#### Regulatory sequence analysis

## Matrix-based pattern matching

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# Regulatory motif: position-specific scoring matrix (PSSM) Binding motif of the yeast TF Pho4p (TRANSFAC matrix F\$PHO4\_01)

Pos	1	2	3	4	5	6	7	8	9	10	11	12
Base												
A	1	3	2	0	8	0	0	0	0	0	1	2
C	2	2	3	8	0	8	0	0	0	2	0	2
G	1	2	3	0	0	0	8	0	5	4	5	2
T	4	1	0	0	0	0	0	8	3	2	2	2
			V	С	Α	С	G	T	K	В		



#### Frequency matrix

Pos	1	2	3	4	5	6	7	8	9	10	11	12
A	0.13	0.38	0.25	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.13	0.25
C	0.25	0.25	0.38	1.00	0.00	1.00	0.00	0.00	0.00	0.25	0.00	0.25
G	0.13	0.25	0.38	0.00	0.00	0.00	1.00	0.00	0.63	0.50	0.63	0.25
Т	0.50	0.13	0.00	0.00	0.00	0.00	0.00	1.00	0.38	0.25	0.25	0.25
Sum	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

$$f_{i,j} = \frac{n_{i,j}}{\sum_{i=1}^{A} n_{i,j}}$$

A alphabet size (=4)  $n_{i,j,}$  occurrences of residue i at position j  $p_i$  prior residue probability for residue i  $f_{i,i}$  relative frequency of residue i at position j

Reference: Hertz (1999). Bioinformatics 15:563-577.

#### Pseudo-count correction

Pos	1	2	3	4	5	6	7	8	9	10	11	12
Α	0.15	0.37	0.26	0.04	0.93	0.04	0.04	0.04	0.04	0.04	0.15	0.26
C	0.24	0.24	0.35	0.91	0.02	0.91	0.02	0.02	0.02	0.24	0.02	0.24
G	0.13	0.24	0.35	0.02	0.02	0.02	0.91	0.02	0.58	0.46	0.58	0.24
Т	0.48	0.15	0.04	0.04	0.04	0.04	0.04	0.93	0.37	0.26	0.26	0.26
Sum	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

1st option: identically distributed pseudo-weight

$$f'_{i,j} = \frac{n_{i,j} + k/A}{\sum_{i=1}^{A} n_{i,j} + k}$$

2nd option: pseudo-weight distributed according to residue priors

$$f'_{i,j} = \frac{n_{i,j} + p_i k}{\sum_{i=1}^{A} n_{i,j} + k}$$

A alphabet size (=4)  $n_{i,j}$ , occurrences of residue i at position j  $p_i$  prior residue probability for residue i  $f_{i,j}$  relative frequency of residue i at position j k pseudo weight (arbitrary, 1 in this case)  $f_{i,j}$  corrected frequency of residue i at position j

Reference: Hertz (1999). Bioinformatics 15:563-577.

#### Probability of a sequence segment under the matrix model

Pos	1	2	3	4	5	6	7	8	9	10	11	12
Α	0.15	0.37	0.26	0.04	0.93	0.04	0.04	0.04	0.04	0.04	0.15	0.26
С	0.24	0.24	0.35	0.91	0.02	0.91	0.02	0.02	0.02	0.24	0.02	0.24
G	0.13	0.24	0.35	0.02	0.02	0.02	0.91	0.02	0.58	0.46	0.58	0.24
Т	0.48	0.15	0.04	0.04	0.04	0.04	0.04	0.93	0.37	0.26	0.26	0.26
Sequence S	Α	Т	G	С	G	Т	Α	Α	Α	G	С	Т
P(res)	0.15	0.15	0.35	0.91	0.02	0.04	0.04	0.04	0.04	0.46	0.02	0.26
P(S M)	5.32E-1	3									N	V
Let										$P(S \mid M)$		$T_{f'}$
<ul> <li>M be a f</li> </ul>	reauenc	v matrix	of width	) w						_ (~	- / <b>1</b> j=	$\int_{-1}^{J} r_{j} J$

- Let
  - M be a frequency matrix of width w
  - $S = \{r_1, r_2, ..., r_w\}$  be a sequence segment of length w (same length as the matrix)
  - $r_i$  is the residue found at position j of the sequence segment S.
- The corrected frequencies  $F'_{ij}$  can be used to estimate the probability to observe residue i at position j of the motif described by the matrix
- The probability to generate the sequence segment *S* under the model described by the matrix M is the product of the frequencies of residues at the corresponding columns of the matrix.

#### Probability of the best sequence segment under the matrix model

Pos	1	2	3	4	5	6	7	8	9	10	11	12
A	0.15	0.37	0.26	0.04	0.93	0.04	0.04	0.04	0.04	0.04	0.15	0.26
С	0.24	0.24	0.35	0.91	0.02	0.91	0.02	0.02	0.02	0.24	0.02	0.24
G	0.13	0.24	0.35	0.02	0.02	0.02	0.91	0.02	0.58	0.46	0.58	0.24
Т	0.48	0.15	0.04	0.04	0.04	0.04	0.04	0.93	0.37	0.26	0.26	0.26
Sequence S	T	Α	G	С	Α	С	G	Т	G	G	G	T
P(res)	0.48	0.37	0.35	0.91	0.93	0.91	0.91	0.93	0.58	0.46	0.58	0.26
P(S M)	1.59E-0	)3							Г		ν	v

This segment of sequence is associated to the highest possible probability given the matrix : P(S|M)

Each nucleotide of the sequence corresponds to the residue with the highest probability in the corresponding column of the matrix.

$$P(S \mid M) = \prod_{j=1}^{w} f'_{r_j j}$$

#### Probability of a sequence segment under a Bernoulli background model

	Pos	Prior											
-	Α	0.325											
Ī	С	0.175											
Ī	G	0.175											
Ī	Т	0.325											
Sequ	ence S	Α	Т	G	С	G	Т	Α	Α	Α	G	С	Т
	P(res)	0.325	0.325	0.175	0.175	0.175	0.325	0.325	0.325	0.325	0.175	0.175	0.325
	P(S B)	6.29E-	08										

- A background model (B) should be defined to estimate the probability of a sequence motif outside of the motif.
- Various possibilities can be envisaged to define the background model
  - Bernoulli model with equiprobable residues (this should generally be avoided, because most biological sequences are biased towards some residues)
  - Bernoulli model with residue-specific probabilities  $(p_r)$
  - Markov chains
- Under a Bernoulli model, the probability of a sequence motif S is the probability of the prior frequencies of its residues  $r_i$ .

$$P(S \mid B) = \prod_{j=1}^{w} p_{r_j}$$

#### Weight of a sequence segment

<b>\</b> /	Weight -11.67 =SUM[W(r)]											
W(r)	-0.79	-0.79	0.70	1.65	-2.20	-2.20	-2.20	-2.20	-2.20	0.97	-2.20	-0.23
residue r	Α	Т	G	С	G	Т	Α	Α	Α	G	С	T
Т	0.39	-0.79	-2.20	-2.20	-2.20	-2.20	-2.20	1.05	0.13	-0.23	-0.23	-0.23
G	-0.29	0.32	0.70	-2.20	-2.20	-2.20	1.65	-2.20	1.19	0.97	1.19	0.32
С	0.32	0.32	0.70	1.65	-2.20	1.65	-2.20	-2.20	-2.20	0.32	-2.20	0.32
Α	-0.79	0.13	-0.23	-2.20	1.05	-2.20	-2.20	-2.20	-2.20	-2.20	-0.79	-0.23
Pos	1	2	3	4	5	6	7	8	9	10	11	12

$$W_{S} = \ln \left( \frac{P(S \mid M)}{P(S \mid B)} \right)$$

- The weight of a sequence segment is defined as the log-ratio between
  - P(S/M), the sequence probability under the model described by the PSSM, and
  - *P*(*S*/*B*), the sequence probability under the background model.
- The weight  $W_s$  represents the likelihood that segment S is an occurrence of the motif M rather than being issued from the background model B.
- Under Bernoulli asumption, the weight matrix  $W_{ij}$  can be used to simplify the computation of segment weights.

**Under assumption of a Bernoulli** background model, this formula becomes

$$W_{S} = \ln\left(\frac{P(S \mid M)}{P(S \mid B)}\right) = \ln\left(\frac{\prod_{j=1}^{w} f'_{r_{j}j}}{\prod_{j=1}^{w} p_{r_{j}}}\right) = \sum_{j=1}^{w} \ln\left(\frac{f'_{r_{j}j}}{p_{r_{j}}}\right) = \sum_{j=1}^{w} W_{r_{j}j}$$

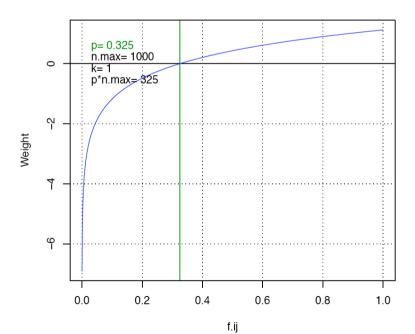
- 1		
	$W_S$	weight of sequence segment $S$
	P(S M)	probability of the sequence segment, given
		the matrix
	P(S B)	probability of the sequence segment, given
		the background
	j	position within the segment and within the
		matrix
	$r_{i}$	residue at position $j$ of the sequence
	J	segment
	$p_{rj}$	prior probability of residue $r_i$
	$f_{rij}^{j}$	probability of residue $r_i$ at position j of the
	· JJ	matrix

#### Position-weight matrix

Prior	Pos	1	2	3	4	5	6	7	8	9	10	11	12
0.33	A	-0.79	0.13	-0.23	-2.20	1.05	-2.20	-2.20	-2.20	-2.20	-2.20	-0.79	-0.23
0.18	C	0.32	0.32	0.70	1.65	-2.20	1.65	-2.20	-2.20	-2.20	0.32	-2.20	0.32
0.18	G	-0.29	0.32	0.70	-2.20	-2.20	-2.20	1.65	-2.20	1.19	0.97	1.19	0.32
0.33	Т	0.39	-0.79	-2.20	-2.20	-2.20	-2.20	-2.20	1.05	0.13	-0.23	-0.23	-0.23
1	Sum	-0.37	-0.02	-1.02	-4.94	-5.55	-4.94	-4.94	-5.55	-3.08	-1.13	-2.03	0.19

$$W_{i,j} = \ln\left(\frac{f'_{i,j}}{p_i}\right) \int_{i=1}^{r_{i,j}} \frac{n_{i,j} + p_i k}{\sum_{i=1}^{A} n_{i,j} + k} \qquad \sum_{i=1}^{A} f'_{i,j} = \frac{n_{i,j} + p_i k}{\sum_{i=1}^{A} n_{i,j} + k}$$

alphabet size (=4)  $p_i$  prior residue probability for residue i  $f_{i,j}$  relative frequency of residue i at position j k pseudo weight (arbitrary, 1 in this case)  $f'_{i,j}$  corrected frequency of residue i at position j



#### Scanning a sequence with a weight matrix

 The weight matrix is successively aligned to each position of the sequence, and the score is the sum of weights for the letters aligned at each position (Hertz & Stormo, 1999).

Ex: sequence .... GCTGCACGTGGCCC..

#### **Weight matrix**

	1	2	3	4	5	6	7	8	9	10	11	12
Α	-0.8	0.1	-0.2	-2.2	1.0	-2.2	-2.2	-2.2	-2.2	-2.2	-0.8	-0.2
С	0.3	0.3	0.7	1.6	-2.2	1.6	-2.2	-2.2	-2.2	0.3	-2.2	0.3
G	-0.3	0.3	0.7	-2.2	-2.2	-2.2	1.6	-2.2	1.2	1.0	1.2	0.3
A C G T	0.4	-0.8	-2.2	-2.2	-2.2	-2.2	-2.2	1.0	0.1	-0.2	-0.2	-0.2

#### **Scanning**

1	SUM -10.54													С	С
2		С	т	G	С	A	С	G	т	G	G	С	С	С	
	7.55	0.3	-0.8	0.7	1.6	1.0	1.6	1.6	1.0	1.2	1.0	-2.2	0.3		
3		Т	G	С	A	С	G	т	G	G	С	С	С		
	-9.93	0.4	0.3	0.7	-2.2	-2.2	-2.2	-2.2	-2.2	1.2	0.3	-2.2	0.3		

#### Markov chains and transition matrices

$$P(r_i \mid S_{i-m,i-1})$$

- The two tables below show the transition matrices for a Markov model of order 1 (top) and 2 (bottom), respectively.
- The two models were trained with yeast non-coding upstream sequences.
- Notice the strong probability of transitions from AA to A and TT to T.

#### Transition matrix, order 1

Pre/Suffix	Α	С	G	Т	P(Prefix)	N(Suffix)
Α	0.359	0.171	0.187	0.283	0.313	1,467,035
C	0.329	0.199	0.163	0.308	0.191	894,658
G	0.317	0.211	0.198	0.274	0.187	874,683
Т	0.255	0.193	0.193	0.359	0.310	1,451,623
P(Suffix)	0.313	0.191	0.187	0.310		
N(Suffix)	1,467,895	894,543	874,444	1,451,117	1	

#### **Transition matrix, order 2**

Prefix/Suffix	Α	С	G	Т	P(Prefix	N(Prefix
AA	0.388	0.161	0.200	0.251	0.112	525,000
AC	0.339	0.198	0.173	0.290	0.054	251,072
AG	0.345	0.204	0.196	0.255	0.059	274,601
AT	0.311	0.184	0.182	0.323	0.088	413,946
CA	0.347	0.178	0.189	0.286	0.063	293,750
cc	0.341	0.190	0.161	0.309	0.038	178,110
CG	0.293	0.221	0.196	0.290	0.031	145,876
СТ	0.229	0.195	0.205	0.371	0.059	275,634
GA	0.394	0.155	0.187	0.264	0.059	277,053
GC	0.330	0.205	0.169	0.297	0.039	184,192
GG	0.318	0.217	0.187	0.277	0.037	173,266
GT	0.285	0.175	0.204	0.336	0.051	239,384
TA	0.300	0.193	0.168	0.339	0.079	369,426
TC	0.313	0.203	0.152	0.332	0.060	280,131
TG	0.302	0.209	0.208	0.282	0.060	279,783
TT	0.210	0.208	0.189	0.392	0.111	520,906
P(Suffix)	0.313	0.191	0.187	0.310		
N(suffix)	1,466,075	893,444	873,260	1,449,351		

#### Scoring a sequence segment with a Markov model

• The example below illustrates the computation of the probability of a sequence segment (CCTACTATATGCCCAGAATT) with a Markov chain of order 2, calibrated from 3nt frequencies on the yeast genome.

pos

_	$L_{\perp}$
$P(S) = P(S_{1,m})$	$\prod_{i=m+1} P(r_i \mid S_{i-m,i-1})$
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**Transition matrix, order 2** 

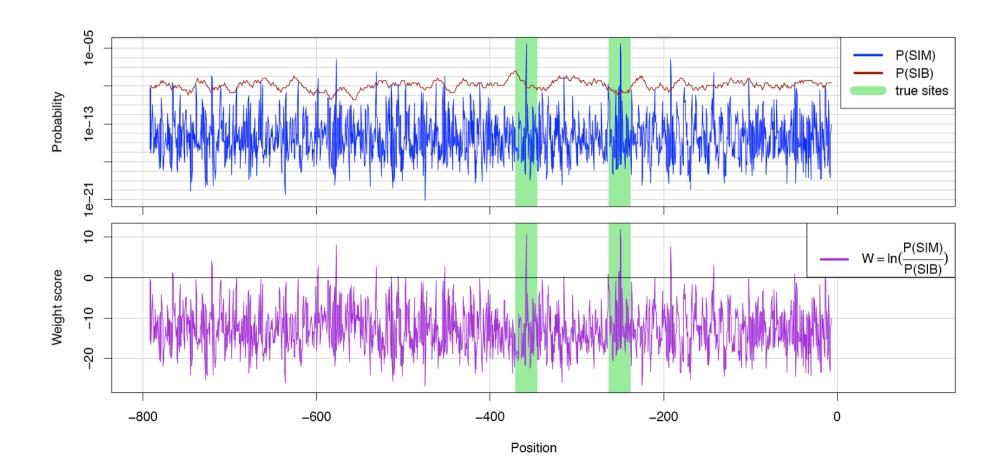
Transition matrix, order 2						
Prefix/Suffix	Α	С	G	T	P(Prefix	N(Prefix
AA	0.388	0.161	0.200	0.251	0.112	525,000
AC	0.339	0.198	0.173	0.290	0.054	251,072
AG	0.345	0.204	0.196	0.255	0.059	274,601
AT	0.311	0.184	0.182	0.323	0.088	413,946
CA	0.347	0.178	0.189	0.286	0.063	293,750
CC	0.341	0.190	0.161	0.309	0.038	178,110
CG	0.293	0.221	0.196	0.290	0.031	145,876
CT	0.229	0.195	0.205	0.371	0.059	275,634
GA	0.394	0.155	0.187	0.264	0.059	277,053
GC	0.330	0.205	0.169	0.297	0.039	184,192
GG	0.318	0.217	0.187	0.277		173,266
GT	0.285	0.175	0.204	0.336	0.051	239,384
TA	0.300	0.193	0.168	0.339	0.079	369,426
TC	0.313	0.203	0.152	0.332	0.060	280,131
TG	0.302	0.209	0.208	0.282	0.060	279,783
TT	0.210	0.208	0.189	0.392	0.111	520,906
P(Suffix)	0.313	0.191	0.187	0.310		
N(suffix)	1,466,075	893,444	873,260	1,449,351		

P(R W)	wR	S	P(S)
1 P(CC)	0.038 cc	CC	3.80E-02
2 P(T CC)	0.309 ccT	CCT	1.17E-02
3 P(A CT)	0.229 ctA	CCTA	2.69E-03
4 P(C TA)	0.193 taC	CCTAC	5.19E-04
5 P(T AC)	0.290 acT	CCTACT	1.50E-04
6 P(A CT)	0.229 ctA	CCTACTA	3.45E-05
7 P(T TA)	0.339 taT	CCTACTAT	1.17E-05
8 P(A AT)	0.311 atA	CCTACTATA	3.63E-06
9 P(T TA)	0.339 taT	CCTACTATAT	1.23E-06
10 P(G AT)	0.182 atG	CCTACTATATG	2.25E-07
11 P(C TG)	0.209 tgC	CCTACTATATGC	4.69E-08
12 P(C GC)	0.205 gcC	CCTACTATATGCC	9.61E-09
13 P(C CC)	0.190 ccC	CCTACTATATGCCC	1.82E-09
14 P(A CC)	0.341 ccA	CCTACTATATGCCCA	6.21E-10
15 P(G CA)	0.189 caG	CCTACTATATGCCCAG	1.17E-10
16 P(A AG)	0.345 agA	CCTACTATATGCCCAGA	4.04E-11
17 P(A GA)	0.394 gaA	CCTACTATATGCCCAGAA	1.59E-11
18 P(T AA)	0.251 aaT	CCTACTATATGCCCAGAAT	4.00E-12
19 P(T AT)	0.323 atT	CCTACTATATGCCCAGAATT	1.29E-12

### Scanning a sequence with a position-specific scoring matrix

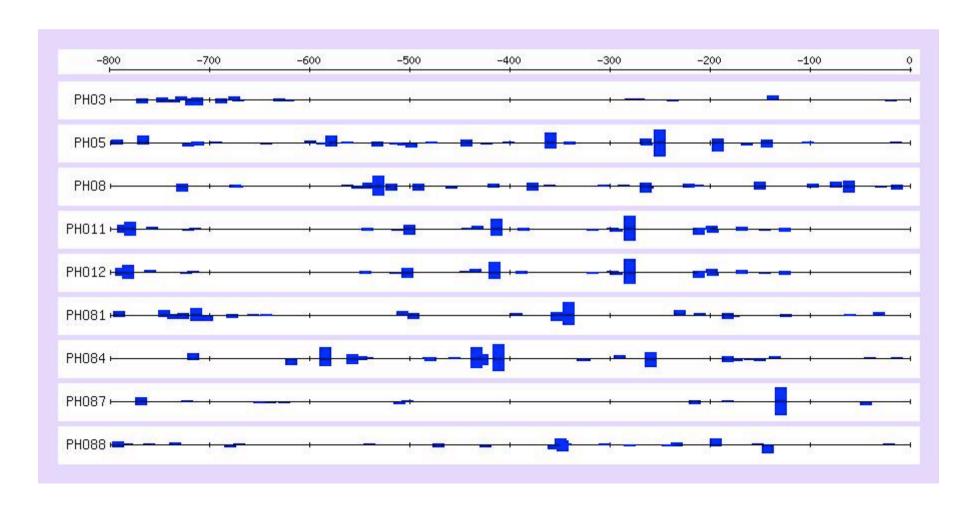
- P(S|M) probability for site S to be generated as an instance of the motif.
- P(S|B) probability for site S to be generated as an instance of the background.
- weight, i.e. the log ratio of the two above probabilities.
  - A positive weight indicates that a site is more likely to be an instance of the motif than of the background.

$$W_{S} = \ln \left( \frac{P(S \mid M)}{P(S \mid B)} \right)$$



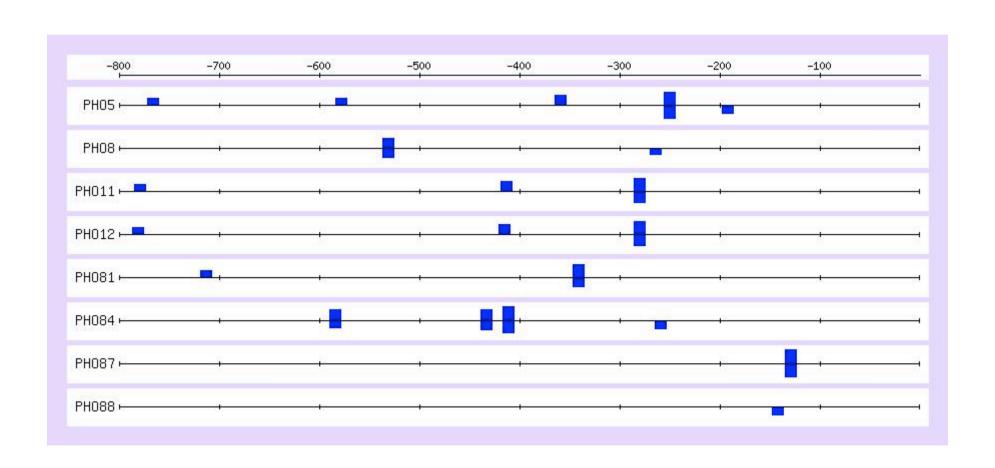
#### Matrix search : matching positions

- Matrix-based pattern matching is more sensitive than string-based pattern matching.
- How to choose the threshold?



#### Matrix search: threshold selection

- Patser includes an option to automatically select a threshold on the basis of
  - the information content of the matrix
  - the length of the sequence to be scanned
- Another approach is to select the threshold on the basis of scores returned when the matrix is used to scan known binding sites for the factor.

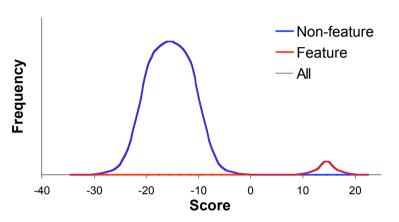


#### Matrix search

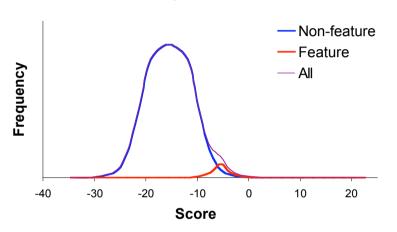
- The sequence is scanned with the matrix, and a score is assigned to each position.
- The highest score reflects the highest probability of having a functional site.
- How to define the threshold? There is a trade:
  - high selectivity ⇔ low sensitivity
  - high confidence in the predicted sites, but many real sites are missed
  - low selectivity 
     ⇔ high sensitivity
     the real sites are drawn in a see of false positive

## Discrimination power of a matrix

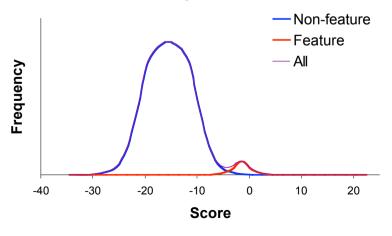




#### **Poorly discriminant**



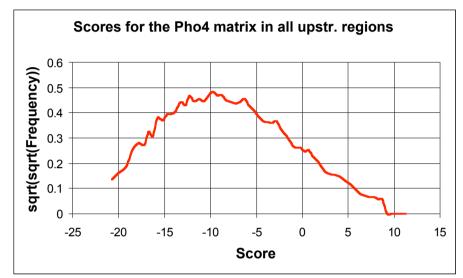
#### **Reasonably discriminant**

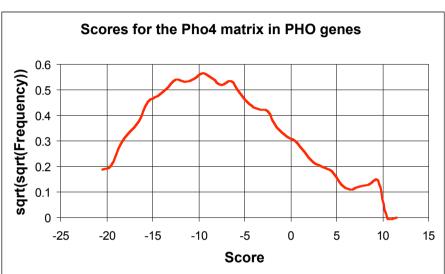


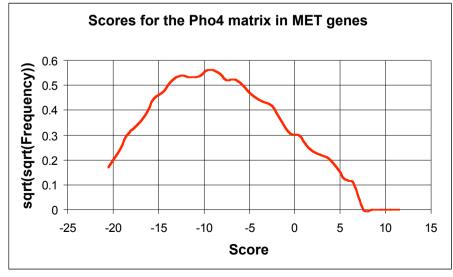
#### Regulatory sequence analysis

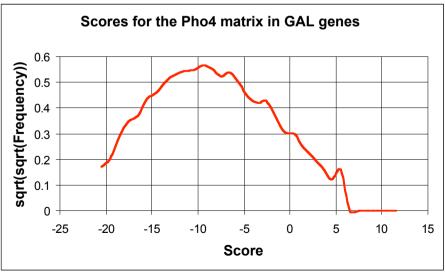
# Genome-scale matrix-based pattern matching

#### Pho4p matrix: score distribution in all upstream sequences









# Genome-scale pattern matching: top scoring upstream sequences for the Pho4p matrix

ORF	strand	start	end	score	gene description
YMR255W	D	-326	-315	10.2	hypothetical protein
YKR050W	D	-744	-733	9.83	TRK2; moderate-affinity potassium transport protein
YKR048C	D	-442	-431	9.83	NAP1; nucleosome assembly protein I
YKR047W	D	-689	-678	9.83	questionable ORF
YKR031C	D	-597	-586	9.83	SPO14; phospholipase D
YCR037C	D	-135	-124	9.83	PHO87; member of the phosphate permease family
YAL038W	D	-525	-514	9.83	CDC19; pyruvate kinase
YML123C	D	<del>-4</del> 17	-406	9.56	PHO84; high-affinity inorganic phosphate/H+ symporter
YJL067W	D	-442	<del>-4</del> 31	9.56	questionable ORF
YCR051W	D	-298	-287	9.56	weak similarity to ankyrins
YBR296C	D	-326	-315	9.56	strong similarity to phosphate-repressible phosphate permease
YHR215W	D	-286	-275	9.46	PHO12; secreted acid phosphatase
YDR281C	D	-282	-271	9.46	hypothetical protein
YBR093C	D	-256	-245	9.46	PHO5; repressible acid phosphatase precursor
YAR071W	D	-286	-275	9.46	PHO11; secreted acid phosphatase
YNR050C	D	-516	-505	9.35	LYS9; saccharopine dehydrogenase (NADP+, L-glutamate forming)
YNL062C	D	-68	-57	9.35	GCD10; translation initiation factor eIF3 RNA-binding subunit
YJR059W	D	-246	-235	9.19	PTK2; involved in polyamine uptake
YHR107C	D	-506	-495	9.19	CDC12; septin
YGR233C	D	-347	-336	9.19	PHO81; cyclin-dependent kinase inhibitor
YFR040W	D	-81	-70	9.19	SAP155; Sit4p-associated protein
YJR067C	D	-505	-494	9.08	YAE1; protein of unknown function
YDR163W	D	-668	-657	9.08	hypothetical protein

#### Improving genome-scale predictions

- The prediction of single binding sites is notoriously noisy. However, one can
  try to combine different types of information in order to predict the regulation
  of a gene as a whole, rather than each potential binding site.
- Include as much biological information as possible
  - Site repetition (e.g. GATA boxes)
  - Combination of heterologous sites (e.g. Met4p and Met31p)
  - Information about site positions: distribution of position for known sites and impose a constraint on putative site positions
- Supervised classification: train a program with
  - a set of reliable positive sites (from known target genes)
  - a set of reliable negative sites (genes known not to respond to the factor)

#### Regulatory sequence analysis

# Matching a sequence with a library of patterns

#### Match a sequence with a library of patterns

- Goal: given a sequence, find matches for any known regulatory site
  - → identify transcription factors that could regulate the gene
- Strategy: apply systematically pattern search with all patterns stored in the library
- Problem: how to set the threshold for the different patterns?
- Warning: generates many false positive

### Transfac Matsearch result - PHO5 upstream region

Inspecting sequence F	PHO5_4 [?] (1 - 81	б):		
F\$NIT2_01	141 (+)	1.000	0.995	TATCtc
F\$PHO4_01	561 (+)	1.000	0.990	tcaCACGtggga
F\$PHO4_01	561 (-)	1.000	0.982	tccCACGtgtga
F\$NIT2_01	634 (+)	1.000	0.972	TATCaa
F\$NIT2_01	543 (-)	1.000	0.967	TATCga
F\$NIT2_01	676 (-)	1.000	0.945	TATCcc
F\$NIT2_01	31 (-)	1.000	0.937	TATCag
F\$PHO4_01	452 (+)	1.000	0.935	tagCACGttttc
F\$MCM1_01	666 (-)	0.961	0.929	tatCCCAaatgggtat
F\$MATA1_01	202 (+)	1.000	0.926	<b>tGATGtcagt</b>
f\$GCR1_01	323 (-)	1.000	0.922	gaCTTCcaa
f\$GCN4_C	536 (+)	0.837	0.902	aaaTGAATcg
F\$ABAA_01	292 (-)	1.000	0.889	atttgcgCATTcttgttga
F\$ABF_C	205 (+)	0.887	0.885	tgtcagtccccACGC
F\$MATA1_01	727 (+)	1.000	0.882	<b>tGATGttttg</b>
F\$MIG1_01	210 (-)	1.000	0.881	gctattagcgtGGGGac
f\$GCR1_01	69 (+)	0.826	0.880	ggCATCcaa
F\$PHO4_01	90 (-)	1.000	0.879	ggtCACGtttct
F\$MAT1MC_02	696 (+)	1.000	0.875	tgaaTTGTcg
F\$GCN4_C	589 (+)	0.882	0.862	ttaTGATTct
F\$STE11_01	415 (+)	1.000	0.860	ctttttCTTTgtctgcac
F\$GCR1_01	249 (-)	0.783	0.859	ggCGTCctg
F\$STE11_01	425 (-)	1.000	0.859	atatttCTTTgtgcagac
F\$MCM1_01	484 (+)	0.831	0.855	atgCCAAaaaaagtaa

#### Transfac Matsearch result - random sequence (mkv 5)

r				
Inspecting sequence ra	ndom mkv5 [?] (1	- 817):		
F\$NIT2_01	176 (+)	1.000	1.000	TATCta
F\$NIT2_01	656 (+)	1.000	1.000	TATCta
F\$NIT2_01	275 (+)	1.000	0.995	TATCtc
F\$NIT2_01	455 (+)	1.000	0.995	TATCtc
F\$NIT2_01	298 (-)	1.000	0.980	TATCtt
F\$MATA1_01	506 (-)	1.000	0.980	tGATGtatgt
F\$ABF_C	84 (+)	0.991	0.973	aatcattcttgACGT
F\$MIG1_01	264 (-)	1.000	0.958	gagataaaactGGGGtt
F\$NIT2_01	701 (+)	1.000	0.947	TATCgt
F\$NIT2_01	802 (-)	1.000	0.947	TATCgt
F\$ABF1_01	81 (+)	0.976	0.944	gtaaatcattcttgACGTtttt
F\$MAT1MC_02	665 (-)	1.000	0.918	cctaTTGTga
F\$NIT2_01	280 (-)	1.000	0.915	TATCcg
F\$ABAA_01	42 (+)	1.000	0.902	tccccatCATTctaacagt
F\$PACC_01	331 (-)	1.000	0.897	acgaGCCAagaaaagtt
F\$ABAA_01	201 (+)	1.000	0.883	accatagCATTctggatct
F\$MAT1MC_02	442 (-)	1.000	0.882	tataTTGTat
F\$ABF_C	638 (-)	0.991	0.882	agtcaaatgaaACGT
F\$ABF_C	609 (-)	0.949	0.874	tttctttaaacACGG
F\$MATA1_01	558 (-)	1.000	0.868	tGATGgaaga
F\$HSF_03	713 (-)	1.000	0.859	AGAAttgaaattttt
F\$MAT1MC_02	134 (-)	1.000	0.858	cacaTTGTgt
F\$ABAA_01	80 (+)	1.000	0.856	agtaaatCATTcttgacgt
F\$HAP234_01	332 (-)	1.000	0.851	acgagCCAAgaaaagt
	: :	:		

#### Transfac Matsearch result - random sequence (iid)

Inspecting sequence	random iid [?] (1	- 817):		
F\$NIT2_01	534 (-)	· · · · · ·	1.000	TATCta
F\$NIT2_01	294 (+)	1.000	0.995	TATCtc
F\$NIT2_01	634 (-)	1.000	0.972	TATCaa
F\$NIT2_01	216 (-)	1.000	0.965	TATCtg
F\$STUAP_01	808 (-)	1.000	0.959	attCGCGtct
F\$NIT2_01	24 (+)	1.000	0.952	TATCat
F\$NIT2_01	343 (+)	1.000	0.952	TATCat
<b>F\$NIT2_01</b>	413 (-)	1.000	0.952	TATCat
F\$STUAP_01	441 (+)	1.000	0.930	aagCGCGcct
F\$NIT2_01	244 (-)	1.000	0.930	TATCct
F\$STUAP_01	808 (+)	1.000	0.926	agaCGCGaat
F\$GCR1_01	499 (+)	1.000	0.922	gaCTTCcta
F\$PACC_01	647 (-)	1.000	0.920	ctccGCCAggcactgaa
<b>F\$NIT2_01</b>	475 (+)	1.000	0.915	TATCcg
F\$ABF_C	235 (-)	0.949	0.904	tatcctgcaacACGG
F\$PHO4_01	246 (-)	1.000	0.882	gctCACGttatc
F\$GCR1_01	763 (-)	1.000	0.866	acCTTCcgc
F\$STUAP_01	441 (-)	1.000	0.859	aggCGCGctt
<b>F\$MIG1_01</b>	371 (+)	1.000	0.857	accgaaacagtGGGGtt
F\$MAT1MC_02	375 (-)	0.769	0.855	cccaCTGTtt

#### Regulatory sequence analysis

## Old slides

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#### Pho4p matrix : score distribution in upstream regions of PHO and MET genes

