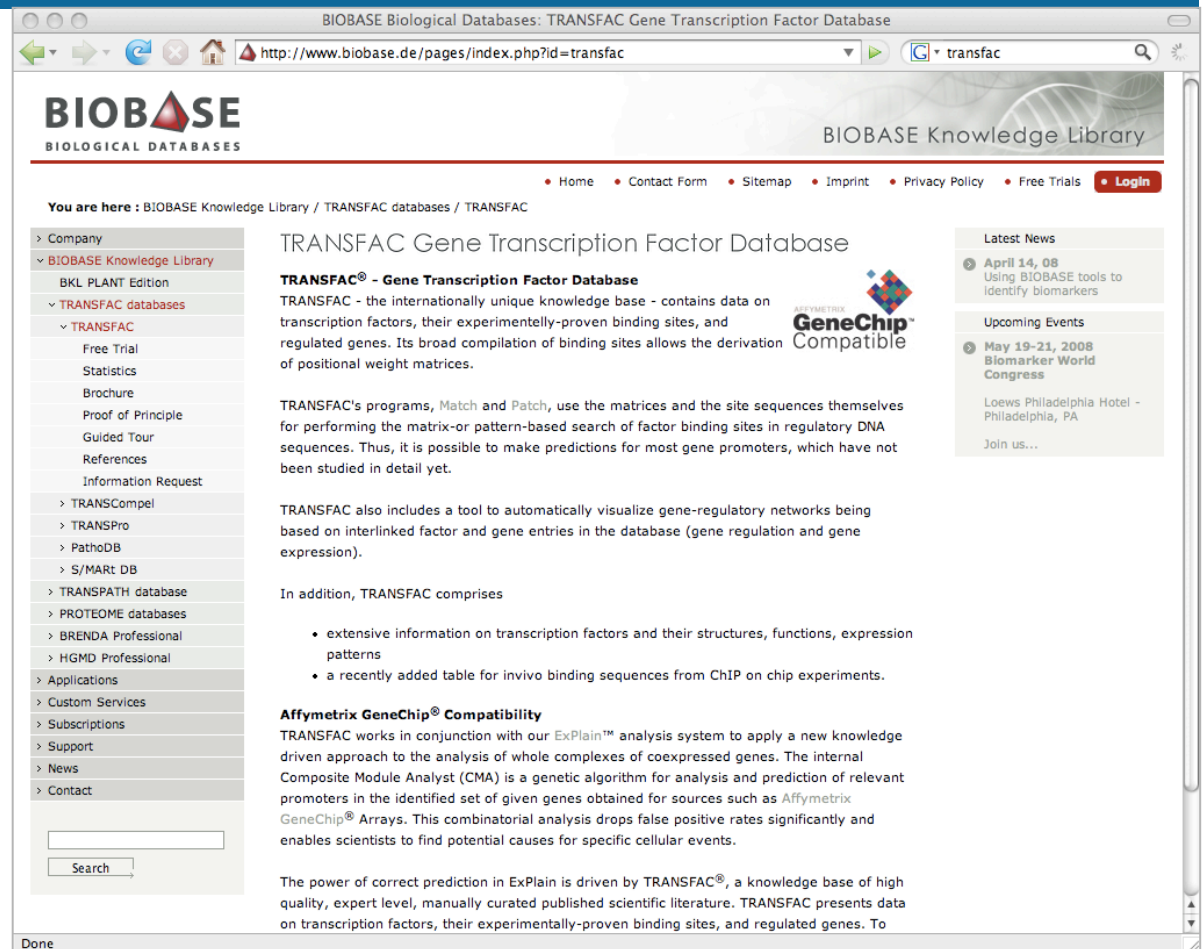


Transcription factor databases

TRANSFAC - Gene transcription factor database

- Organisms
 - Eukaryotes
 - Particular emphasis on mammals (specially human, mouse, rat)
- Distribution
 - The public version is not updated anymore
 - Commercial version (TRANSFAC PRO)
 - Distributed by BioBase™
 - <http://www.biobase.de/>
- Data content
 - Transcription factors
 - Binding sites
 - **Evidences !**
 - **Publications !**
 - Position-specific scoring matrices
- Pattern matching tools (patch, match)



TRANSFAC – matrix example – V\$SOX2_Q6

Field descriptions

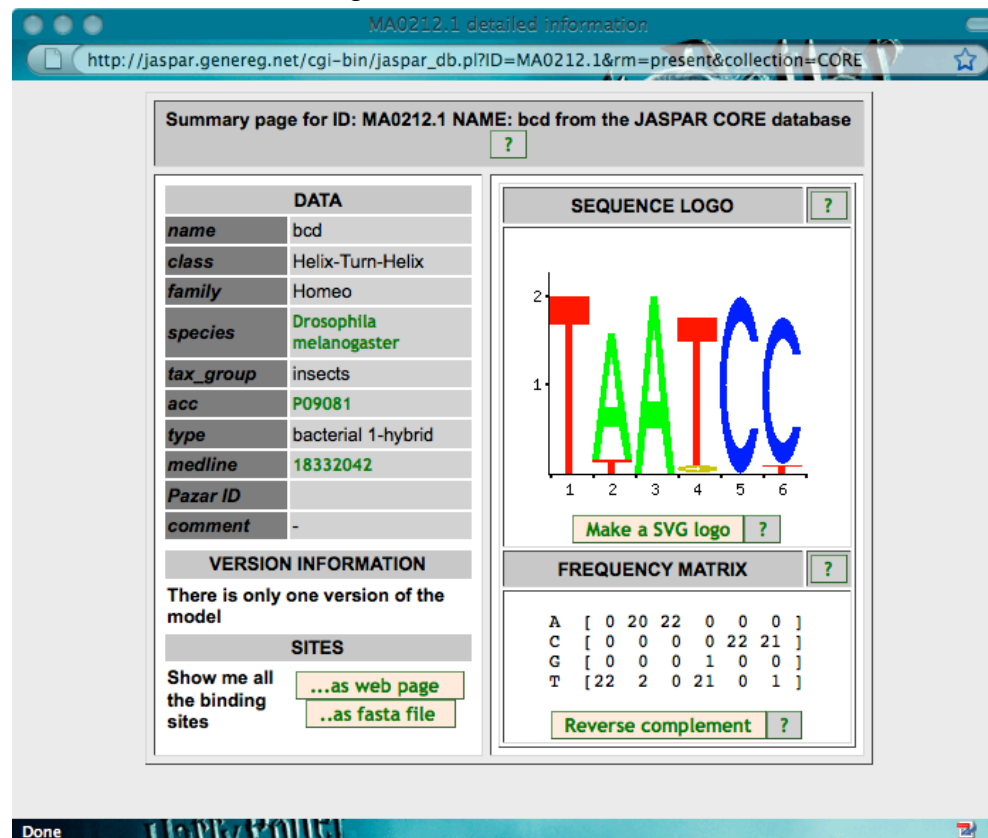
AC Accession no.
 XX (field separator)
 ID Identifier
 DT Date; author
 NA Name of the binding factor
 DE Short factor description
 BF List of linked factor entries

 PO A C G T Position within the aligned sequences,
 01 frequency of A, C, G, T residues, resp.;
 02 last column: deduced consensus in
 03 IUPAC 15-letter code
 BA Statistical basis
 BS Factor binding sites underlying the matrix
 BS (SITE accession no.; Start position for matrix sequence;
 length of sequence used;
 BS number of gaps inserted; strand orientation)
 CC Comments
 RX MEDLINE ID
 RN Reference no.
 RA Reference authors
 RT Reference title
 RL Reference data
 //

```
AC M01272
XX
ID V$SOX2_Q6
XX
DT 08.07.2009 (created); dtc.
CO Copyright (C), Biobase GmbH.
XX
NA SOX2
XX
BF T09507; Sox-xbb1; Species: mouse, Mus musculus.
BF T01836; Sox2; Species: mouse, Mus musculus.
BF T04915; Sox2; Species: human, Homo sapiens.
BF T01837; Sox2; Species: chick, Gallus gallus.
BF T10231; Sox2; Species: Mammalia.
BF T09970; Sox2; Species: human, Homo sapiens.
BF T10885; Sox2; Species: monkey, Cercopithecus aethiops.
XX
PO      A      C      G      T
01      6      2      4      4      N
02      7      2      3      4      N
03      4      6      2      4      N
04      4      5      4      3      N
05      2      9      1      4      C
06      0     12      0      4      C
07      8      0      0      8      W
08      0      0      0     16      T
09      0      0      0     16      T
10      0      0     16      0      G
11      0      0      0     16      T
12      2      2      2      9      T
13      7      2      0      6      W
14      0      2      2     11      T
15      1      0      9      5      K
16      4      6      3      2      N
XX
BA 16 compiled sequences
XX
BS gccctcattggttatgc; R15133; 13; 16;; n.
BS AAACCTCTTTGTTTGGA; R15201; -1; 16;; p.
BS ttcaccattgttctag; R15231; 11; 16;; n.
BS GACTCTATTGTCTCTG; R15267; 11; 16;; p.
BS GATATCTTTGTTTCTT; R16367; -4; 16;; p.
BS tgcacctttggttatgc; R17099; 5; 16;; n.
BS aattccattggttatga; R19276; 15; 16;; n.
BS aaactctttgtttgga; R19367; 20; 16;; n.
BS atggacattgtaatgc; R19510; 15; 16;; n.
BS AGGCCTTTTGTCTCTGG; R22342; 21; 16;; p.
BS tgtgCTTTTGTnnnnn; R22344; 1; 16;; p.
```

JASPAR

- <http://jaspar.genereg.net/>
- Public database
- Data content
 - PSSM
 - “sites” (i.e. sequences having served to build the matrix, but no genomic position)
 - Core: transcription factor-specific matrices
 - Collection: matrices for families of transcription factors
- Tools
 - Pattern matching, matrix randomization



Sequences for model MA0212.1

Site	Occurences
tgtTAATCCc	1
tgGGATTAta	1
ttacTAATCC	1
gctTAATCCg	1
ggtTAATCCg	1
agcTTATCC	1
gagaTAATCC	1
gtccTAATCC	1
cgtTAATCTc	1
atGGATTAGA	2
cgcTAAATCC	1
cgggTAATCC	1
GGCTTAagcc	1
tgtTAATCCg	1
tgtTAATCC	1
tctTAATCCc	1
ggTTATCCg	1
gcgTAATCCa	1
gggtTAATCC	1
tctaTAATCC	1
ggttTAATCC	1

- <http://www.oreganno.org/oreganno/Index.jsp>
- Also available from the UCSC genome browser
 - <http://genome.ucsc.edu/>
- Community-based annotation (Jamboree)
- Data content
 - Transcription factor binding sites
 - Mapping on the genomes
 - NO MATRICES
- Scope: all organisms (with specific focus on metazoan)

The screenshot displays the ORegAnno website interface. At the top, the browser address bar shows the URL <http://www.oreganno.org/oreganno/Index.jsp>. The page features a logo for ORegAnno (open regulatory annotation database) and a navigation menu on the right with links for login, new user, logout, search, annotate, queue, tools, dump, help, and cite. The main content area includes a description of the database, a 'NEWS' section with recent updates, and a 'MOST RECENTLY ANNOTATED PUBLICATIONS' section listing recent research papers. The footer mentions 'INCORPORATED DATASETS' and provides contact information.

ORegAnno
open regulatory annotation database

AN OPEN ACCESS DATABASE FOR GENE REGULATORY ELEMENT AND POLYMORPHISM ANNOTATION

The Open REGulatory ANNOtation database (ORegAnno) is an open database for the curation of known regulatory elements from scientific literature. Annotation is collected from users worldwide for various biological assays and is automatically cross-referenced against PubMed, Entrez Gene, Ensembl, dbSNP, the eVOC: Cell type ontology, and the Taxonomy database, where appropriate, with information regarding the original experimentation performed (evidence). ORegAnno further provides an open validation process for all regulatory annotation in the public domain. Assigned validators receive notification of new records in the database and are able to cross-reference the citation to ensure record integrity. Validators have the ability to modify any record (deprecating the old record and creating a new one) if an error is found. Further, any contributor to the database can comment on any annotation by marking errors, or adding special reports into function as they see fit. These features of ORegAnno ensure that the collection is of the highest quality and uniquely provides a dynamic view of our changing understanding of gene regulation in the various genomes. As a first step, we recommend reading through our [Help](#) page.

The ORegAnno data and web application are all [LGPL open-source](#) to encourage the development and maintenance of the database to new information and experimentation techniques. Please use our [current citation information](#) when referring to ORegAnno data in publication. We encourage interested contributors to send email to the ORegAnno mailing list at oreganno@bcgsc.ca or to visit the [mailing-list archives](#).

NEWS

October 17th, 2007 Warning: there are persistent case sensitivity issues with the Boolean search features. A fix will be availability shortly.

September 21st, 2007 There will be an interruption of ORegAnno service on the 21st as the BCGSC systems undergo maintenance

July 26th, 2007 A set of NRSF/REST binding sites identified using ChipSeq by Caltech/Stanford has been added [\[more\]](#)

[More news...](#)

MOST RECENTLY ANNOTATED PUBLICATIONS

Gao H et al., Genome-wide identification of estrogen receptor alpha-binding sites in mouse liver. *Mol Endocrinol* 2008

Harbison CT et al., Transcriptional regulatory code of a eukaryotic genome. *Nature* 2004

Lim CA et al., Genome-wide mapping of RELA(p65) binding identifies E2F1 as a transcriptional activator recruited by NF-kappaB upon TLR4 activation. *Mol Cell* 2007

Lin CY et al., Whole-genome cartography of estrogen receptor alpha binding sites. *PLoS Genet* 2007

MacIsaac KD et al., An improved map of conserved regulatory sites for *Saccharomyces cerevisiae*. *BMC Bioinformatics* 2006

INCORPORATED DATASETS

ORegAnno provides the ability to incorporate well-established datasets and provide relevant citation and ongoing maintenance

RegulonDB

Transcriptional regulation in *Escherichia coli*

- RegulonDB Web site
 - <http://regulondb.ccg.unam.mx/>
- Model organism: *Escherichia coli*
- Data content
 - Transcription factors
 - Transcription factor binding sites (TFBS)
 - Position-specific scoring matrices (PSSM)
 - Promoters
 - Operons
- Collaboration with EcoCyc
 - EcoCyc is the reference database about metabolism in *Escherichia coli*
 - RegulonDB is integrated in the EcoCyc database



Example of regulon in RegulonDB

RegulonDB 6.1

http://regulondb.ccg.unam.mx/RegulonControllerServlet?regulon_id=ECK12R054548

RegulonDB
Escherichia coli K12 Transcriptional Network

Main Page Using RegulonDB Tools Downloads About RegulonDB

Search: Gene Go

Export to: XML

REGULON LexA, in Escherichia coli K12 genome

TRANSCRIPTION FACTOR: [Info](#)

Name: LexA [Tractordb tool](#)

Connectivity: Local Regulator

Sensing Class: LexA transcriptional repressor

Synonym(s): [lexA](#)

Gene name(s): [lexA](#)

Conformation(s): LexA

Coregulator(s): [ArcA](#), [LexA](#)

Note(s): [Note\(s\): ...\[more\]](#)

REGULATION EXERTED BY LexA, [Info](#)

Transcription Factor		Regulated		Binding Sites				Evidences	References
Conformation	Function	Promoter	Gene(s)	LeftPos	RigthPos	CenterPos	Sequence		
KNOWN BINDING SITES (The centerpos is relative to the promoter +1)									
LexA repressor									
LexA	repressor	lexAp	lexA,dinF	4255050	4255069	-50.5	ttcgataaatCTCTGGTTTATTGTGCAGTTtatggtcca	[HIBSCS]	[1] [2]
LexA	repressor	lexAp	lexA,dinF	4255091	4255110	-9	aatgccttTGCTGTATATACTACAGCAtaactgtata	[BPP] [HIBSCS]	[3] [2]
LexA	repressor	lexAp	lexA,dinF	4255112	4255131	13	ctcagcagcatAACTGTATATACACCCAGGGggcggaatga	[BPP] [HIBSCS]	[3] [2]
LexA	repressor	phrBp	phr	738568	738587	-66.5	gccagcagctGGCTGCGCTTATCGACAGTTatgcctggg	[HIBSCS]	[1] [4]
LexA	repressor	phrBp	phr	738659	738678	25.5	ttatcctgacGCCTGGCTTTCAGGGCAGCGttattcgaa	[GEA] [HIBSCS]	[5]
LexA	repressor	rpsUp3	dnaG,rpoD,rpsU	3208751	3208770	4.5	attttgaaatAAGCTGGCGTTGATGCCAGCggcaaacga	[BCE] [SM]	[6] [7]
LexA	repressor	recAp	recA,recX	2821851	2821870	-21	aaacacttgaTACTGTATGAGCATACAGTAtaattgctc	[BPP]	[3] [2]
LexA	repressor	sulAp	sulA	1020162	1020181	-2	ctggatgtacTGTACATCCATACAGTAACTcacaggggct	[BCE]	[8]
LexA	repressor	uvrBp2	uvrB	812655	812674	-20	tatggtgatgAACTGTTTTTTTATCCAGTAtaattgtg	[HIBSCS]	[9]
LexA	repressor	uvrDp1	uvrD	3995930	3995949	11	taatcagcaaATCTGTATATATACCCAGCTtttggcgga	[HIBSCS]	[10]
LexA	repressor	umuDp	umuC,umuD	1229951	1229970	-0.5	aagaacagacTACTGTATATAAAAAACAGTAtaactcagg	[BPP]	[11] [1]
LexA	repressor	umuDp	umuC,umuD	1229931	1229950	-20.5	atcaglattgATCTGCTGGCAAGAACAGACtactgtatat	[HIBSCS]	[11] [1] [12]
LexA	repressor	insKp	insK					[AIBSCS] [GEA]	[13]
LexA	repressor	dinQp	dinQ					[AIBSCS] [GEA]	[13]
LexA	repressor	polBp	polB	65834	65853	-40.5	gggcagtaatGACTGTATAAAACCACAGCCaatcaaacga	[AIBSCS] [GEA]	[14]
LexA	repressor	ruvAp1	ruvA,ruvB	1944102	1944121	-63.5	aataaattatACTGTGCCATTTTTCAGTTcatcgagacac	[HIBSCS]	[15] [1]
LexA	repressor	ruvAp1	ruvA,ruvB	1944051	1944070	-12.5	tctcatcctTCGCTGGATATCTATCCAGCatttttat	[BPP] [HIBSCS]	[15] [13] [1] [16]
LexA	repressor	ruvAp2	ruvA,ruvB	1944103	1944122	-72.5	gaataaattaTACTGTGCCATTTTTCAGTTcatcgagaca	[HIBSCS]	[15] [1]

Done

PSSM in RegulonDB

- RegulonDB contains a collection of PSSM built by aligning annotated binding sites.
 - http://regulondb.ccg.unam.mx/data/Matrix_AlignmentSet.txt
- This collection can be used to scan genomes and predict new TFBS.

```
...
-----

Transcription Factor Name      LexA
Total of uniq binding sites    23

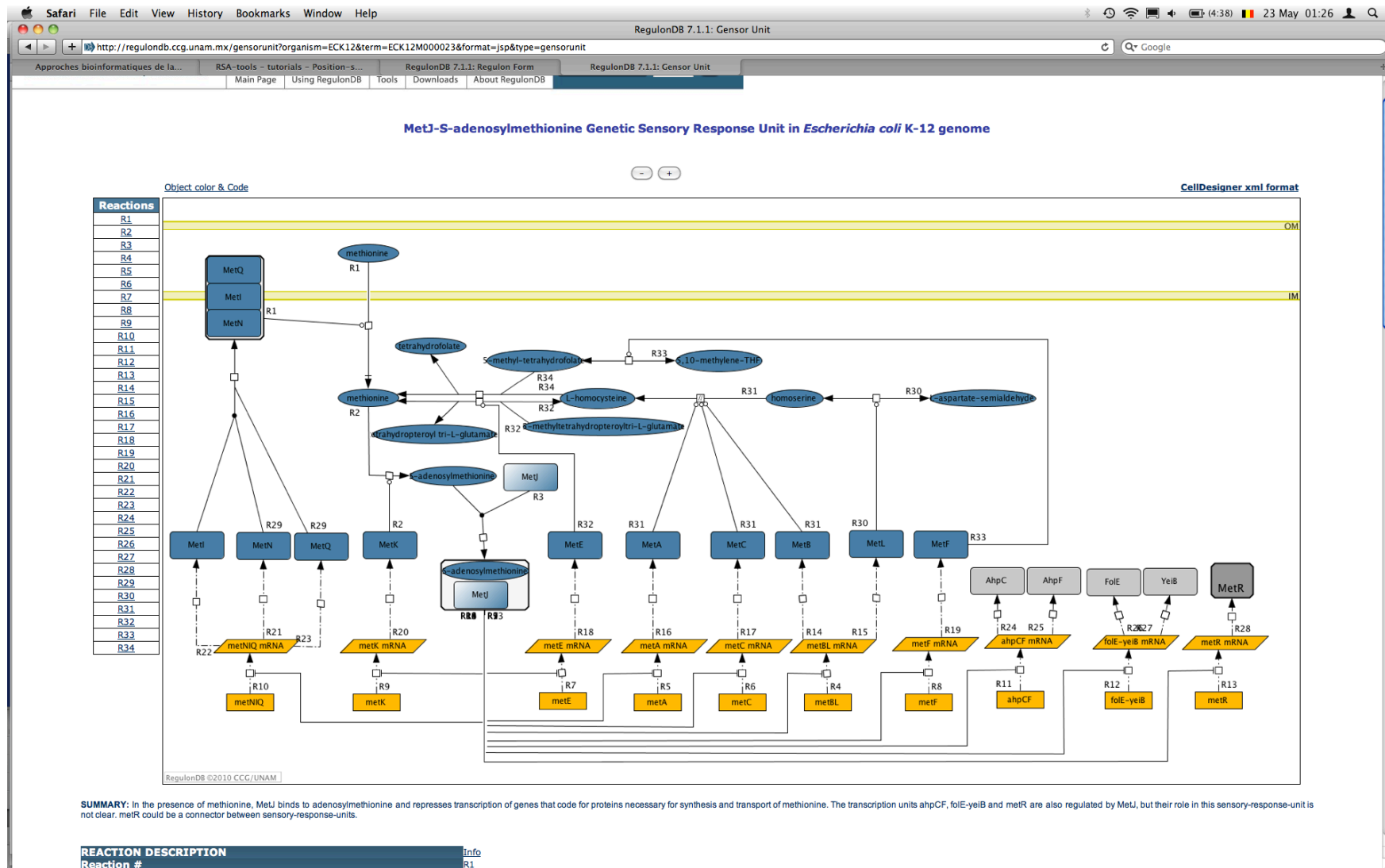
Matrix
A   12  0  0  0  1 12  1 12  6 10  7 13  4 12  0 23  0  1 12  6 11
C   3 22  0  0  2  3  5  2  2  5  5  2  4  7 23  0  0  8  2  2  3
G   5  0  0 23  6  3  2  4  0  2  0  3  3  2  0  0 23  1  3  2  1
T   3  1 23  0 14  5 15  5 15  6 11  5 12  2  0  0  0 13  6 13  8

Alignment      Score
ACTGTATAAAACCACAGCCAA      12.05
GCTGCGCTTATCGACAGTTAT      8.48
CCTGGCTTTCAGGGCAGCGTT      7.51
ACTGTTTTTTTATCCAGTATA      16.18
ATTGGCTGTTTATACAGTATT      12.01
CCTGTTAATCCATACAGCAAC      10.7
ACTGTACATCCATACAGTAAC      14.66
TCTGCTGGCAAGAACAGACTA      3.36
ACTGTATATAAAAACAGTATA      17.23
GCTGGATATCTATCCAGCATT      15.55
GCTGGATATCTATCCAGCATT      15.55
ACTGTGCCATTTTTCAGTTCA      8.61
ACTGTGCCATTTTTCAGTTCA      8.61
ACTGTATATAAAACCAGTTTA      16.16
ACTGTACACAATAACAGTAAT      12.47
ACTGTATGAGCATACAGTATA      14.73
GCTGGCGTTGATGCCAGCGGC      4.27
ACTGTTTATTTATACAGTAAA      16.67
TCTGTATATATACCCAGCTTT      14.73
TCTGGTTTATTGTGCAGTTTA      9.97
GCTGTATATACTCACAGCATA      15.05
ACTGTATATACACCCAGGGGG      9.28
CCTGAATGAATATACAGTATT      12.9

-----
....
```


“Gensor units” (RegulonDB)

- RegulonDB defines the concept of “Gensor unit” as “a unit that initiates with the signal, continues with the signal transduction to the core of regulation to modify expression of the affected set of target genes, and ends with an adequate response.”
- Example: **MetJ-S-adenosylmethionine Genetic Sensory Response Unit in *Escherichia coli* K-12 genome**



Other databases

- PAZAR <http://www.pazar.info/>
 - Unification of independent collection of transcription factor binding sites and motifs.
- YeasTract <http://www.yeasttract.com/>
 - Yeast-specific database. Factors, binding sites and motifs + tools.
- FlyReg <http://www.flyreg.org/>
 - Drosophila DNase I Footprint Database
- PlantCARE <http://bioinformatics.psb.ugent.be/webtools/plantcare/html/>
 - Plant Cis-Acting Regulatory Elements

Practical – Transcription factor databases

- Take some matrix from either of those database
 - JASPAR (<http://jaspar.genereg.net/>)
 - TRANSFAC public version (<http://www.gene-regulation.com/>)
- Open a connection to RSAT (<http://rsat.ulb.ac.be/rsat/>).
- Use the tool convert-matrix to obtain information on the matrix
 - Display the logo. How do you interpret
 - the information content in each column ?
 - the error bars
 - Redo the conversion, but set the option “Multiply counts” to 10. How does it affect the logo ?
 - Redo the conversion, but set the option “Multiply counts” to 0.1. How does it affect the logo ?
 - Convert counts to weights
 - How do you justify your choice of the background model ?
 - Explore the statistical parameters
- Tips:
 - don't forget to specify the input format
 - pay a particular attention to the choice of the background model.
- Examples:
 - TRANSFAC e.g. V\$OCT1_01
 - JASPAR: compare the two matrices for the factor Klf4 (identifiers [MA0039.1](#) and [MA0039.2](#) resp.)