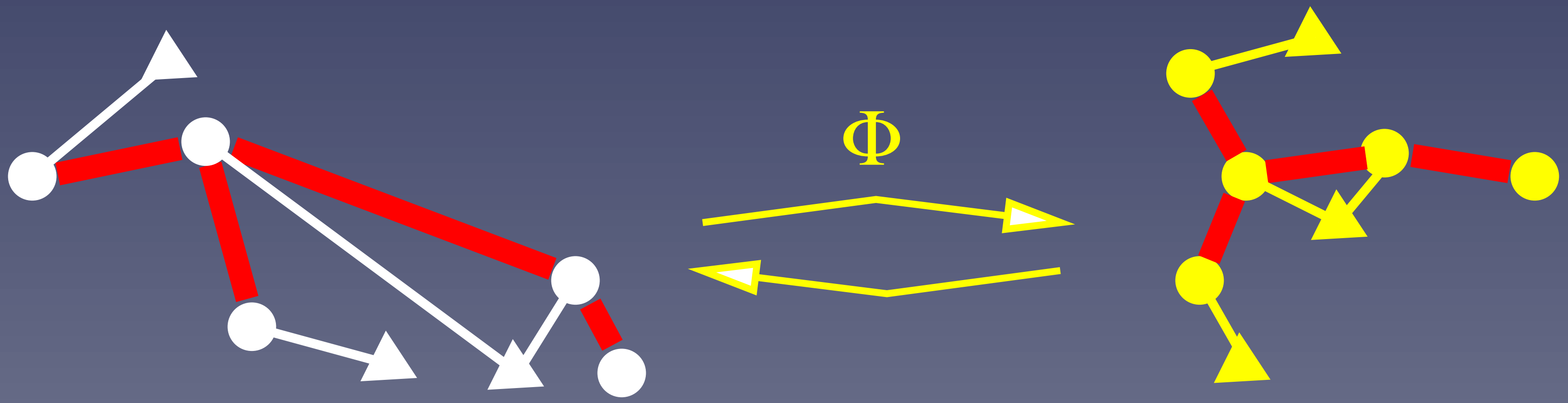

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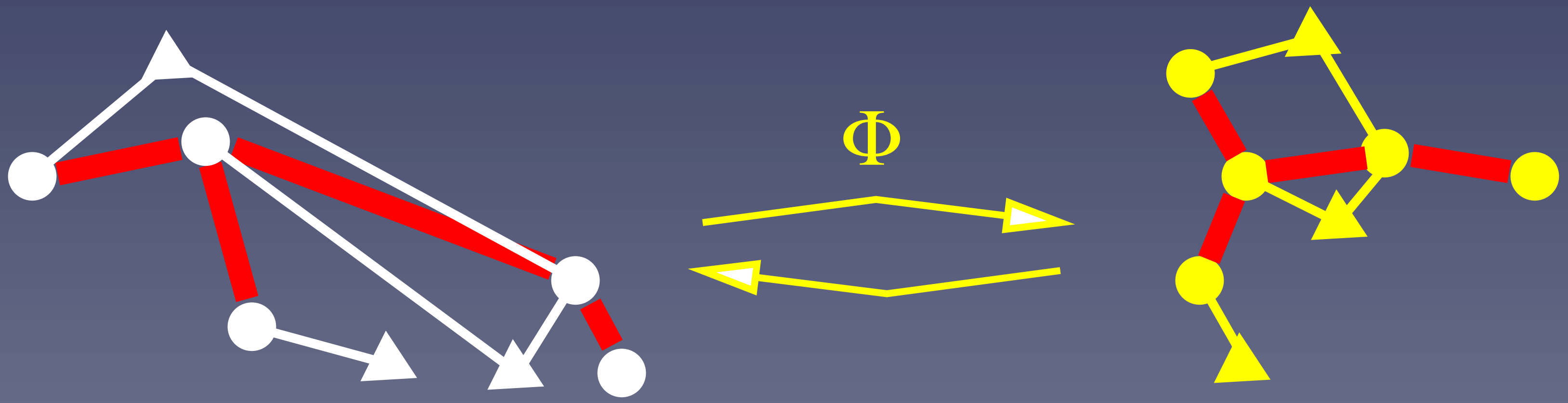

Learning the mapping Φ

- Let us consider mappings $\mathcal{X} \to \mathbb{R}^d$ ($\mathcal{X}$ being endowed with a p.d. kernel K):

$$\Phi(x) = (f_1(x), \ldots, f_d(x))' \in \mathbb{R}^d$$

  made of orthogonal features $f_i \in \mathcal{H}_K$ in the RKHS

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- A possible criterion to ensure that connected genes in the known network have similar value is to minimize:

$$\min_{f \in \mathcal{H}_K} \frac{\sum_{(i,j) \in E} \left(f(x_i) - f(x_j)\right)^2 - \sum_{(i,j) \notin E} \left(f(x_i) - f(x_j)\right)^2}{\sum_{i=1}^{n} f(x_i)^2}$$

Regularized risk

- If the data are centered ($\sum_i x_i = 0$), then this is equivalent to minimizing:

$$\min_{f \in \mathcal{H}_K} \frac{\sum_{i \sim j} \left(f(x_i) - f(x_j) \right)^2}{\sum_{i=1}^{n} f(x_i)^2}.$$

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- For statistical reasons (particularly in large dimension), it is safer to minimize:

$$\min_{f \in \mathcal{H}_K} \frac{\sum_{i \sim j} \left(f(x_i) - f(x_j) \right)^2 + \lambda || f ||^2}{\sum_{i=1}^n f(x_i)^2}$$

Influence of λ

- $\lambda \to +\infty$: kernel PCA
  - Useful for noisy, high-dimensional data.
  - Used in spectral clustering. The graph does not play any role (unsupervised)
- $\lambda \to 0$: second smallest eigenvector of the graph
  - Useful to embed the graph in a Euclidean space (used in graph partitioning)
  - Sensitive to noise. Mapping of points outside of the graph unstable (overfitting)

Extracting successive features

- Successive features to form Φ can be obtained by:

$$f_i = \underset{f \perp \{f_1, \ldots, f_{i-1}\}}{\arg\min} \left\{ \frac{\sum_{i \sim j} \left(f(x_i) - f(x_j)\right)^2 + \lambda ||f||^2}{\sum_{i=1}^{n} f(x_i)^2} \right\}.$$

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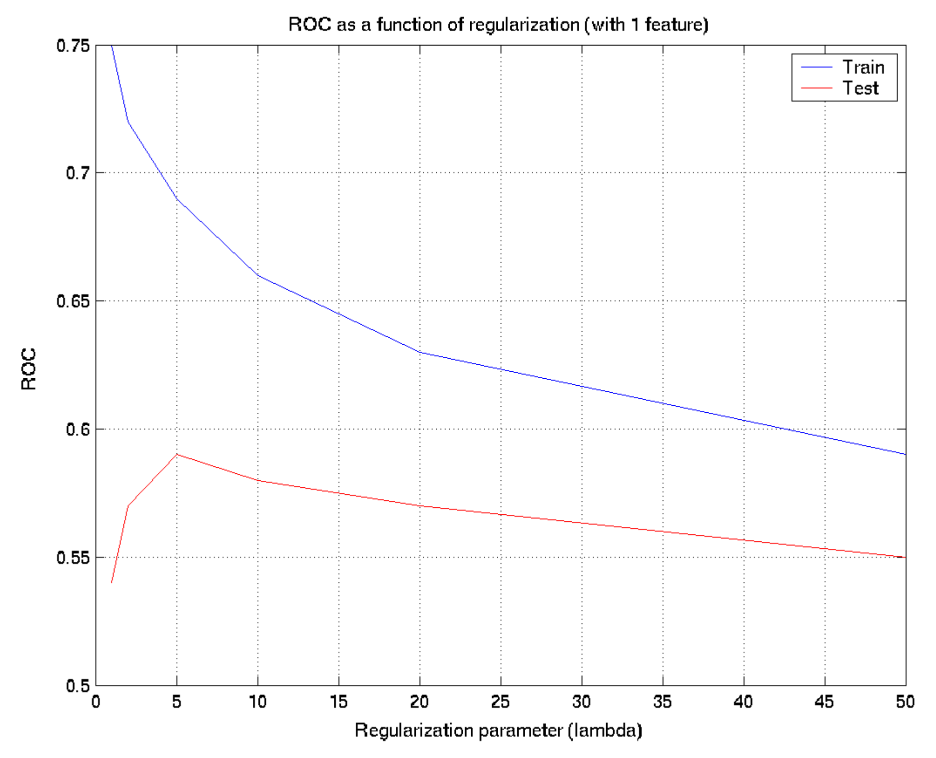
- The solution satisfies $f_i(x) = \sum_j \alpha_{i,j} K(x_j, x)$, where α_i are the successive generalized eigenvectors of

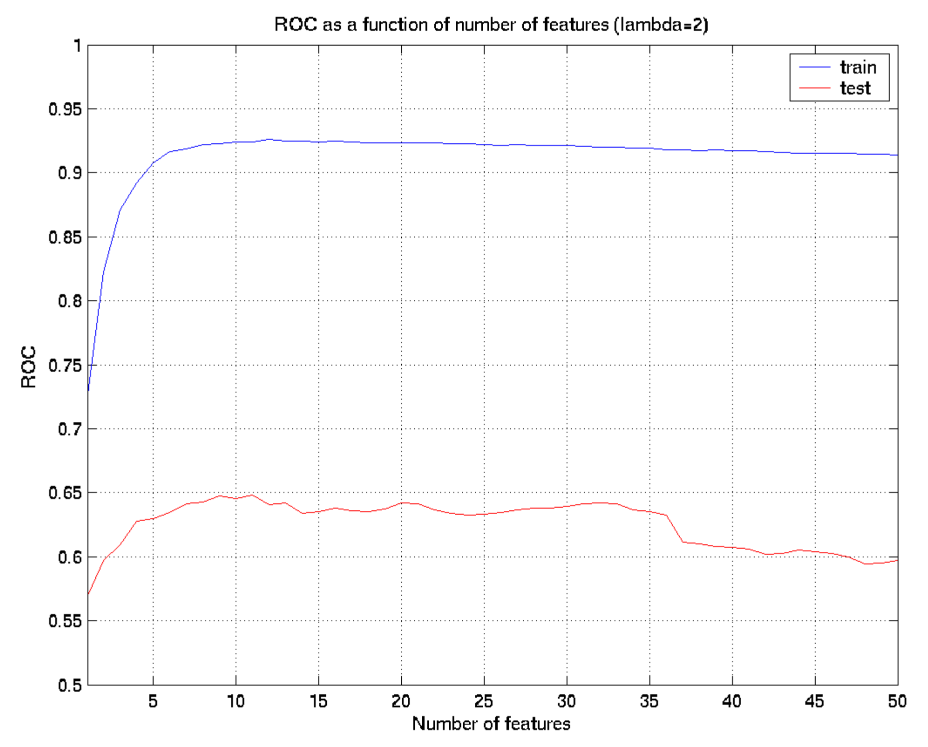
$$(LK_V + \lambda I)\alpha = \mu K_V \alpha.$$

Evaluation of the supervised approach: effect of λ



Metabolic network, 10-fold cross-validation, 1 feature

Evaluation of the supervised approach: number of features ($\lambda = 2$)

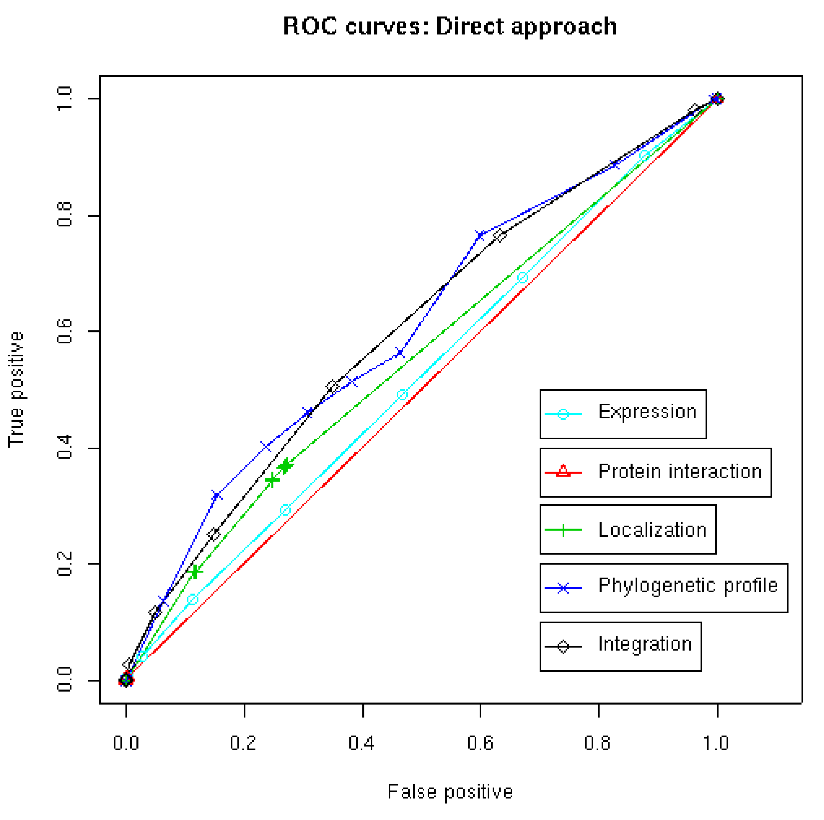


Learning from heterogeneous data

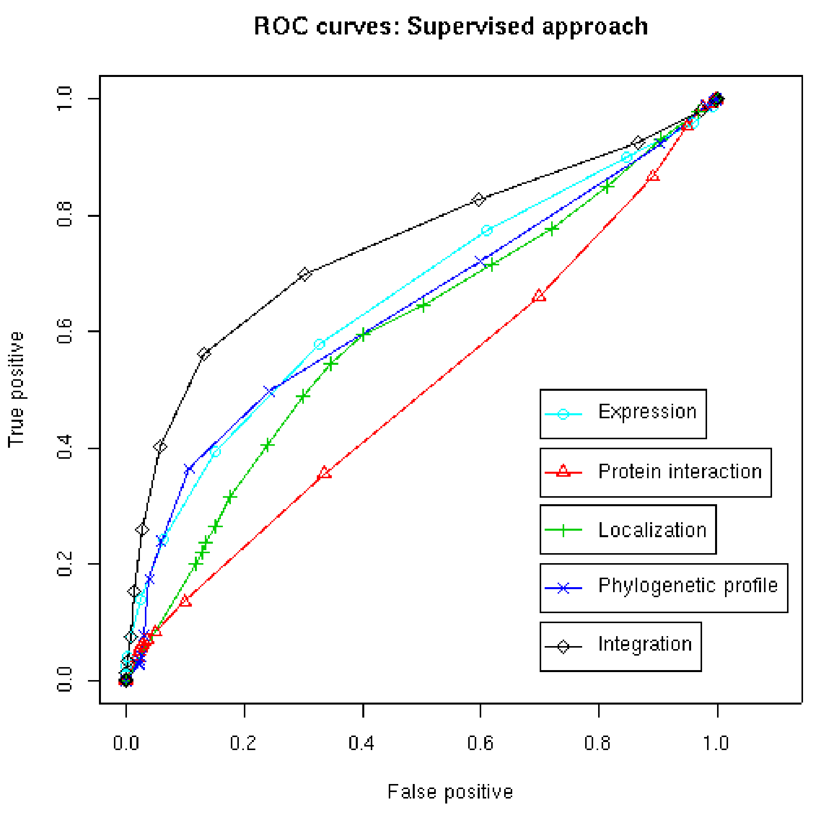
- Suppose several data are available about the genes, e.g., expression, localization, struture, predicted interaction etc...
- Each data can be represented by a positive definite similarity matrix $K_1, \ldots, K_p$ called kernels
- Kernel can be combined by various operations, e.g., addition:

$$K = \sum_{i=1}^{p} K_i$$

Learning from heterogeneous data (unsupervised)



Learning from heterogeneous data (supervised)



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2. Supervised graph inference can be performed by distance metric learning

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2. Supervised graph inference can be performed by distance metric learning
3. Data integration with kernels is simple and powerful

See you at poster 49