

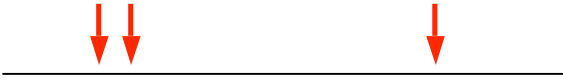




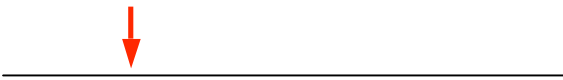
Regulatory Sequence Analysis

String-based pattern matching

Jacques van Helden
Jacques.van.Helden@ulb.ac.be

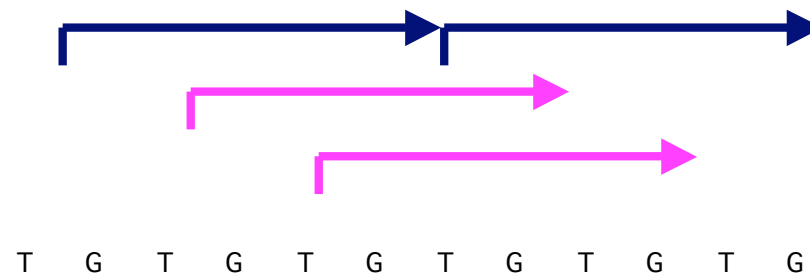
Word counting - Occurrences or matching sequences

- If a sequence contains multiple occurrences of a given pattern, one can score either
 - *all of them*, or
 - only count the *first occurrence per sequence*. In this case, each sequence is scored as "matching" the pattern or not.

		All occurrences	First occurrence
Seq 1		3	true
Seq 2		0	false
Seq 3		4	true
Seq 4		1	true
Seq 5		0	false
Seq 6		1	true
Total		9 occ	4 mseq

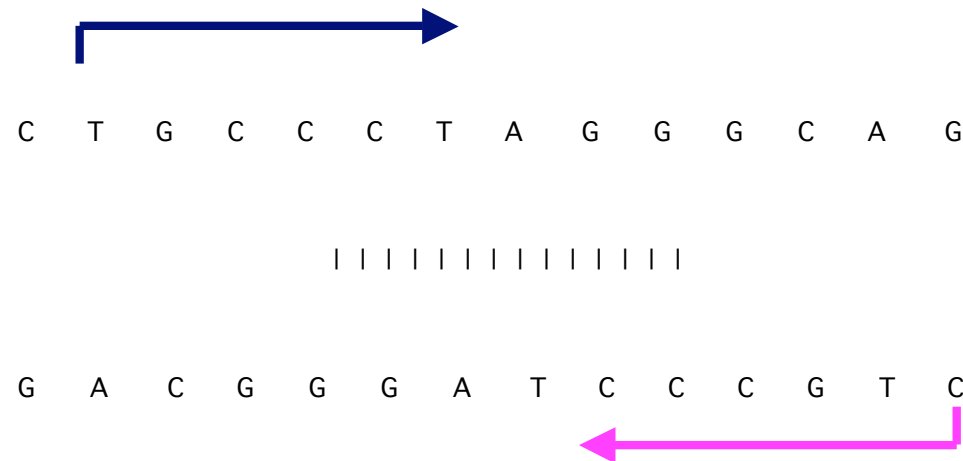
Treatment of self-overlap

Mutually overlapping occurrences of the same word.



2 or 4 occurrences of TGTGTG ?

Single or double strand count



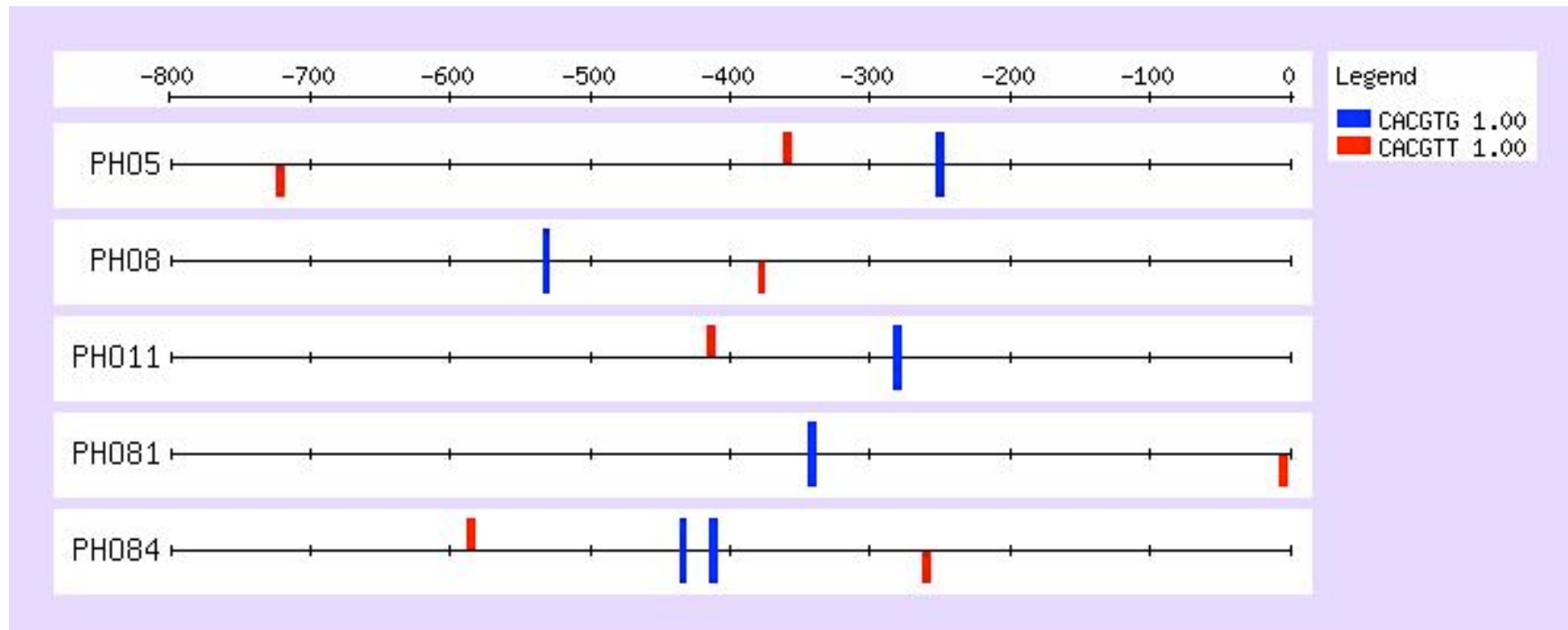
1 or 2 occurrences of CTGCCC ?

Software : *dna-pattern*

- Specialized program for pattern matching in DNA sequences
 - Supports IUPAC code for partly specified nucleotides (e.g. TSWNATTK)
 - Supports spaces of fixed or variable length within the patterns (e.g. GGGWn_{0,30}WCCC)
 - Single or both strands
 - Allow substitutions but no insertion or deletion
- Extract neighbourhood of the match (flanking bases)
- Return
 - matching positions
 - match count per sequence
- Sliding window
 - Detection of regions containing combinations of multiple patterns
 - A specific weight can be associated to each pattern

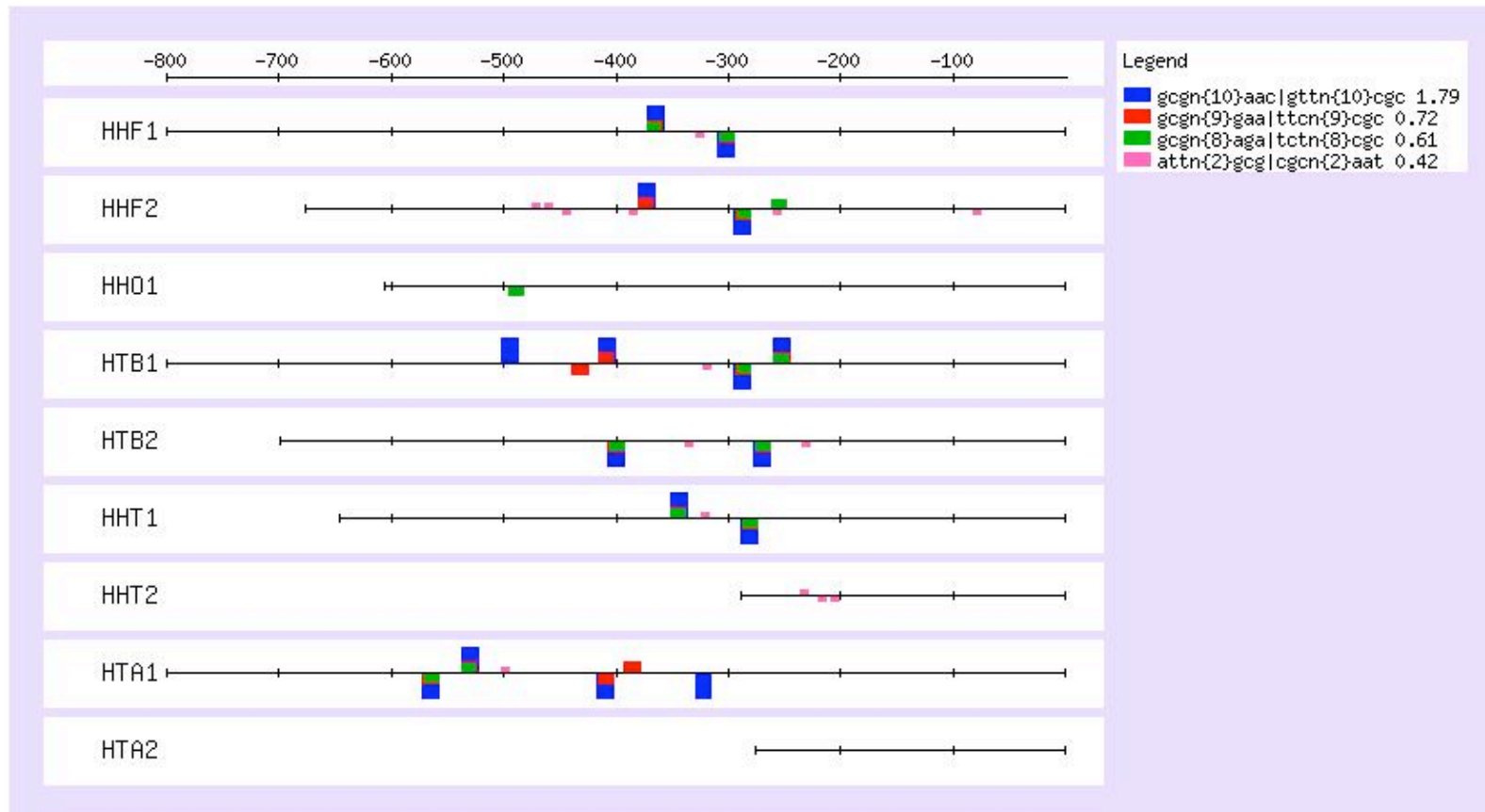
Matching simple patterns

- A simple string-based pattern matching is usually poorly informative.
 - spurious matches are expected to be found anywhere
 - the presence of the consensus does not necessarily mean that the factor binds
 - some patterns have a higher significance than other ones (e.g. the core of the consensus).



Matching a collection of overlapping patterns

- Pattern matching results can be improved by matching a collection of mutually overlapping patterns (words or spaced dyads)
 - Multiple patterns can be used to represent fragments of a larger binding site, or the variants arising from the degeneracy of the consensus.
 - Specific weights can be assigned to the elements of the collection, to represent their relative importance for the binding.



Regulatory Sequence Analysis

Genome-scale pattern matching

Jacques van Helden
Jacques.van.Helden@ulb.ac.be

Genome-scale pattern matching

- Knowing the consensus binding site for a given transcription factor, one would be tempted to use this information for predicting its target genes in the whole genome.
- This approach is however very inaccurate, because
 - The consensus poorly reflects the binding specificity
 - Binding is not synonymous of regulation
- As an experiment, we counted the number of occurrences for the consensus of various yeast transcription factors (source: TRANSFAC + our annotations). For each one of the
 - 800bp upstream sequences, clipped to prevent upstream ORFs.
 - For each gene, we counted the number of occurrences of each consensus.

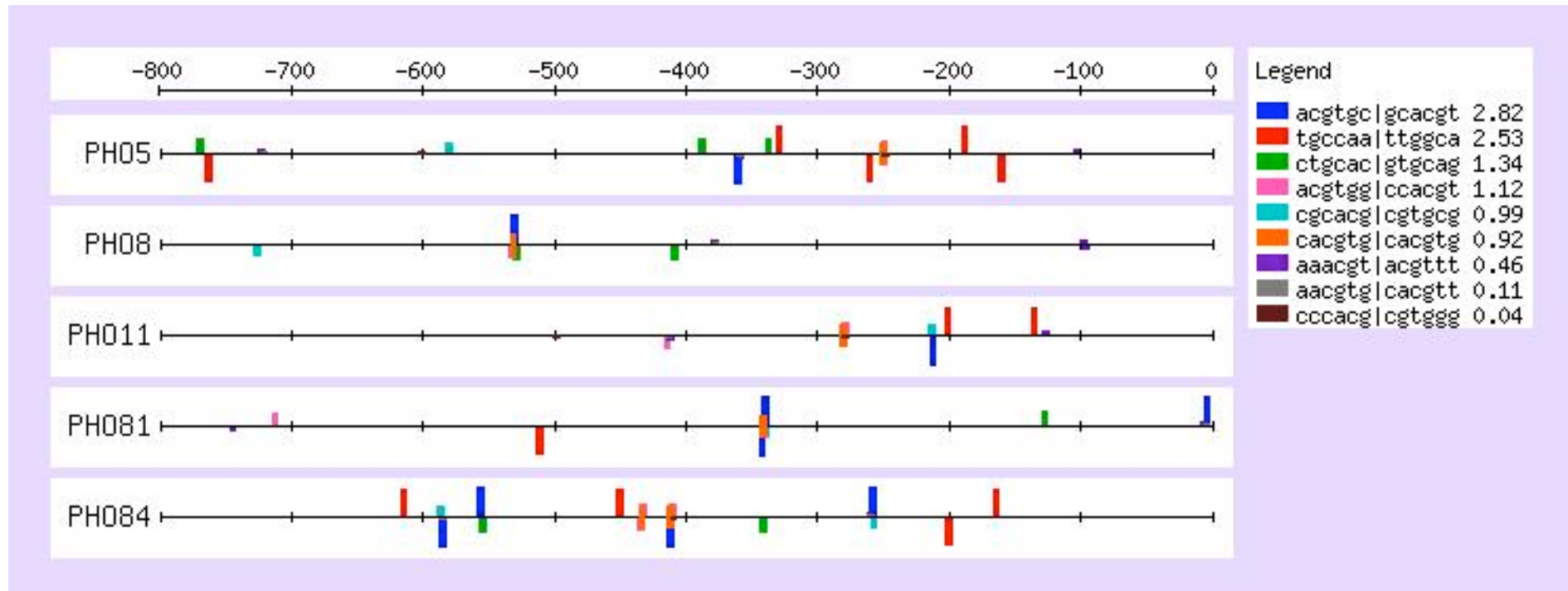
Occurrences of consensus per promoter

- *Saccharomyces cerevisiae*, 5864 genes, 800bp (clipped if upstream ORF)

factor	sequence	mean	>= 1	>=2	>=3	>=4	>=5	>=6	7
ABF1	TCNNNNNNNACG	0.62	788	196	43	13	5	0	0
ABF1.1	RTCRYNNNNNACG	0.15	61	5	2	0	0	0	0
ADR1	GGRGK	1.52	2187	1283	725	414	230	113	72
CBF1	RTCACRTG	0.07	70	10	6	0	0	0	0
CCBF	RNNYCACGAAAA	0.01	1	1	1	1	1	0	0
GAL4	CGGNNNACWNTCSTCCGARS	0.00	0	0	0	0	0	0	0
GATA_L5	GATAA	1.63	2588	1322	685	322	168	89	40
GATA_L6	GATAAG	0.28	266	46	14	7	2	1	0
GCN4	SKRTGASTCAYMS	0.00	2	0	0	0	0	0	0
GCN4.1	SNSNNNNNRTGACTCATNS	0.00	0	0	0	0	0	0	0
GCR1	RGCTTCCWC	0.03	14	1	0	0	0	0	0
GFII	RTCACRTG	0.07	70	10	6	0	0	0	0
HAP1	aaCttCCGWTAWCtCCNtNCNNNT	0.00	0	0	0	0	0	0	0
HAP2	YCINNCCAATNANM	0.01	0	0	0	0	0	0	0
HAP3	YCINNCCAATNANM	0.01	0	0	0	0	0	0	0
HAP4	YCINNCCAATNANM	0.01	0	0	0	0	0	0	0
MATa1	TGATGTANNT	0.04	4	0	0	0	0	0	0
MATalpha2	CRTGTNNW	0.74	1088	345	87	15	6	2	1
MCM1	WTWCCYAAWNNGGTAA	0.00	0	0	0	0	0	0	0
MET4_core	CACGTG	0.16	401	49	49	8	8	2	2
MET4_L8	TCACGTGA	0.04	101	2	2	0	0	0	0
MIG1	KANWWWWATSYGGGGW	0.00	0	0	0	0	0	0	0
PHO4	CACGTKBG	0.04	17	2	0	0	0	0	0
PHO4_both	CACGTK	0.32	460	118	61	28	10	3	3
PHO4_high	CACGTG	0.16	401	49	49	8	8	2	2
PHO4_medium	CACGTT	0.16	74	5	0	0	0	0	0
RAP1	aCAcCCataCAAt	0.00	0	0	0	0	0	0	0
REB1	YNNYYACCCG	0.11	22	2	0	0	0	0	0
repr of CAR1	TAGCCGCCRANR	0.01	2	0	0	0	0	0	0
TAF	RTCRYNNNNNACG	0.22	130	10	2	0	0	0	0
YAP1	TGASTMA	0.23	282	56	8	0	0	0	0

Assigning scores to patterns

- Pattern-specific scores can improve the interpretation by highlighting the most significant patterns.
- Scores can be assigned arbitrarily (e.g. on the basis of prior biological knowledge) or reflect the significance calculated by pattern discovery programs.



Sliding windows - scoring mutually overlapping matches

Sliding windows - scoring successions of matches
