Probabilistic kernels for structured objects

Jean-Philippe.Vert@mines.org

Ecole des Mines de Paris
Groupe bioinformatique

SVM seminar, Orsay University, Jan. 10, 2003.

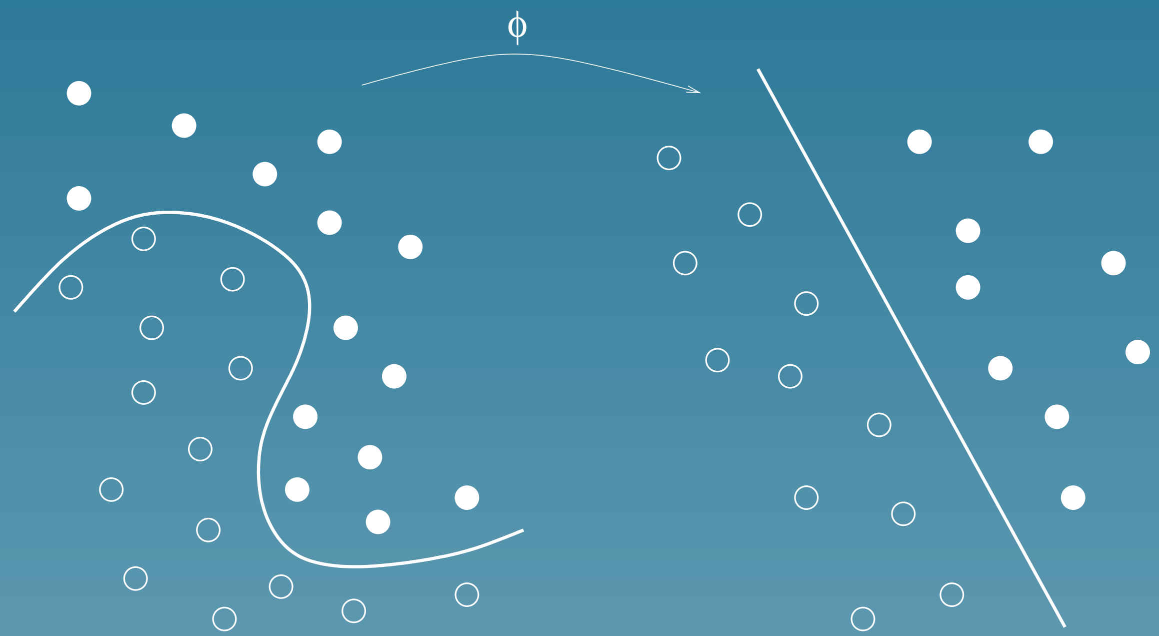
Outline

1. SVM and kernel methods
2. Probabilistic kernels for structured objects
3. Application: gene function prediction from phylogenetic profile

Part 1

SVM and kernel methods

Support vector machines



- Objects to classified x mapped to a feature space
- Largest margin separating hyperplan in the feature space

The kernel trick

- Implicit definition of $x \longrightarrow \Phi(x)$ through the kernel:

$$K(x,y) \stackrel{def}{=} < \Phi(x), \Phi(y) >$$

The kernel trick

- Implicit definition of $x \longrightarrow \Phi(x)$ through the kernel:

$$K(x, y) \stackrel{def}{=} < \Phi(x), \Phi(y) >$$

- Simple kernels can represent complex Φ

The kernel trick

- Implicit definition of $x \rightarrow \Phi(x)$ through the kernel:

$$K(x,y) \stackrel{def}{=} < \Phi(x), \Phi(y) >$$

- Simple kernels can represent complex Φ
- For a given kernel, not only SVM but also clustering, PCA, ICA... possible in the feature space = kernel methods

Kernel examples

- "Classical" kernels: polynomial, Gaussian, sigmoid...
  but the objects x must be vectors

Kernel examples

- “Classical” kernels: polynomial, Gaussian, sigmoid...
  but the objects x must be vectors
- “Exotic” kernels for strings:

Kernel examples

- "Classical" kernels: polynomial, Gaussian, sigmoid... but the objects x must be vectors
- "Exotic" kernels for strings:
  - $\star$ Fisher kernel (Jaakkoola and Haussler 98)

Kernel examples

- "Classical" kernels: polynomial, Gaussian, sigmoid...
  but the objects x must be vectors
- "Exotic" kernels for strings:
  - ⋆ Fisher kernel (Jaakkoola and Haussler 98)
  - ⋆ Convolution kernels (Haussler 99, Watkins 99)

Kernel examples

- “Classical” kernels: polynomial, Gaussian, sigmoid...
  but the objects x must be vectors
- “Exotic” kernels for strings:
  - ⋆ Fisher kernel (Jaakkoola and Haussler 98)
  - ⋆ Convolution kernels (Haussler 99, Watkins 99)
  - ⋆ Kernel for translation initiation site (Zien et al. 00)

Kernel examples

- "Classical" kernels: polynomial, Gaussian, sigmoid... but the objects x must be vectors
- "Exotic" kernels for strings:
  - ⋆ Fisher kernel (Jaakkoola and Haussler 98)
  - ⋆ Convolution kernels (Haussler 99, Watkins 99)
  - ⋆ Kernel for translation initiation site (Zien et al. 00)
  - ⋆ String kernel (Lodhi et al. 00)

Kernel examples

- "Classical" kernels: polynomial, Gaussian, sigmoid...
  but the objects x must be vectors

- "Exotic" kernels for strings:
  - ⋆ Fisher kernel (Jaakkoola and Haussler 98)
  - ⋆ Convolution kernels (Haussler 99, Watkins 99)
  - ⋆ Kernel for translation initiation site (Zien et al. 00)
  - ⋆ String kernel (Lodhi et al. 00)
  - ⋆ Spectrum kernel (Leslie et al., PSB 2002)

Kernel engineering

- Let $\mathcal{X}$ be a finite set

Kernel engineering

- Let $\mathcal{X}$ be a finite set
- A fonction $K : \mathcal{X}^2 \longrightarrow \mathbb{R}$ is a valid kernel if it is symmetric positive definite.

Kernel engineering

- Let $\mathcal{X}$ be a finite set
- A fonction $K : \mathcal{X}^2 \longrightarrow \mathbb{R}$ is a valid kernel if it is symmetric positive definite.
- Kernel engineering:Use prior knowledge to build the geometry of the feature space through $K(.,.)$

Part 2

Probabilistic kernels for structured objects

The problem

- $\mathcal{X}$ a finite set of (structured) objects

The problem

- $\mathcal{X}$ a finite set of (structured) objects
- $p(x)$ a probability distribution on $\mathcal{X}$

The problem

- $\mathcal{X}$ a finite set of (structured) objects
- $p(x)$ a probability distribution on $\mathcal{X}$
- How to build $K(x, y)$ from $p(x)$?

The problem

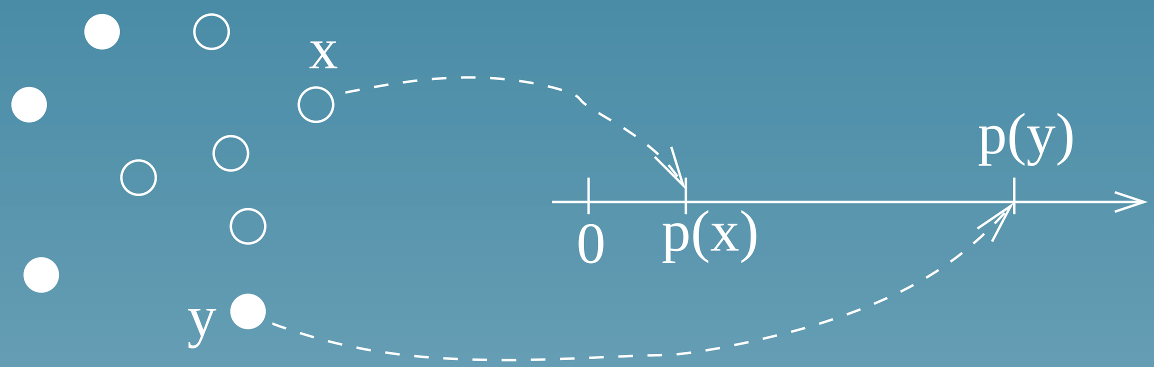
- $\mathcal{X}$ a finite set of (structured) objects
- $p(x)$ a probability distribution on $\mathcal{X}$
- How to build $K(x, y)$ from $p(x)$?
- *Remark: up to translation and scaling, we can restrict K to be a probability on $\mathcal{X} \times \mathcal{X}$ (P-kernel)*

Product kernel

$$K_{prod}(x, y) = p(x)p(y)$$

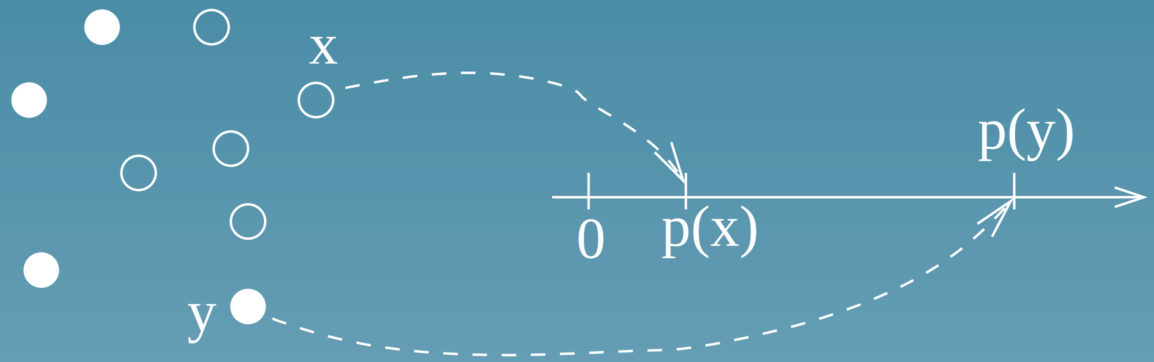
Product kernel

$$K_{prod}(x,y) = p(x)p(y)$$



Product kernel

$$K_{prod}(x, y) = p(x)p(y)$$



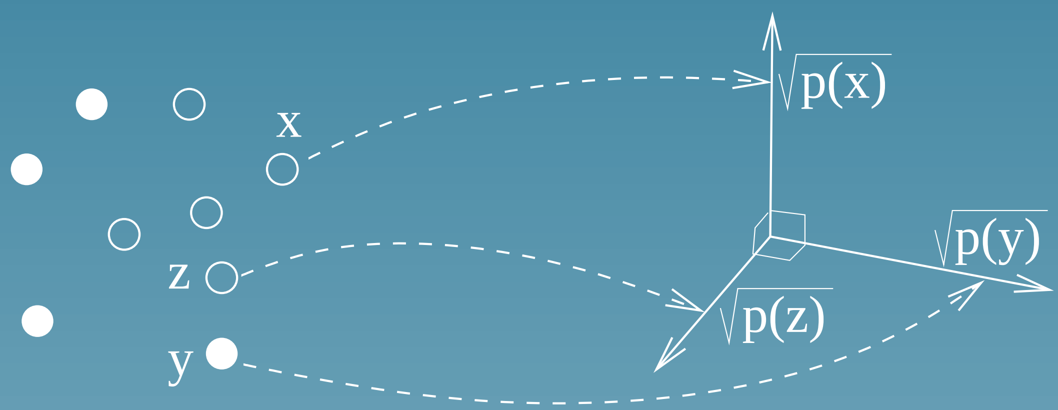
SVM = probability threshold classifier

Diagonal kernel

$$K_{diag}(x, y) = p(x)\delta(x, y)$$

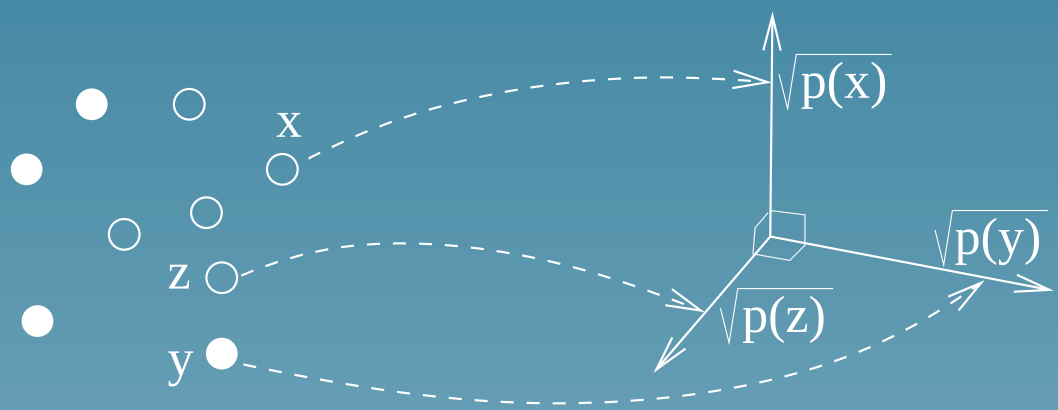
Diagonal kernel

$$K_{diag}(x, y) = p(x)\delta(x, y)$$



Diagonal kernel

$$K_{diag}(x, y) = p(x)\delta(x, y)$$



No learning

Interpolated kernel

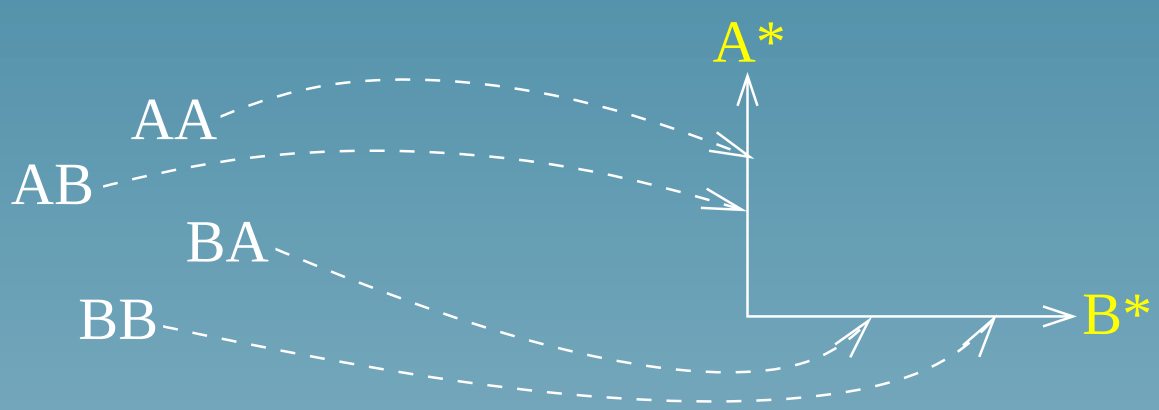
If objects are composite: $x = (x_1, x_2)$:

$$K(x, y) = K_{diag}(x_1, y_1) K_{prod}(x_2, y_2)$$

Interpolated kernel

If objects are composite: $x = (x_1, x_2)$:

$$K(x, y) = K_{diag}(x_1, y_1) K_{prod}(x_2, y_2)$$
$$= p(x_1)\delta(x_1, y_1) \times p(x_2|x_1)p(y_2|y_1)$$



General interpolated kernel

- Composite objects $x = (x_1, \ldots, x_n)$

General interpolated kernel

- Composite objects $x = (x_1, \ldots, x_n)$
- A list of index subsets: $\mathcal{V} = \{I_1, \ldots, I_v\}$ where $I_i \subset \{1, \ldots, n\}$ for $i = 1, \ldots, v$.

General interpolated kernel

- Composite objects $x = (x_1, \ldots, x_n)$
- A list of index subsets: $\mathcal{V} = \{I_1, \ldots, I_v\}$ where $I_i \subset \{1, \ldots, n\}$ for $i = 1, \ldots, v$.
- Interpolated kernel:

$$K_{\mathcal{V}}(x, y) = \frac{1}{|\mathcal{V}|} \sum_{I \in \mathcal{V}} K_{diag}(x_I, y_I) K_{prod}(x_{I^c}, y_{I^c})$$

Examples

- If $\mathcal{V} = \{\emptyset\}$, then:

$$K_{\mathcal{V}}(x, y) = K_{prod}(x, y).$$

- If $\mathcal{V} = \{[1, n]\}$, then:

$$K_{\mathcal{V}}(x, y) = K_{diag}(x, y).$$

Rare common subparts

For a given $p(x)$ and $p(y)$, we have:

$$K_{\mathcal{V}}(x,y) = K_{prod}(x,y) \times \frac{1}{|\mathcal{V}|} \sum_{I \in \mathcal{V}} \frac{\delta(x_I, y_I)}{p(x_I)}$$

Rare common subparts

For a given $p(x)$ and $p(y)$, we have:

$$K_{\mathcal{V}}(x, y) = K_{prod}(x, y) \times \frac{1}{|\mathcal{V}|} \sum_{I \in \mathcal{V}} \frac{\delta(x_I, y_I)}{p(x_I)}$$

x and y get closer in the feature space when they share rare common subparts

Implementation

- For many applications, computation time of the kernel is a limiting factor
- The sum in the interpolated might involve up to 2^n terms...
- Good news: factorization possible for particular choices of $p(.)$ and $\mathcal{V}$

Example 1: Weight matrix kernel

$$p(x) = \prod_{i=1}^{n} p_i(x_i)$$

$$\mathcal{V} = \mathcal{P}([1, n])$$

then:

$$K_{\mathcal{V}}(x, y) = \frac{1}{2^n} \prod_{i=1}^{n} \phi_i(x_i, y_i),$$

with:

$$\phi_i(x_i, y_i) = \begin{cases} p_i(x_i) + p_i(x_i)^2 & \text{if } x_i = y_i \\ p_i(x_i)p_i(y_i) & \text{if } x_i \neq y_i \end{cases}$$

Weight matrix kernel: Proof

$$K(x, y) = \frac{1}{2^n} \sum_{\mathcal{V} \subset [1,n]} \left[\prod_{i \in \mathcal{V}} p(x_i) \delta(x_i, y_i) \times \prod_{i \notin \mathcal{V}} p(x_i) p(y_i) \right]$$

$$= \frac{1}{2^n} \prod_{i=1}^{n} \left[p(x_i) \delta(x_i, y_i) + p(x_i) p(y_i) \right].$$

Example 2: Markov block kernel

$$p(x) = p_1(x_1) \prod_{i=2}^{n} p_i(x_i | x_{i-1})$$

$$\mathcal{V} = \{[k, l] : 1 \leq k \leq l \leq n\} \cap \{\emptyset\}$$

then:

$$K_{\mathcal{V}}(x, y) = \phi_0(n) + \phi_1(n) + \phi_2(n),$$

with:

$$\begin{cases} \phi_0(1) = p_1(x_1)p_1(y_1) \\ \phi_1(1) = p_1(x_1)\delta(x_1, y_1) \\ \phi_2(1) = 0 \end{cases}$$

and for $i = 2, \ldots, n$

$$\begin{cases} \phi_0(i) = p_i(x_i|x_{i-1})p_i(y_i|y_{i-1}) \times \phi_0(i-1) \\ \phi_1(i) = p_i(x_i|x_{i-1})\delta(x_i, y_i) \\ \qquad\qquad \times \left[\phi_1(i-1) + \frac{p_i(y_i|y_{i-1})}{p_i(x_i)}\phi_0(i-1)\right] \\ \phi_2(i) = p_i(x_i|x_{i-1})p_i(y_i|y_{i-1}) \times [\phi_1(i-1) + \phi_2(i-1)] \end{cases}$$

Weight matrix kernel: Proof

Classical dynamic programming.

Example 3: common subtree kernel

- Let T be a rooted tree
- λ the root, $f(s)$ the father node of any node $s \in T$
- Graphical model and common subtrees:

$$p(x) = p_\lambda(x_\lambda) \prod_{s \in T \setminus \{\lambda\}} p_s(x_s | x_{f(s)})$$

$$\mathcal{V} = \{ S \text{ rooted subtree of } \}$$

Then:

$$K(x,y) = \sum_{S \in \mathcal{V}} \Big[\prod_{s \in S} p(x_s | x_{f(s)}) \delta(x_s, y_s)$$

$$\times \prod_{s \notin S} p(x_s | x_{f(s)} p(y_s | y_{f(s)}) \Big]$$

Can be computed in linear time by one post-order traversal of the tree (similar to the CTW algorithm by Willems et al.)

Example 4: common subtree kernel with latent variables

- Same as example 3 but some variables are not observed:

$$K(x_{obs}, y_{obs}) = \sum_{S \in \mathcal{V}} \sum_{z_S \in \mathcal{A}^S} p(z_S) p(x_{obs} | z_S) p(y_{obs} | z_S)$$

- A bit longer to write, but still possible

- Linear time computation

Part 3

Application:
Gene functional prediction from phylogenetic profiles

Mini introduction

- Genes are small parts of the DNA which encode proteins.
- About 6,000 genes in the baker yeast, 30,000 in human
- The sequence of the genes are (almost) known (sequencing projets)
- Next big challenge: understand the function of the genes

Definition

- The phylogenetic profile of a gene is a vector of bits which indicates the presence (1) or absence (0) of the gene in every fully sequenced genome.

Gene	aero	aful	...	tpal	worm
YAL001C	1	1	...	0	0
YAB002W	0	0	...	0	1
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$

- Can be estimated *in silico* by sequence similarity search

From profile to function

- Genes are likely to be transmitted together during evolution when they participate:
  - ⋆ to a common structural complex,
  - ⋆ to a common pathway.
- Consequently genes with similar phylogenetic profiles are likely to have similar functions
- How to measure the similarity between profiles?

Naive approach

- Count the number of bits in common:

x	1	1	0	1	0	0	0	1	1	0
y	1	0	1	0	0	0	0	1	0	1

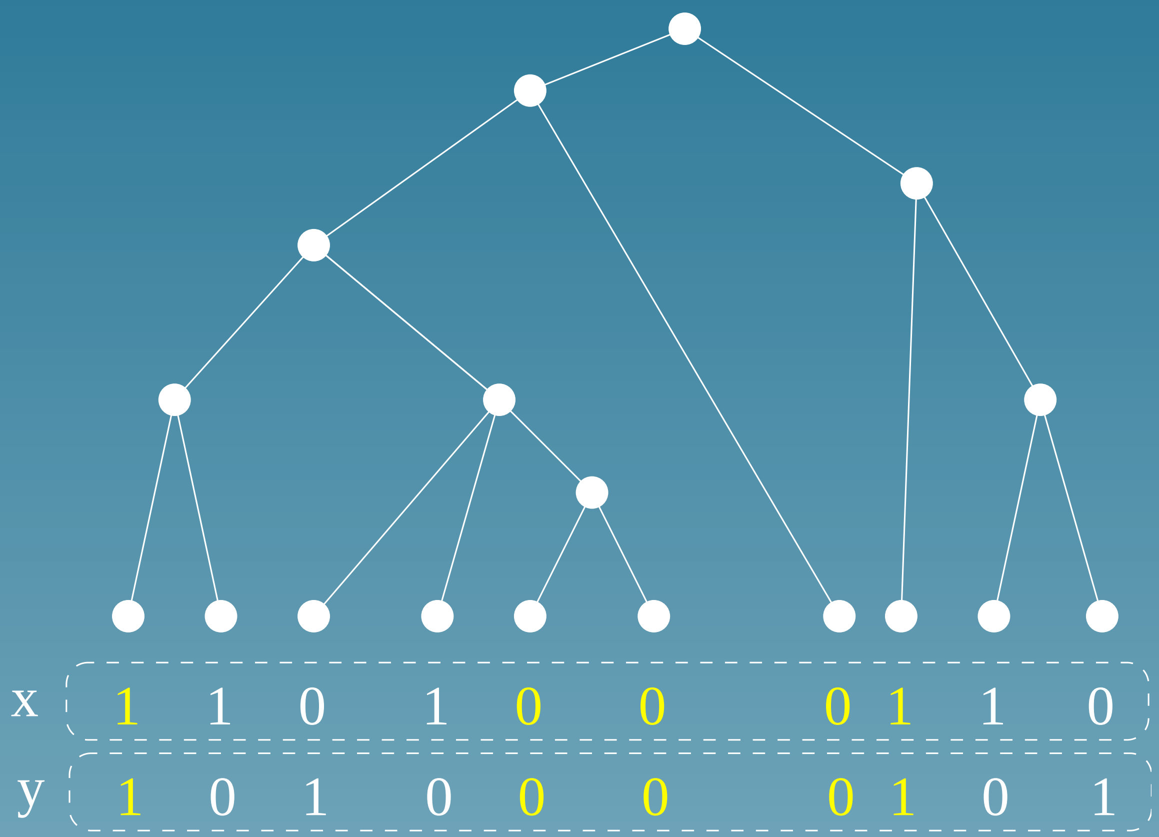
$$s(x, y) = 5$$

- Cluster or use k-NN for gene function prediction with this similarity measure (Pellegrini et al., 1999)

Limitations of the naive approach

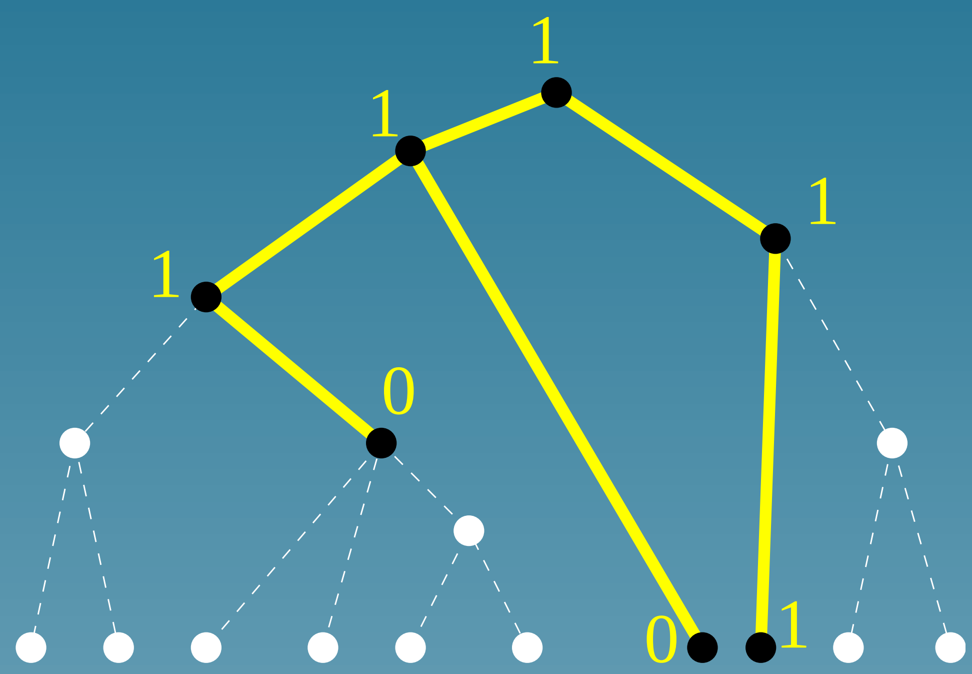
- The set of sequenced organisms has a strong influence on the similarity score (e.g., eukaryotes are under-represented)
- A more detailed understanding of when two proteins were transmitted together or not during evolution could be useful
- A function could be characterized by only a subset of the bits (e.g., 1 in eukaryotes, 0 in bacteria, whatever in archae)

What is not used in the naive approach



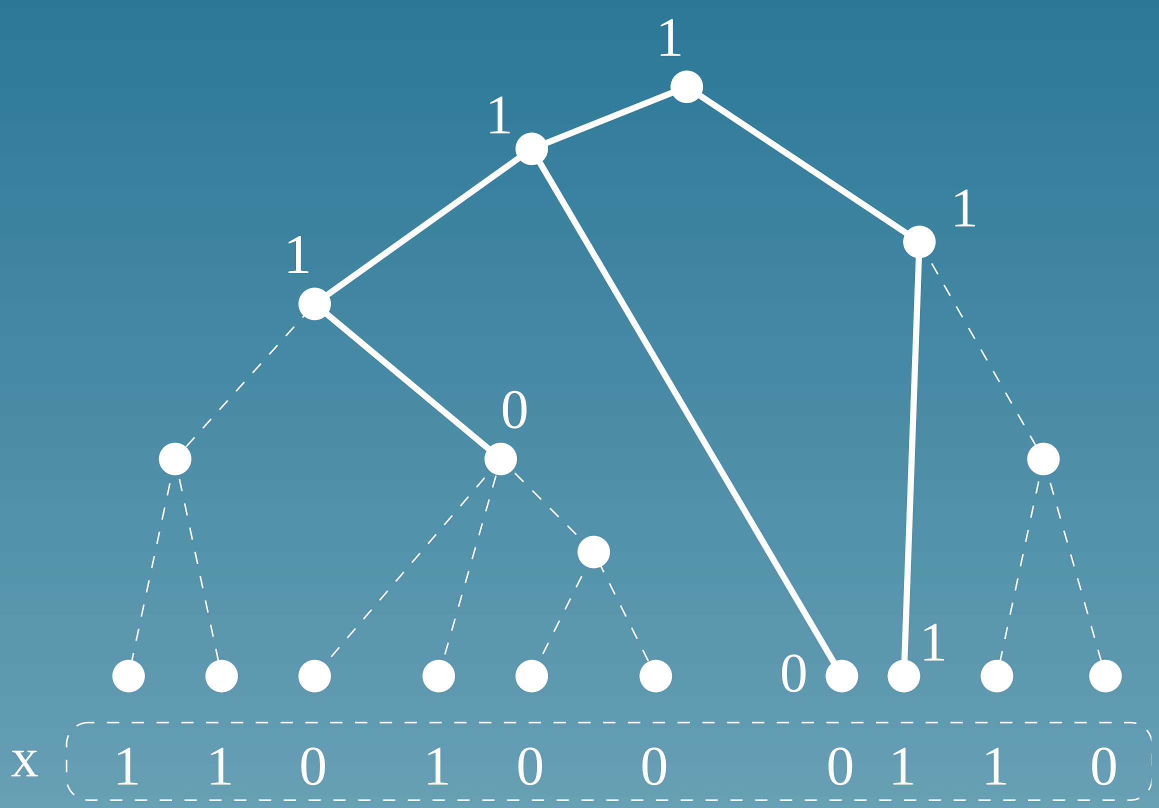
The knowledge of the phylogenetic tree.

Evolution pattern



- A possible pattern of transmission during evolution
- Mathematically, a rooted subtree with nodes labeled 0 or 1.

Evolution patterns and phylogenetic profiles



Impossible to know for sure if the gene followed exactly this evolution pattern

Probabilistic model of gene transmission

- The phylogenetic tree as a tree graphical model
- Simplified model:
  - ⋆ $P(1) = 1 - P(0) = 0.9$, at the root,
  - ⋆ Along each branch transmission follows the transition matrix:

$$\begin{pmatrix} 0.9 & 0.1 \\ 0.1 & 0.9 \end{pmatrix}$$

Probabilistic assignment of evolution pattern

For a phylogenetic profile x and an evolution pattern e:

- $P(e)$ quantifies how "natural" the pattern is
- $P(x|e)$ quantifies how likely the pattern e is the "true history" of the profile x

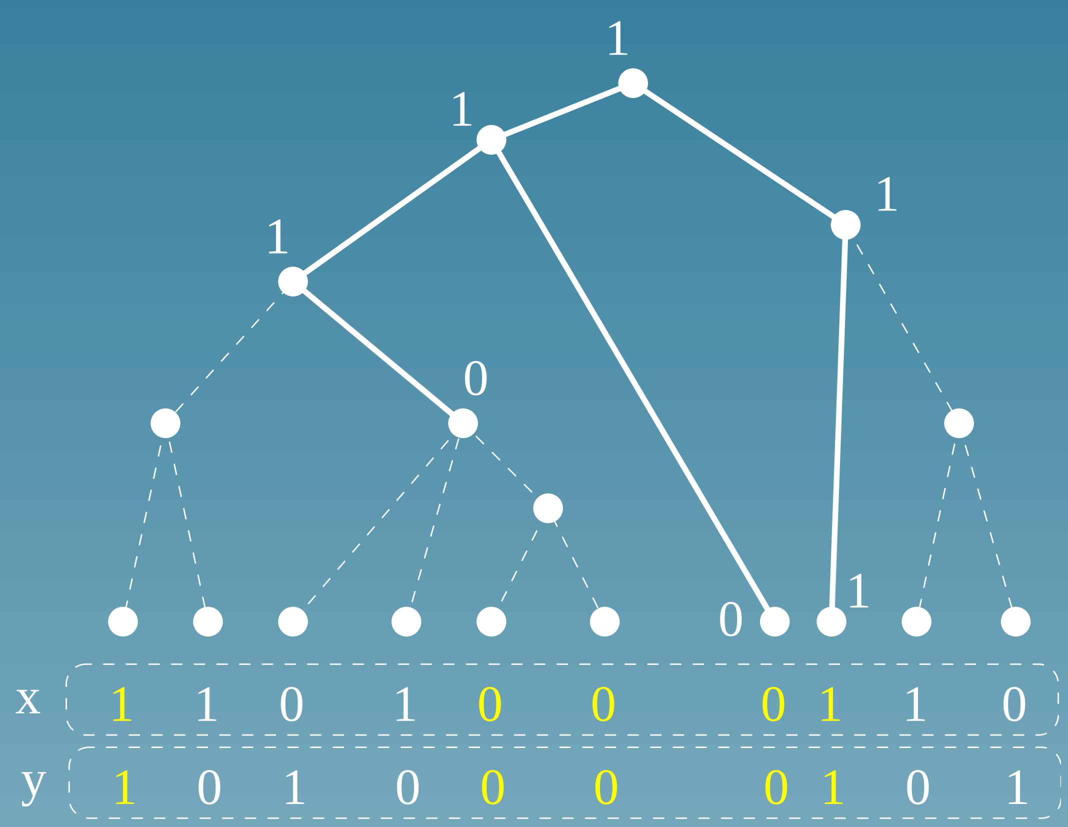
Representation of a profile in terms of evolution patterns

- Consider all possible evolution patterns $(e_1, \ldots, e_N)$. A profile x can be represented by the N-dimensional vector:

$$\Phi(x) = \begin{pmatrix} \sqrt{P(e_1)}P(x|e_1) \\ \vdots \\ \sqrt{P(e_N)}P(x|e_N) \end{pmatrix}$$

- This leads to the probabilistic kernel described before

Comparing two profiles through evolution patterns



Gene function prediction with SVM

- Profiles for 2465 genes of *S. Cerevisiae* were computed by BLAST search (cf Pavlidis et al. 2001), using 24 genomes.
- Consensus phylogenetic tree (cf. Liberles et al. 2002) with simplified probabilistic model of gene transmission
- SVM trained to predict all functional classes of the MIPS catalog with at least 10 genes (cross-validation)
- Comparison of the tree kernel with the naive kernel

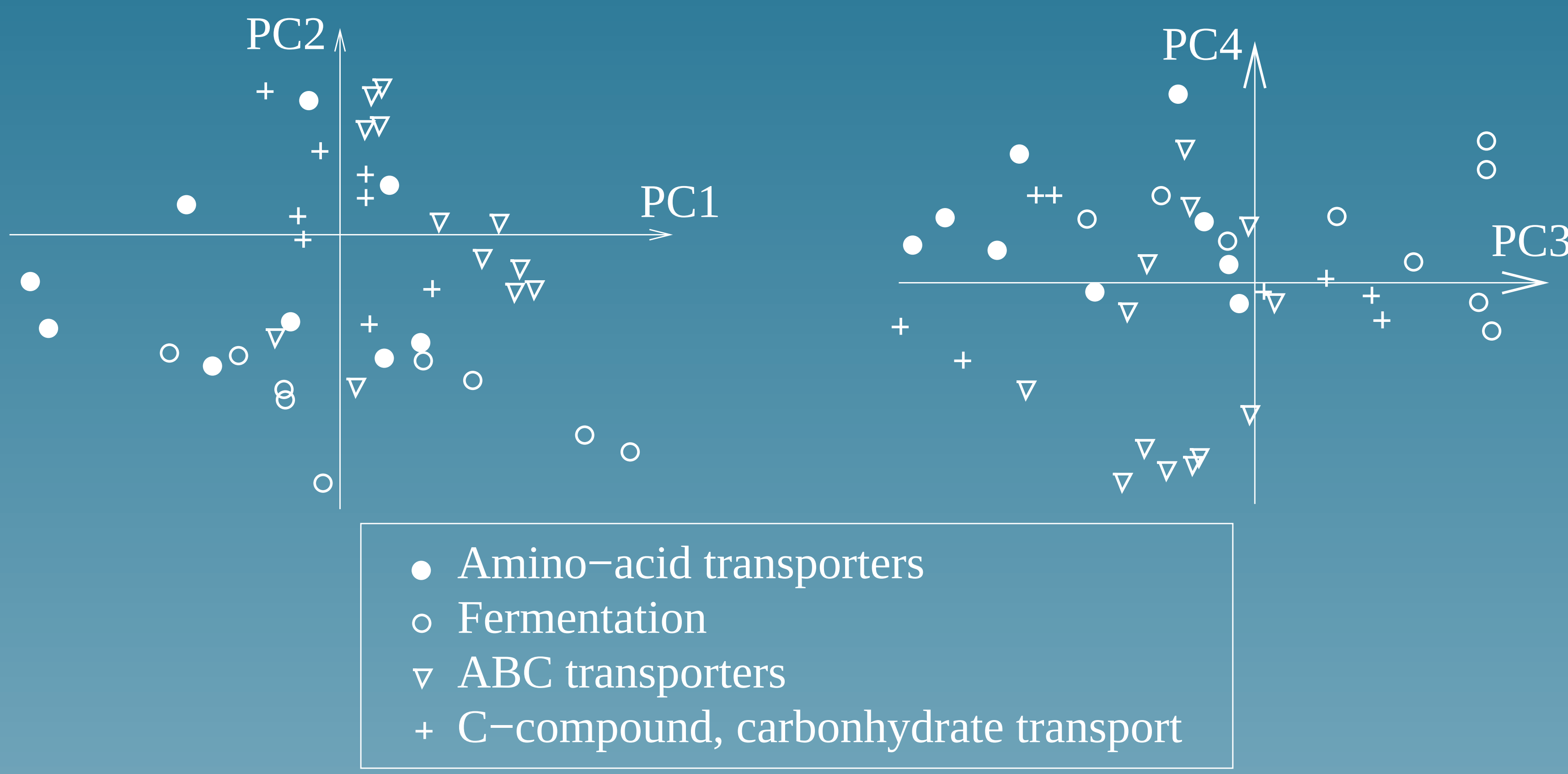
Results (ROC 50)

Functional class	Naive kernel	Tree kernel	Difference
Amino-acid transporters	0.74	0.81	**+ 9%**
Fermentation	0.68	0.73	**+ 7%**
ABC transporters	0.64	0.87	**+ 36%**
C-compound transport	0.59	0.68	**+ 15%**
Amino-acid biosynthesis	0.37	0.46	**+ 24%**
Amino-acid metabolism	0.35	0.32	- *9%*
Tricarboxylic-acid pathway	0.33	0.48	**+ 45%**
Transport Facilitation	0.33	0.28	- *15%*

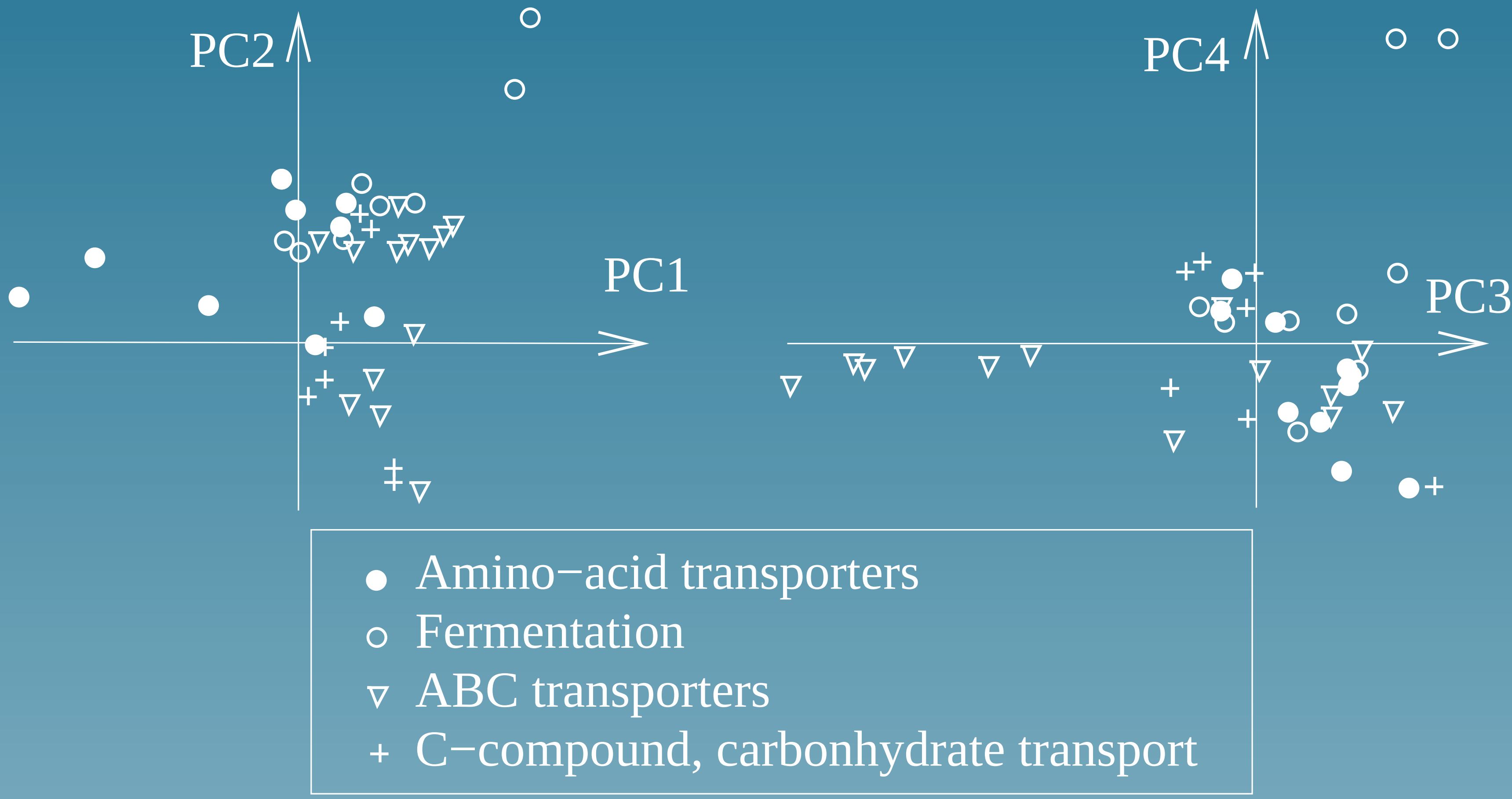
A insight into the feature space

- PCA can be performed implicitly in the feature space with a kernel function: kernel-PCA (Scholkopf et al. 1999)
- Projecting the genes on the first principal components gives an idea of the shape of the features space

Naive kernel PCA



Tree kernel PCA



Conclusion

Conclusion

- A general method to derive a kernel from a probability distribution
- Encouraging results
- Some problems and questions: diagonal dominance? Role of the prior distribution?
- Contributes to a general approach: encode genomic information into kernel functions.