



RegulonDB: Enhancing access to genomic knowledge in *Escherichia coli* K-12

Julio Collado

**Centro de Ciencias Genómicas
UNAM, Cuernavaca**

30 years of TRANSFAC

**Göttingen University, Germany
March 7th, 2018**



We are living a tsunami of data, information and knowledge



Can we make use of the knowledge that is being generated?

Isaac Asimov predicted the internet of today 20 years ago

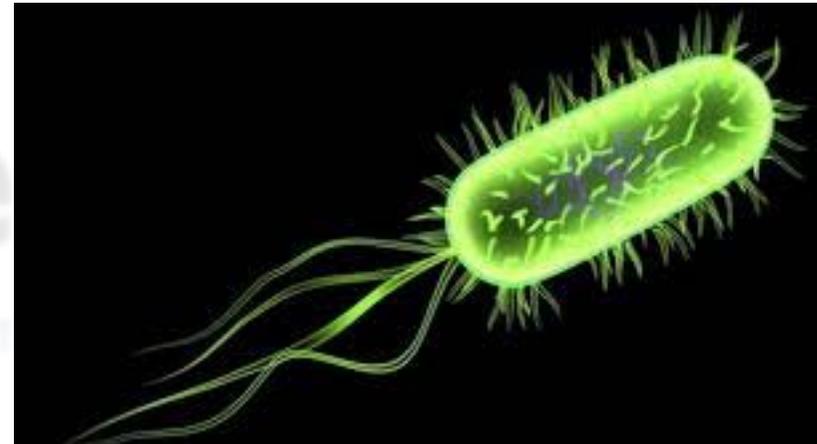
<https://www.youtube.com/watch?v=8ZmFEFO72gA>

Gene regulation in *Escherichia coli* K-12

Table 4. Distribution of *E. coli* proteins among 22 functional groups (simplified schema).

Functional class	Number	Percent of total
Regulatory function	45	1.05
Putative regulatory proteins	133	3.10
Cell structure	182	4.24
Putative membrane proteins	13	0.30
Putative structural proteins	42	0.98
Phage, transposons, plasmids	87	2.03
Transport and binding proteins	281	6.55
Putative transport proteins	146	3.40
Energy metabolism	243	5.67
DNA replication, recombination, modification, and repair	115	2.68
Transcription, RNA synthesis, metabolism, and modification	55	1.28
Translation, posttranslational protein modification	182	4.24
Cell processes (including adaptation, protection)	188	4.38
Biosynthesis of cofactors, prosthetic groups, and carriers	103	2.40
Putative chaperones	9	0.21
Nucleotide biosynthesis and metabolism	58	1.35
Amino acid biosynthesis and metabolism	131	3.06
Fatty acid and phospholipid metabolism	48	1.12
Carbon compound catabolism	130	3.07
Central intermediary metabolism	188	4.3
Putative enzymes	251	5.8
Other known genes (gene product or phenotype known)	26	0.6
Hypothetical, unclassified, unknown	1632	38.0
Total	4288	100.0

*Total of these rounded values is 99.97%.

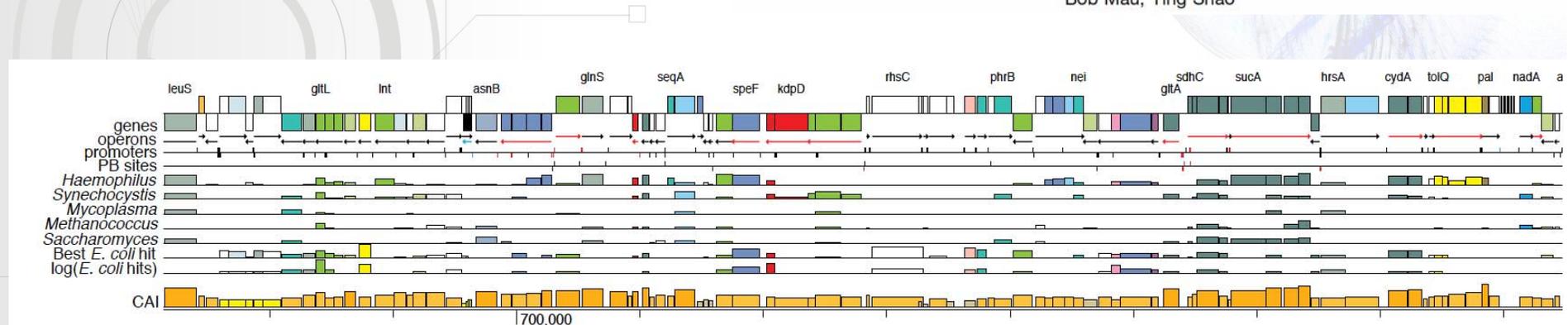


ARTICLE

The Complete Genome Sequence of *Escherichia coli* K-12

Frederick R. Blattner,* Guy Plunkett III,* Craig A. Bloch, Nicole T. Perna, Valerie Burland, Monica Riley, Julio Collado-Vides, Jeremy D. Glasner, Christopher K. Rode, George F. Mayhew, Jason Gregor, Nelson Wayne Davis, Heather A. Kirkpatrick, Michael A. Goeden, Debra J. Rose, Bob Mau, Ying Shao

AAAAAAT TAAAGCGCAAGAT TGT TGGT TGT TGT
CATTACATTGCTGGATAAGAATGTTTAGT19.78



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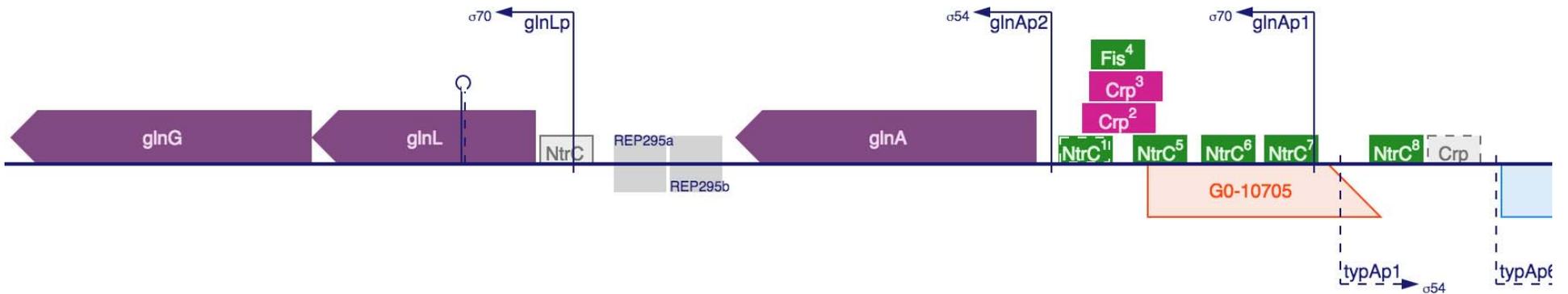
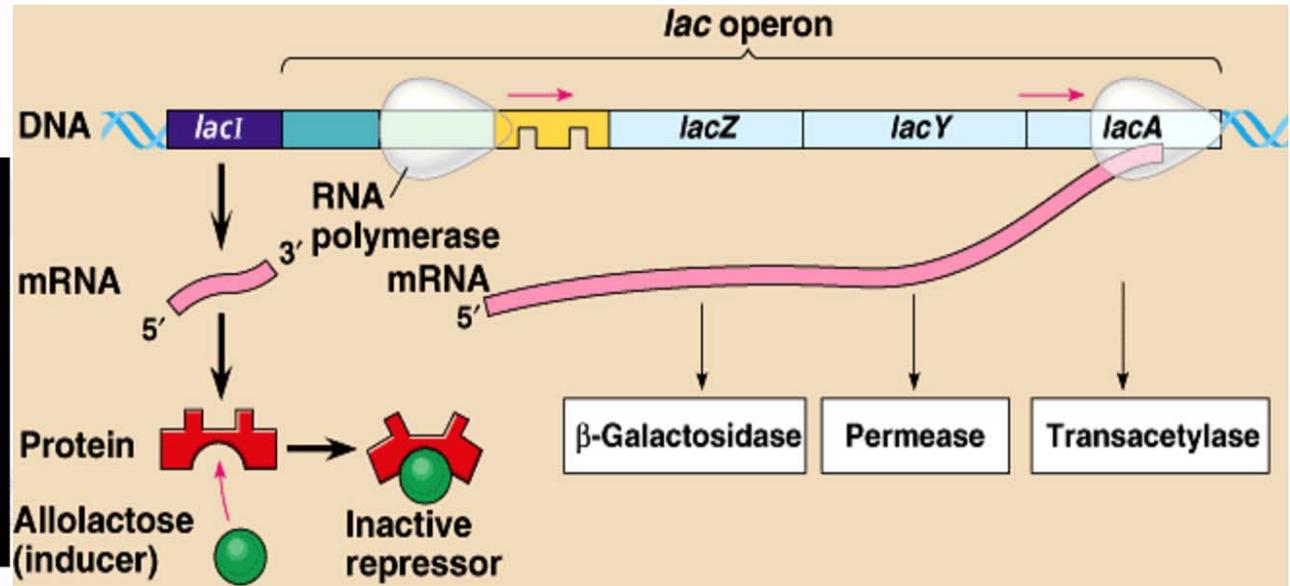
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Total of uniq binding sites3

Matrix
A 2 3 1 1 3 2 3 0 0 1 1 2 0 0 1 0 2 2 0 3 2 0 1 1 0 0 0 1 0
C 1 0 0 1 0 1 0 0 1 0 2 0 0 2 0 1 1 0 0 0 0 0 0 0 1 0 0 0 0
G 0 0 1 0 0 0 0 1 0 2 0 0 3 1 2 0 0 0 3 0 0 0 2 0 0 2 1 0 1
T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0 2 0 1 0 0 1 3 0 2 2 2 2 2 2

AlignmentScore
AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
AAAAAATTAAGCGCAAGATTGTTGGTT21.42
CATTACATTGCTGGATAAGAATGTTTAG19.78



Curation through the years in RegulonDB

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Citation

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update publication conc
Socorro Gama-Castro, I
Alberto Santos-Zavaleta
Moreira,
Juan Segura-Salazar, L
Salgado,
César Bonavides-Martí
Juan Miranda-Rico,
Enrique Morett, Enrique
and Julio Collado-Vides
"RegulonDB (Version 6
beyond transcription, ac
textpresso navigation"
Nucleic Acids Research

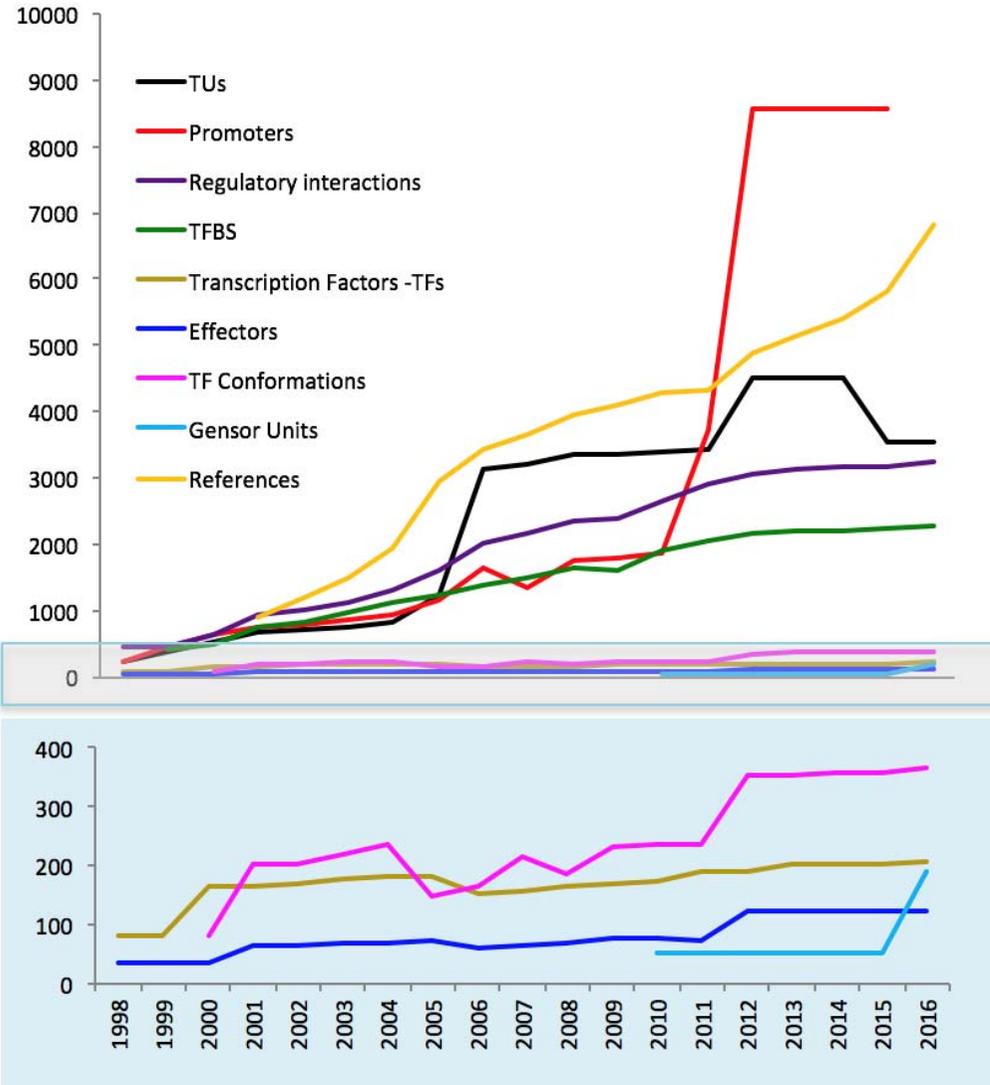
Release: 6.4 Date: 10-A

Transcription Factor N

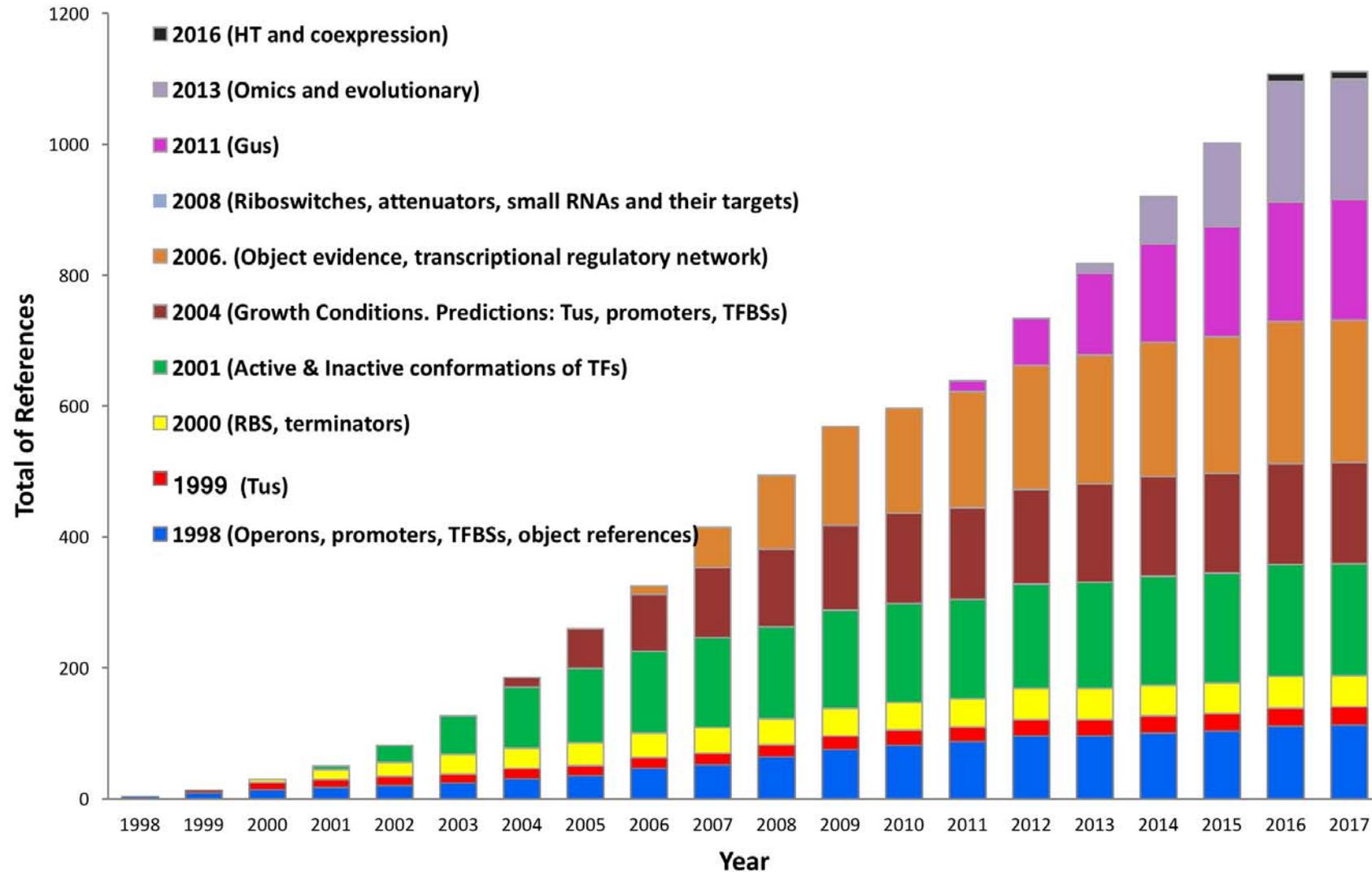
The consensus and p
Transcription Factor N
Total of uniq binding s

Matrix
A 2 3 1 1 3 2
C 1 0 0 1 0 1
G 0 0 1 0 0 0
T 0 0 1 1 0 0

AlignmentScore
AAGCAAAGCGCAGG
AAAAAATTAAGCC
CATTACATTGCTGG



Papers and new objects through the years



The main goal of biocuration:

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"RegulonDB (Version 6.0): gene regulation model of Escherichia coli K-12 beyond transcription, active (experimental) annotated promoters and textpresso navigation"
Nucleic Acids Research, 2008, vol 36, D120-D124

Release: 6.4 Date: 10-AUG-09

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Knowledge

Information

Data

To make data, information and knowledge easily accessible to humans (and computers)

I will illustrate 2 examples

E. coli (K12) Transcriptional Network



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Enrique Morett
and Julio Colla
RegulonDB (V...
beyond transcr...
textpresso nav...
Nucleic Acids R...

Release: 6.4 D

Transcription F

The consensus
Transcription F
Total of uniq b

Matrix
A 2 3 1 1
C 1 0 0 1
G 0 0 1 0
T 0 0 1 1

AlignmentScore
AAGCAAAGC
AAAAAAATTA
CATTACATTG



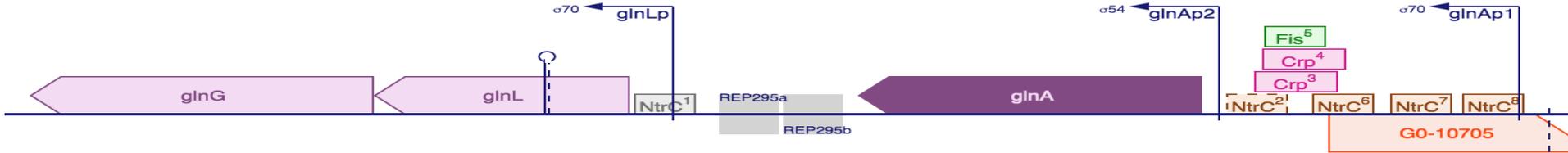
3.- Ontology and NLP strategies

2.- Operons, regulons and GUs

1.- Curating HT experiments

RegulonDB





update publication concerning regulation of the gln operon in *S. pneumoniae*. Socorro Gamero-Castro, Verónica Jiménez-Alberola, Santos-Zavaleta, Monica I. Peña-Moreira, Juan Segura-Salazar, Luis Muñoz-Ramos-Salgado, César Bonavides-Martínez, Cel Abreu-Juan Miranda-Rico, Enrique Moretti, Enrique Merino, Araceli and Julio Collado-Vides. "RegulonDB (Version 6.0): gene regulation beyond transcription, active (experimental) textpresso navigation". Nucleic Acids Research, 2008, vol 36, Release 6.4 Date: 10-AUG-09

Transcription unit

Name: glnALG

Promoter

Name: glnAp2

+1: 4058107

Sigma Factor: Sigma54 Sigmulon

Distance from start of the gene: 73

Sequence: gcatgataacgccttttaggggcaatttaaagt⁻²⁴tgccacagattt⁻¹²cgctttatctcttttt⁺¹acggcgacacggcctaaata

Evidence: [TIM]

Reference(s): [5] Ninfa AJ., et al., 1987
[6] Reitzer LJ., et al., 1989
[7] Tian ZX., et al., 2001

Transcription Factor Matrix and Alignment

The consensus and pater program Transcription Factor NameAda Total of uniq binding sites3

Matrix

```

A 2 3 1 1 1 3 2 3 0 0 1
C 1 0 0 1 0 1 0 0 1 0 0
G 0 0 1 0 0 0 0 1 0 0 0
T 0 0 1 1 0 0 0 2 2 0 0

```

AlignmentScore

```

AAGCAAAGCGCAGCGTCTGAAT
AAAAAATTAAGCGCAAGATTG
CATTACATTGCTGGATAAGAATTG

```

TF binding sites (TFBSs)

[CRP,-] Phrase

Type	Transcription factor	Function	Promoter	Binding Sites			Growth Conditions	Evidence (Confirmed, Strong, Weak)	Reference(s)
				LeftPos	RightPos	Central Rel-Pos			
proximal	CRP-cAMP	repressor	glnAp2	4058152	4058173	-55.5	ttttgcacgaTGGTGCGCATGATAACGCCTTTtaggggcaat nd	[AIBSCS], [BPP], [GEA]	[7]
proximal	CRP-cAMP	repressor	glnAp2	4058154	4058175	-57.5	cctttgcacGATGGTGCGCATGATAACGCCTTTtaggggca nd	[AIBSCS], [BPP], [GEA]	[7]

[Fis,+] Phrase

Type	Transcription factor	Function	Promoter	Binding Sites			Growth Conditions	Evidence (Confirmed, Strong, Weak)	Reference(s)
				LeftPos	RightPos	Central Rel-Pos			
proximal	Fis	activator	glnAp2	4058155	4058169	-55.0	gcacgatggtGCGCATGATAACGCCTTTtaggggca nd	[AIBSCS], [BPP], [GEA]	[12]

[NtrC,+] Phrase

Type	Transcription factor	Function	Promoter	Binding Sites			Growth Conditions	Evidence (Confirmed, Strong, Weak)	Reference(s)
				LeftPos	RightPos	Central Rel-Pos			
proximal	NtrC-Phosphorylated	activator	glnAp2	4058144	4058160	-45.0	tgcgatgatAACGCCTTTTAGGGGCAatttaaagt nd	[GEA], [HIBSCS]	[9], [11]
proximal	NtrC-Phosphorylated	activator	glnAp2	4058167	4058183	-68.0	ggtgcagcccTTTTGCACGATGGTGCGcatgataacg nd	[GEA], [HIBSCS], [SM]	[9], [11]
proximal	NtrC-Phosphorylated	activator	glnAp2	4058188	4058204	-89.0	ttggtgcaacATTACATCGTGGTGCAgcccttttgc nd	[BPP], [GEA], [HIBSCS], [SM]	[5], [6], [8], [9], [11]
remote	NtrC-Phosphorylated	activator	glnAp2	4058207	4058223	-108.0	tttcattgaAGCACTATATTGGTGCAacattcacat nd	[BPP], [GEA], [HIBSCS], [SM]	[5], [6], [9], [10]
remote	NtrC-Phosphorylated	activator	glnAp2	4058239	4058255	-140.0	caaaggtcatTGCACCAACATGGTGCTtaagtgttcc nd	[BPP], [GEA], [HIBSCS], [SM]	[5], [6], [8], [9], [10]

Groups of properties constitute objects, and some objects contain multiple objects

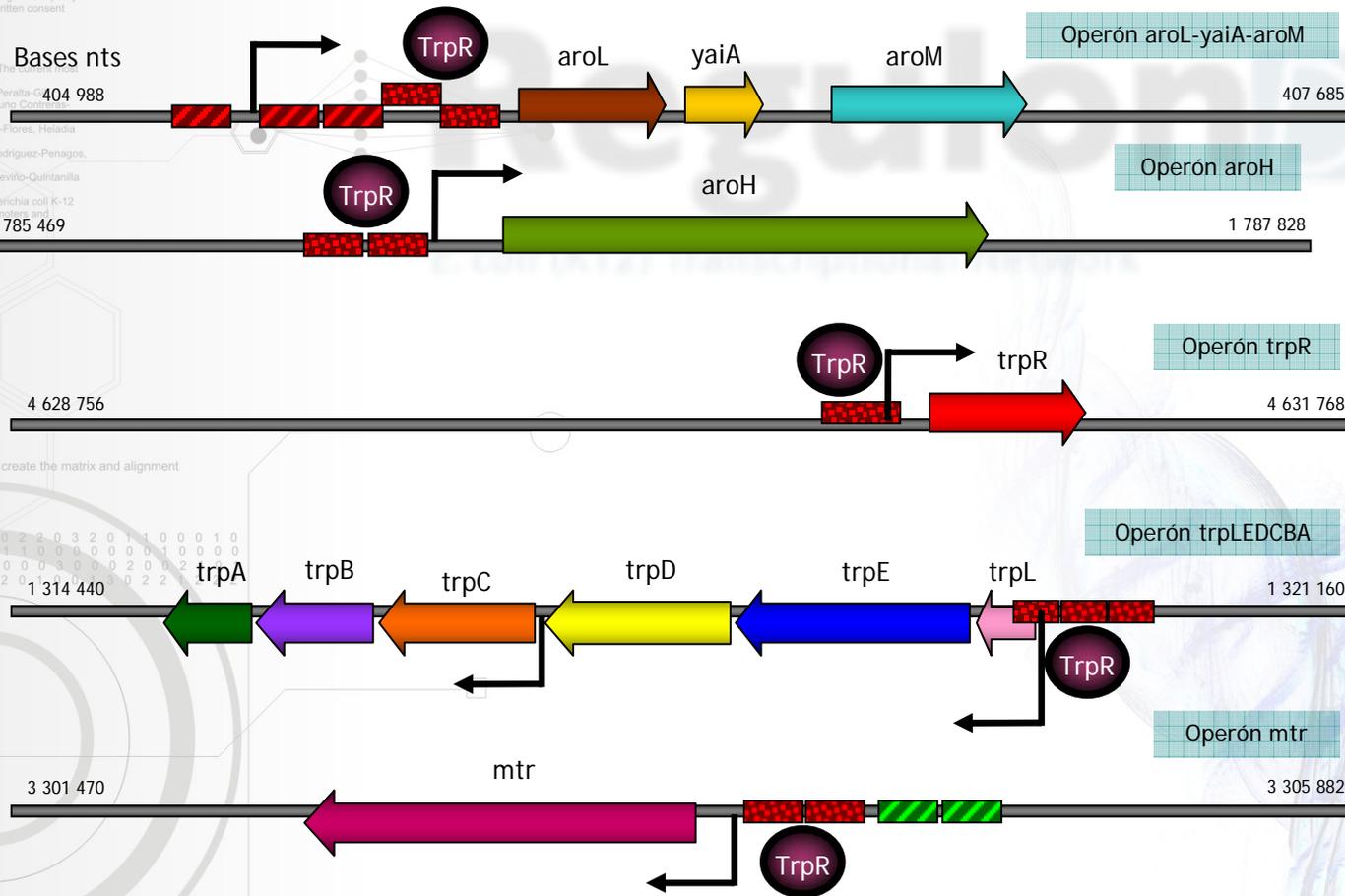
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 Nucleic Acids Research, 2008, vol 36, D120-D124

Release: 6.4 Date: 10-AUG-09



Transcription Factor Matrix and Alignments

The consensus and patser programs were used to create the matrix and alignment
 Transcription Factor NameAda
 Total of uniq binding sites3

Matrix

```

A 2 3 1 1 1 3 2 3 0 0 1 1 2 0 0 1 0 2 0 3 2 0 1 1 0 0 0 1 0
C 1 0 0 1 0 1 0 1 0 1 0 2 0 0 2 0 0 4 1 0 0 0 0 0 0 0 1 0 0 0 0
G 0 0 1 0 0 0 0 0 1 0 2 0 0 3 1 2 0 0 0 3 0 0 0 2 0 0 2 0 0 0
T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0 2 0 0 1 0 0 2 2 0 0 2 0 2 0 0 0
    
```

AlignmentScore

```

AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
AAAAAATAAAGCGCAAGATTGTTGGTT21.42
CATTACATTGCTGGATAAAGATGTTTAG19.78
    
```

What is TrpR controlling ?

A new concept: GENSOR Units

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"RegulonDB (Version 6.0): gene regulation model of Escherichia coli beyond transcription, active (experimental) annotated protein-coding genes (textpresso navigation)"
Nucleic Acids Research, 2008, vol 36, D120-D124

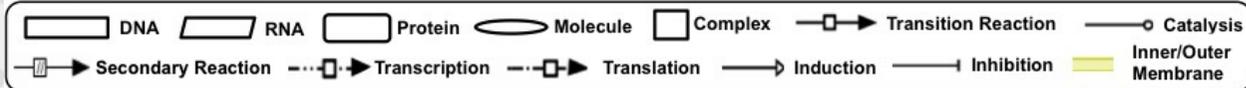
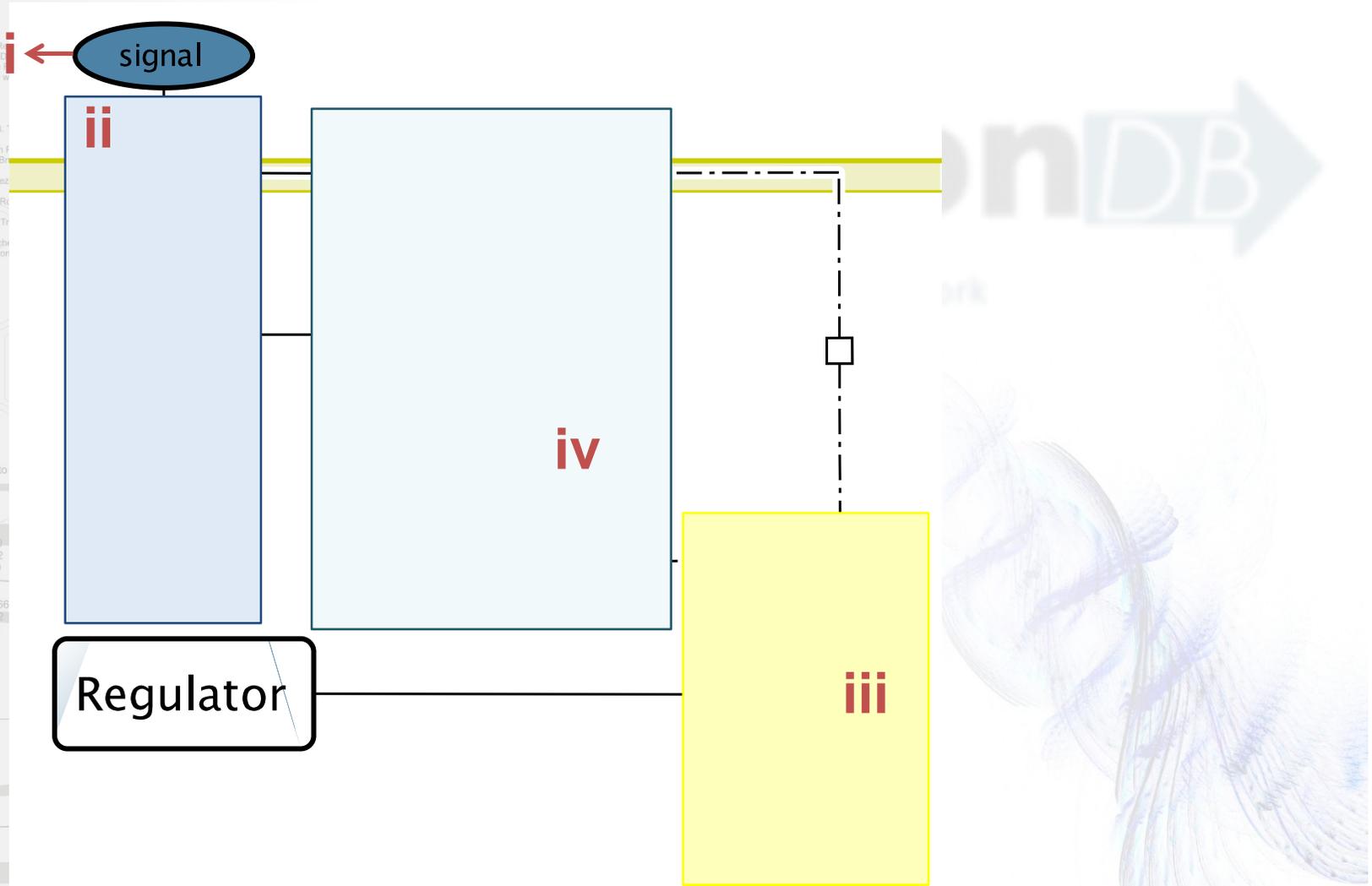
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Total of uniq binding sites3

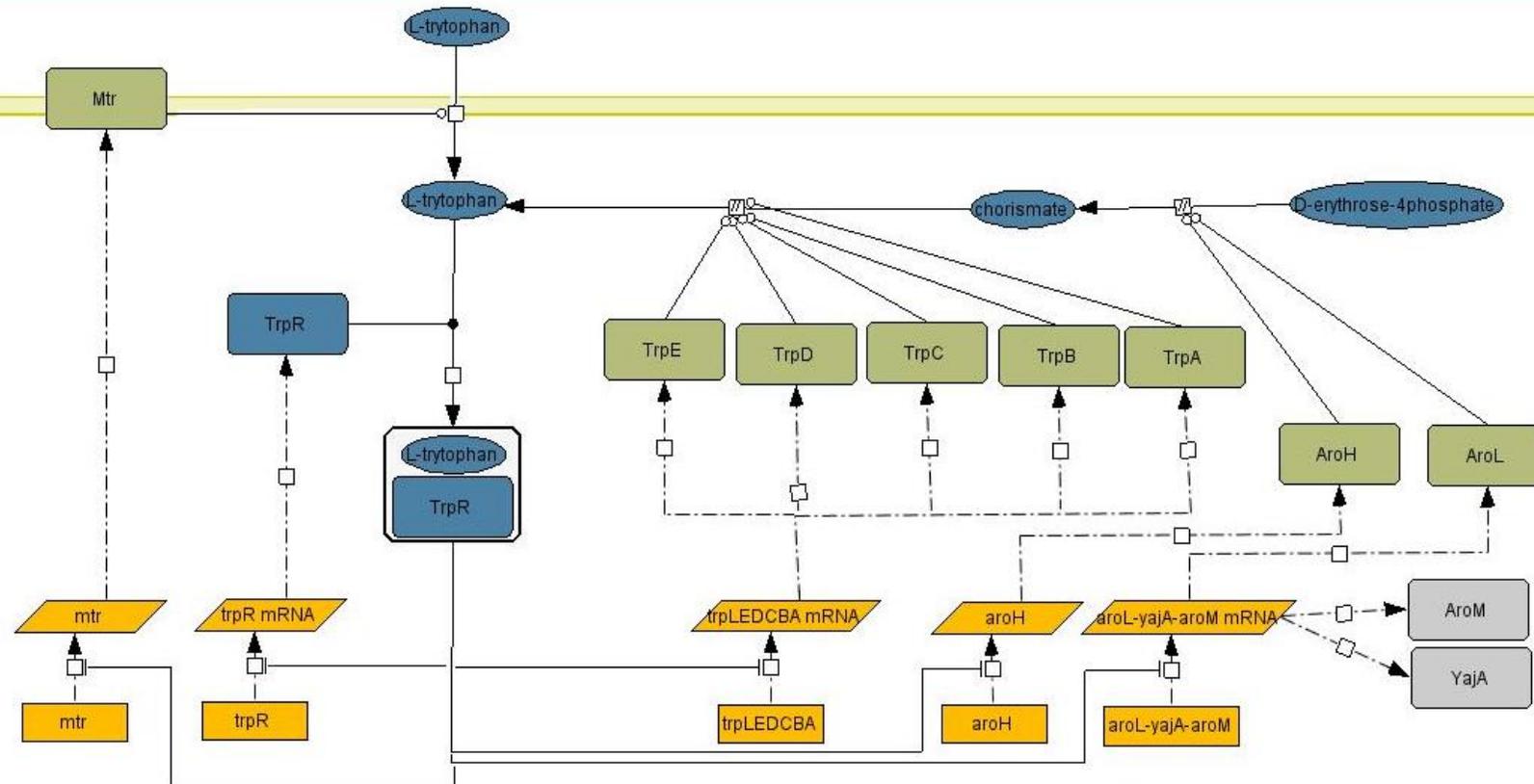
Matrix
A 2 3 1 1 1 3 2 3 0 0 1 1 2 0 0 1
C 1 0 0 1 0 1 0 0 1 0 2 0 0 2 0
G 0 0 1 0 0 0 0 0 1 0 2 0 0 3 1 2
T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0

AlignmentScore
AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
AAAAAATTAAGCGCAAGATTGTTGGT121.42
CATTACATTGCTGGATAAGAATGTTTAG19.78



The TrpR GENSOR Unit

Genes



In the presence of L-tryptophan, TrpR represses transcription of genes that code for proteins necessary for synthesis and transport of tryptophan.

There is no known function for proteins AroM and YanjA.

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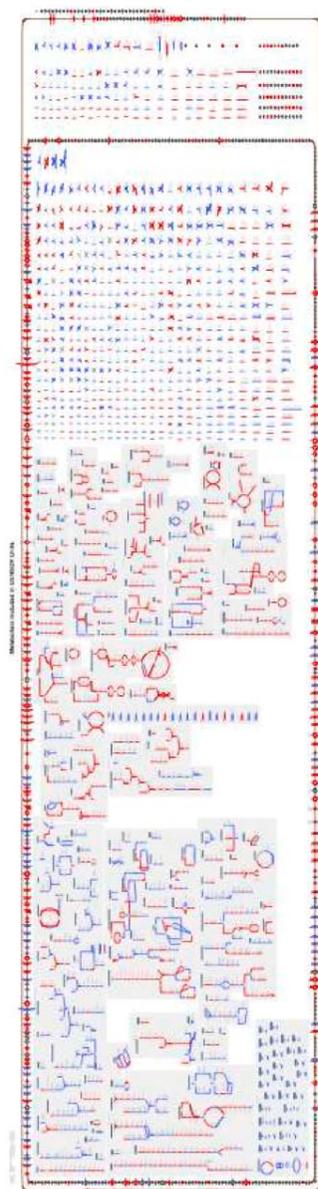
Release: 6.4 Date: 10-AUG-09

Transcription Factor Matrix and Alignment

The consensus and patser programs we Transcription Factor NameAda Total of uniq binding sites3

Matrix
A 2 3 1 1 1 3 2 3 0 0 1 1 2
C 1 0 0 1 0 1 0 0 1 0 2 0 0
G 0 0 1 0 0 0 0 0 1 0 2 0 0
T 0 0 1 1 0 0 0 2 2 0 0 1

AlignmentScore
AAGCAAAGCGCAGCGTCTGAATAACC
AAAAAATTAAGCGCAAGATTGTTGC
CATTACATTGCTGGATAAGAATGTTT



Genome-wide mapping of transcriptional regulation and metabolism describes information-processing units in Escherichia coli

Daniela Ledezma-Tejeida¹, Cecilia Ishida¹, Julio Collado-Vides¹

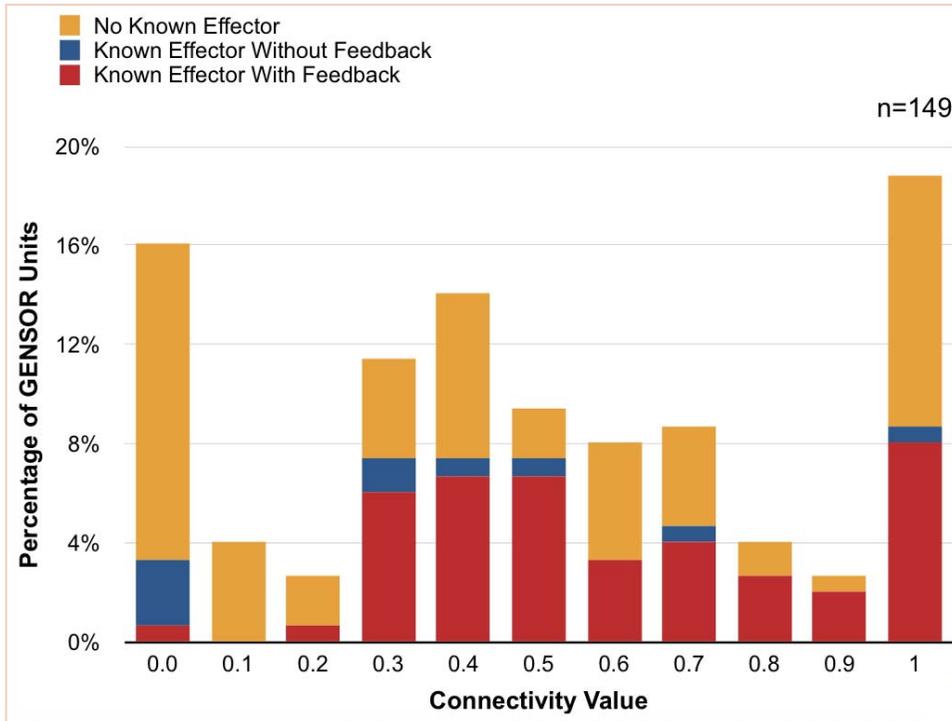
¹Centro de Ciencias Genómicas, Universidad Nacional Autónoma de México, Mexico

Submitted to Journal:
Frontiers in Microbiology

Specialty Section:
Systems Microbiology

Front Microbiol. 2017 Aug 3; 8: 1466.
doi: 10.3389/fmicb.2017.01466.

Table S3. Fraction of metabolism covered by GENSOR Units. Cellular Overview from *EcoCyc* showing in red the reactions included in the GENSOR Unit collection. Most metabolic pathways are covered, especially carbon, aminoacid and lipid metabolism. An SBML map of the 189 merged GENSOR Units is available on demand.



Connectivity

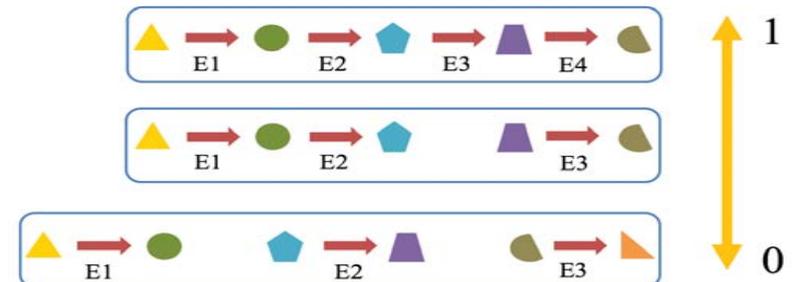
$$C = \frac{E_c}{E_t + (M_f t - 1)}$$

Where:

EC: connected enzymes

Et: Total number of enzymes

Mft: total number of metabolic fluxes



GENSOR Unit	Data sets					Version uploaded to RegulonDB
	RegulonDB	Galagan	ChIP-ChIP	ChIP-exo	SELEX	
ArgR	0.64		0.64	0.64		(ChIP-exo) 0.34
CsiR	1.00	0.08				
Fur	0.52			0.36		(ChIP-exo) 0.51
LexA	0.40		0.24			
MntR	0.00				0.00	
Nac	0.45	0.42				
NsrR	0.43		0.06			
OmpR	0.11	0.07				(ChIP-exo) 0.46 (SELEX) 0.00
PurR	0.81		0.56			
RstA	0.00				0.20	
RutR	0.50		0.09			
UvrY	0.00			0.31		

Work in progress: many questions !

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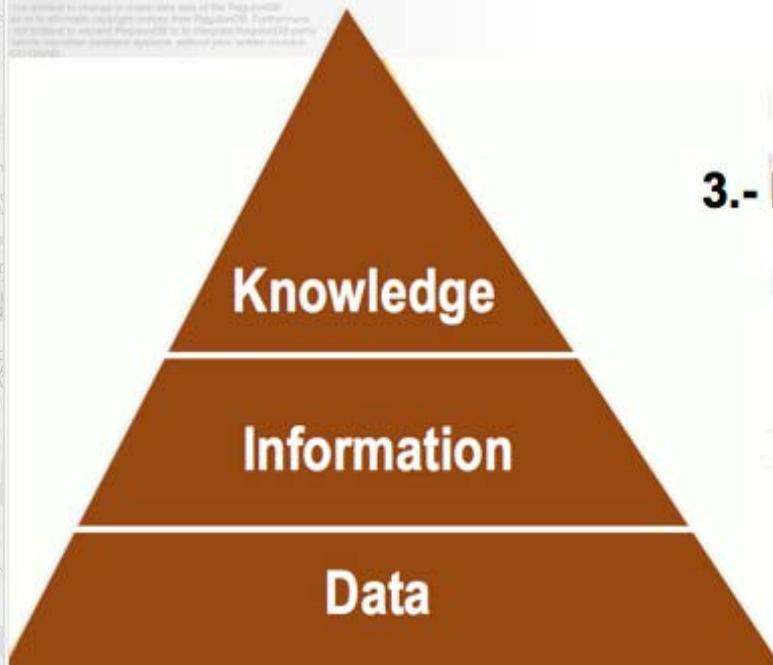
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Transcription Factor Matrix and

The consensus and pattern for
Transcription Factor NameAd
Total of uniq binding sites3

Matrix
A 2 3 1 1 3 2 3 0 0
C 1 0 0 1 0 1 0 0
G 0 0 1 0 0 0 0 1
T 0 0 1 1 0 0 0 2

AlignmentScore
AAGCAAAGCGCAGCGTCTC
AAAAAATTAAGCGCAAG/
CATTACATTGCTGATAAGA

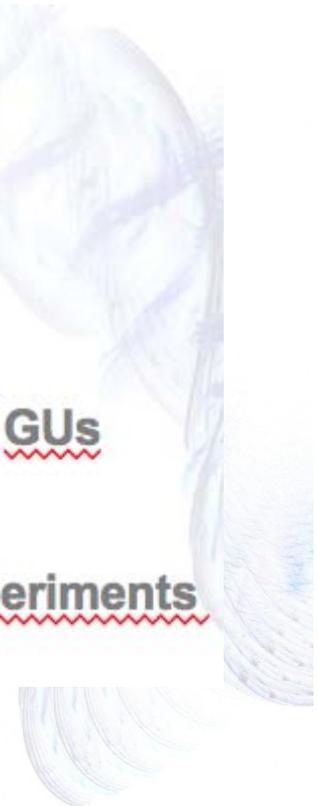


3.- NLP strategies

2.- Operons, regulons and GUs

1.- Curating HT experiments

RegulonDB



The challenge: encoding "knowledge"

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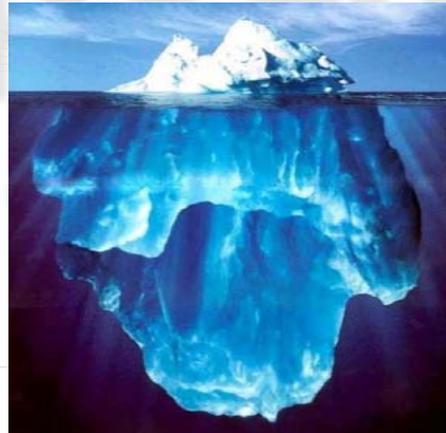
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"RegulonDB (Version 6.0): gene regulation model of Escherichia coli K-12 beyond transcription, active (experimental) annotated promoters and textpresso navigation"
Nucleic Acids Research, 2008, vol 36, D320-D324

Release: 6.4 Date: 10-AUG-09

20 to 25%



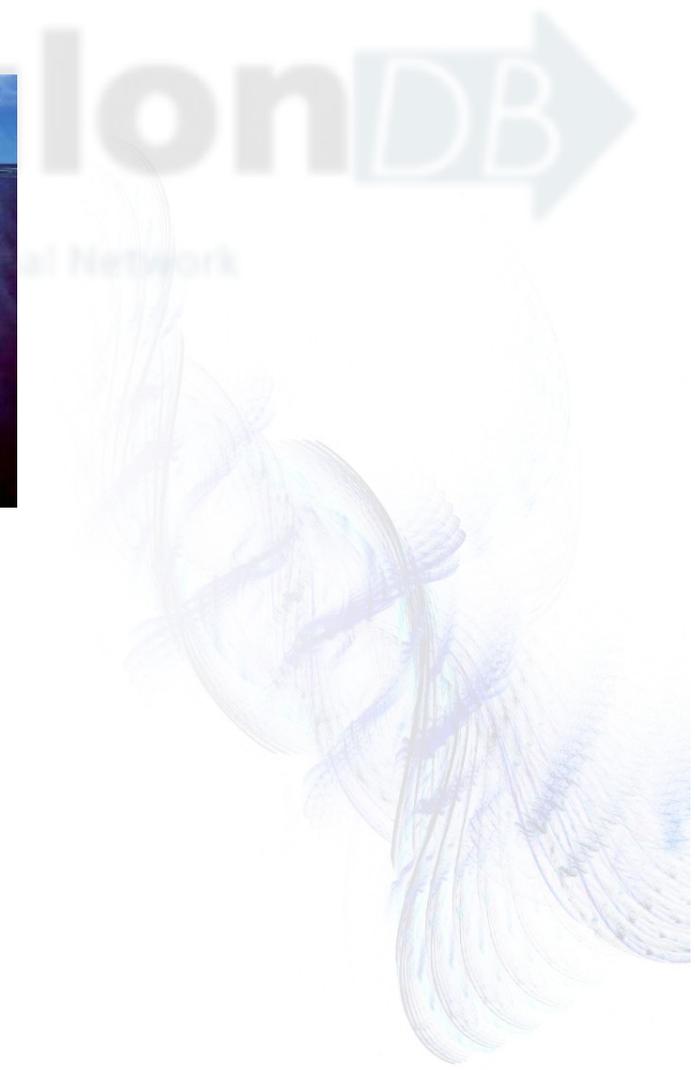
75 to 80%

Transcription Factor Matrix and Alignments

The consensus and patser programs were used to create the matrix and alignment
Transcription Factor NameAda
Total of uniq binding sites3

Matrix
A 2 3 1 1 3 2 3 0 0 1 1 2 0 0 1 0 2 2 0 3 2 0 1 1 0 0 0 1 0
C 1 0 0 1 0 1 0 0 1 0 2 0 0 2 0 1 1 0 0 0 0 0 0 0 1 0 0 0 0
G 0 0 1 0 0 0 0 1 0 2 0 0 3 1 2 0 0 0 3 0 0 0 2 0 0 2 1 0 1
T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0 2 0 1 0 0 1 3 0 2 2 1 2 2 2

AlignmentScore
AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
AAAAAATTAAGCGCAAGATTGTTGGT21.42
CATTACATTGCTGATAAGAATGTTTAG19.78



The challenge: encoding "knowledge"

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Citation

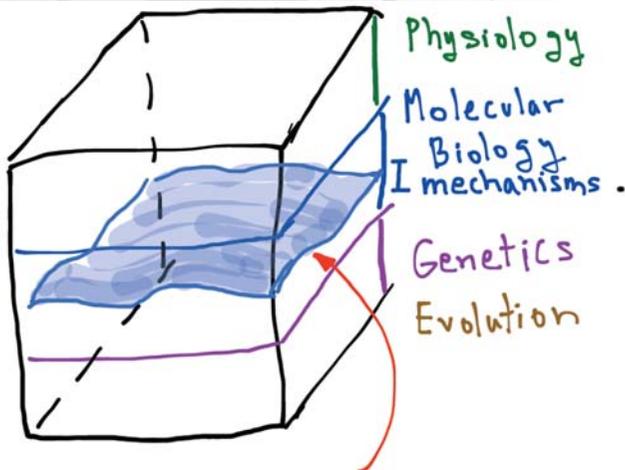
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Socorro Gama-Castro, Verónica Jiménez-Jacinto, Martín Peralta-Gil, Alberto Santos-Zavaleta, Monica I. Peñaloza-Spindola, Bruno Contreras-Moreira, Juan Segura-Salazar, Luis Muñoz-Rascado, Irma Martínez-Flores, Heladia Salgado, César Bonavides-Martínez, Cel Abreu-Goodger, Carlos Rodríguez-Penagos, Juan Miranda-Rico, Enrique Morett, Enrique Merino, Azaceli M. Huerts, Luis Treviño-Quintanilla and Julio Collado-Vides. "RegulonDB (Version 6.0): gene regulation model of Escherichia coli K-12 beyond transcription, active (experimental) annotated promoters and textpresso navigation" Nucleic Acids Research, 2008, vol 36, D320-D124

Release: 6.4 Date: 10-AUG-09

Transcription Factor Matrix and Alignments

The consensus and patser programs were used to create the matrix and alignment
Transcription Factor NameAda
Total of uniq binding sites3

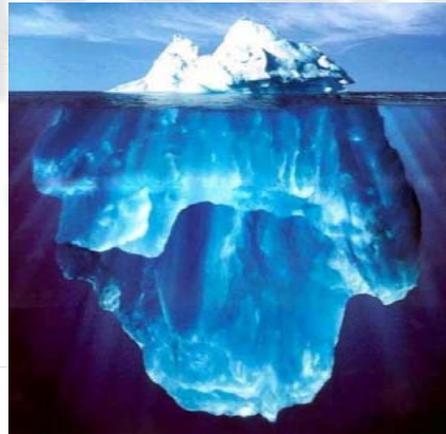
Matrix
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C
G
T
Align
AA
AA
CA



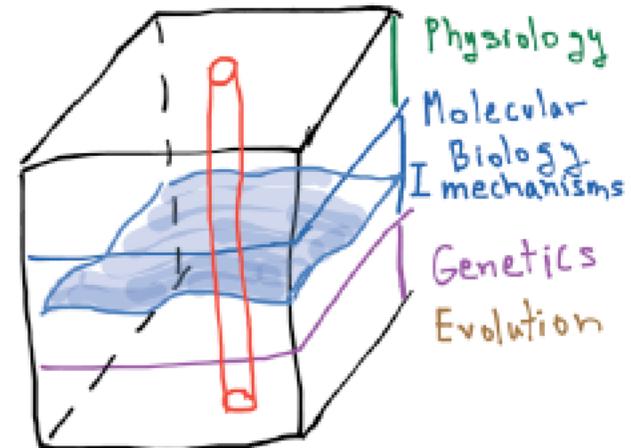
we curate the shadows of mechanisms and transcription on the genome

20 to 25%

75 to 80%



A theme



How to enhance access to knowledge ?

We are using natural language processing tools



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"RegulonDB: a genome regulation model of Escherichia coli K-12 beyond transcription (experimental), annotated promoters and textpresso." Nucleic Acids Res. vol 36. D329-D334. Release: 01/2008.



I. To enhance / improve curation

Curators

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Total of uniq binding sites3

Matrix
A 2 3 1 1 3 2 3 0 0 1 1 2 0 0 1 0 2 2 0 3 2 0 1 1 0 0 0 1 0
C 1 0 0 1 0 1 0 0 1 0 2 0 0 2 0 1 1 0 0 0 0 0 0 0 1 0 0 0 0
G 0 0 1 0 0 0 0 1 0 2 0 0 3 1 2 0 0 0 3 0 0 0 2 0 0 2 1 0 1
T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0 2 0 1 0 0 1 3 0 2 2 2 2 2 2

AlignmentScore
AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
AAAAAATAAAGCGCAAGATTGTTGGTT21.42
CATTACATTGCTGGATAAGAATGTTTAG19.78

II. To enhance navigation through knowledge and its connection to data and information



Users

We are using natural language processing tools



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 Release: 6.0 (2013)



I. To enhance / improve curation

Curators

L-Regulon-DB

Transcription Factor Matrix and Alignments

The consensus and pater programs were used to create the matrix and alignment
 Transcription Factor NameAda
 Total of uniq binding sites3

Matrix
 A 2 3 1 1 1 3 2 3 0 0 1 1 2 0 0 1 0 2 2 0 3 2 0 1 1 0 0 0 1 0
 C 1 0 0 1 0 1 0 0 1 0 2 0 0 2 0 1 1 0 0 0 0 0 0 0 0 1 0 0 0 0
 G 0 0 1 0 0 0 0 0 1 0 2 0 0 3 1 2 0 0 0 3 0 0 0 2 0 0 2 1 0 1
 T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0 2 0 1 0 0 1 3 0 2 2 2 2 2 2

AlignmentScore
 AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
 AAAAAAATAAAGCGCAAGATTGTTGGTT21.42
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Citation

User is commi update publica Succorri Gianu Alberto Santos Moreira, Juan Segura-S Salgado, César Bonavid Juan Miranda- Enrique Morel and Julio Colla "RegulonDB (beyond trans textpresso nav Nucleic Acids I

Release: 6.4 D

Microbiology (1999), 145, 41-55

Printed in Great Britain

Transcriptional regulation of molybdoenzyme synthesis in *Escherichia coli* in response to molybdenum: ModE-molybdate, a repressor of the *modABCD* (molybdate transport) operon is a secondary transcriptional activator for the *hyc* and *nar* operons

William T. Self, Amy M. Grunden,[†] Adnan Hasona and K. T. Shanmugam

Author for correspondence: K. T. Shanmugam. Tel: +1 352 392 2490. Fax: +1 352 392 3922. e-mail: shan@micro.fsu.edu

Department of Microbiology and Cell Science, University of Florida, Gainesville, FL 32611, USA

Escherichia coli growing under anaerobic conditions produces several molybdoenzymes, such as formate hydrogenlyase (formate to H₂ and CO₂); *hyc* and *fdhF* genes) and nitrate reductase (*narGHJ* genes). Synthesis of these molybdoenzymes, even in the presence of the cognate transcriptional activators and effectors, requires molybdate in the medium. Besides the need for molybdopterin cofactor synthesis, molybdate is also required for transcription of the genes encoding these molybdoenzymes. In *E. coli*, ModE was previously identified as a repressor controlling transcription of the operon encoding molybdate transport components (*modABCD*). In this work, the ModE protein was also found to be a required component in the activation of *hyc-lacZ* to an optimum level, but only in the presence of molybdate. Mutant ModE proteins which are molybdate-independent for repression of *modA-lacZ* also restored *hyc-lacZ* expression to the wild-type level even in the absence of molybdate. Nitrate-dependent enhancement of transcription of *narX-lacZ* was completely abolished in a *modE* mutant. Nitrate-response by *narG-lacZ* and *narK-lacZ* was reduced by about 50% in a *modE* mutant. DNase I footprinting experiments revealed that the ModE protein binds the *hyc* promoter DNA in the presence of molybdate. ModE-molybdate also protected DNA in the intergenic region between *narX* and *narK* from DNase I hydrolysis. DNA sequences (5' TAYAT'3 and 5' GTTA 3') found in ModE-molybdate-protected *modABCD* operator DNA were also found in the ModE-molybdate-protected region of *hyc* promoter DNA (5' GTA-7 bp-CATAT 3') and *narX-narK* intergenic region (5' GTTA-7 bp-TACAT 3'). Based on these results, a working model is proposed in which ModE-molybdate serves as a secondary transcriptional activator of both the *hyc* and *narX* operons which are activated primarily by the transcriptional activators, FhA and NarL, respectively.

Keywords: molybdate, regulation, ModE, formate hydrogenlyase, *nar* operon

INTRODUCTION

Under anaerobic growth conditions, *Escherichia coli* produces several molybdoenzymes, almost all of which

serve as terminal enzymes in anaerobic respiratory pathways (Genies & Stewart, 1996). Among the various molybdoenzymes, formate hydrogenlyase (FHL) is unique and is not a component of anaerobic respiration. The FHL complex which catalyses cleavage of formate to H₂ and CO₂, contains a formate dehydrogenase isoenzyme (FDH-H₂ (*fdhF*)), a hydrogenase isoenzyme (HYD3; *hyc*) and intermediate electron carriers also

[†] Present address: Department of Biochemistry and Molecular Biology, University of Georgia, Athens, GA 30602, USA.
Abbreviation: FHL, formate hydrogenlyase.

Regulation of *hyc* and *narXL* expression by ModE

Table 6. Effect of *modE* mutation on nitrate-dependent increase in expression of various *nar-lacZ* fusions

Cells were grown in LBG+Mo and the sodium nitrate concentration (where present) was 30 mM. Values in parentheses represent the percentage of activity in the various strains in comparison to the values obtained with the corresponding wild-type parent strain grown in the same medium.

Strain	Relevant genotype	β -Galactosidase activity*	
		-NO ₃	+NO ₃
<i>narG-lacZ</i> derivatives			
SE2176	Wild-type	2900	19 500
SE2163	Δ modE	2500 (86)	9000 (46)
SE2163(pAG1)	Δ modE pmodE ⁺	2400 (83)	21000 (108)
SE2213	<i>narL</i>	2800 (97)	1300 (7)
<i>narX-lacZ</i> derivatives			
AH121	Wild-type	1300	5500
AH79	Δ modE	1100 (85)	2200 (40)
AH79(pAG1)	Δ modE pmodE ⁺	1100 (85)	5570 (101)
AH107	<i>narL</i>	920 (71)	970 (18)
<i>narX-lacZ</i> derivatives			
AH122	Wild-type	950	2000
AH78	Δ modE	900 (95)	1000 (50)
AH78(pAG1)	Δ modE pmodE ⁺	800 (80)	1800 (90)
AH106	<i>narL</i>	920 (96)	970 (49)

* Expressed as nmol min⁻¹ (mg cell protein)⁻¹.

ModE protein is required for expression of *narXL* operon

The *narXL* operon encodes the two regulatory proteins needed for activation of the *narG* and *narK* operons (Darwin & Stewart, 1996; Egan & Stewart, 1990; Kalman & Gunsalus, 1990; Schröder *et al.*, 1994; Walker & DeMoss, 1993). Since the expression of *narG* and *narK* is influenced by ModE, the effect of mutations in *modE* on *narX-lacZ* expression was investigated. The wild-type strain with λ Ph(*narX-lacZ*) (strain AH122) produced about 400 units of β -galactosidase activity when grown without nitrate and this activity increased by about twofold in the presence of nitrate (Table 6). This nitrate-dependent enhancement of *narX* expression was absent in a *modE* mutant, strain AH78, and as expected, also in a *narL* mutant, strain AH106. Introducing a plasmid containing the *modE*⁺ gene into the *modE* mutant (strain AH78) restored the nitrate response to that of the wild-type. These results suggest that the requirement of ModE for optimum transcription of *narG-lacZ* and *narK-lacZ* is indirect and is mediated through the control of the *narXL* operon.

ModE binds to *hyc* promoter DNA

Since genetic and physiological experiments suggested that ModE is involved in the regulation of both *P_{hyc}-lacZ* and *narX-lacZ*, direct binding experiments consisting of ModE protein and promoter DNA were carried out. Electrophoretic mobility of a 396 bp *hyc* promoter fragment was retarded in the presence of ModE, but

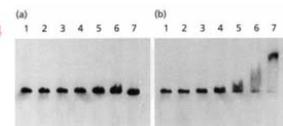


Fig. 2. DNA electrophoretic mobility-shift experiment with purified ModE protein and *hyc* promoter DNA. (a) Without molybdate; (b) with molybdate (0.1 mM) added to binding reactions and electrophoresis buffer. Lane 1, no protein added; lane 2, 85 nM ModE; lane 3, 150 nM ModE; lane 4, 170 nM ModE; lane 5, 212 nM ModE; lane 6, 235 nM ModE; lane 7, 340 nM ModE. The arrow indicates the DNA-protein complex.

only in the presence of molybdate (Fig. 2b). The minimal concentration of ModE-molybdate required for the mobility shift was about 250 nM and this was about a 10-fold higher concentration of ModE than was required for binding to the *modA* operator (Anderson *et al.*, 1997; McNicholas *et al.*, 1997). These results show that the ModE-molybdate complex is capable of binding to *hyc* upstream DNA and efficient binding of ModE to *hyc* promoter DNA requires molybdate. DNase I-footprinting experiments involving ModE and *hyc* promoter DNA revealed that ModE-molybdate protects a 27 bp region in this DNA from DNase I

- Block identification
- Logical sentence extraction
- Reading order discovering

L-RegulonDB: a corpus for navigation

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Release: 6.4 Date: 10-AUG

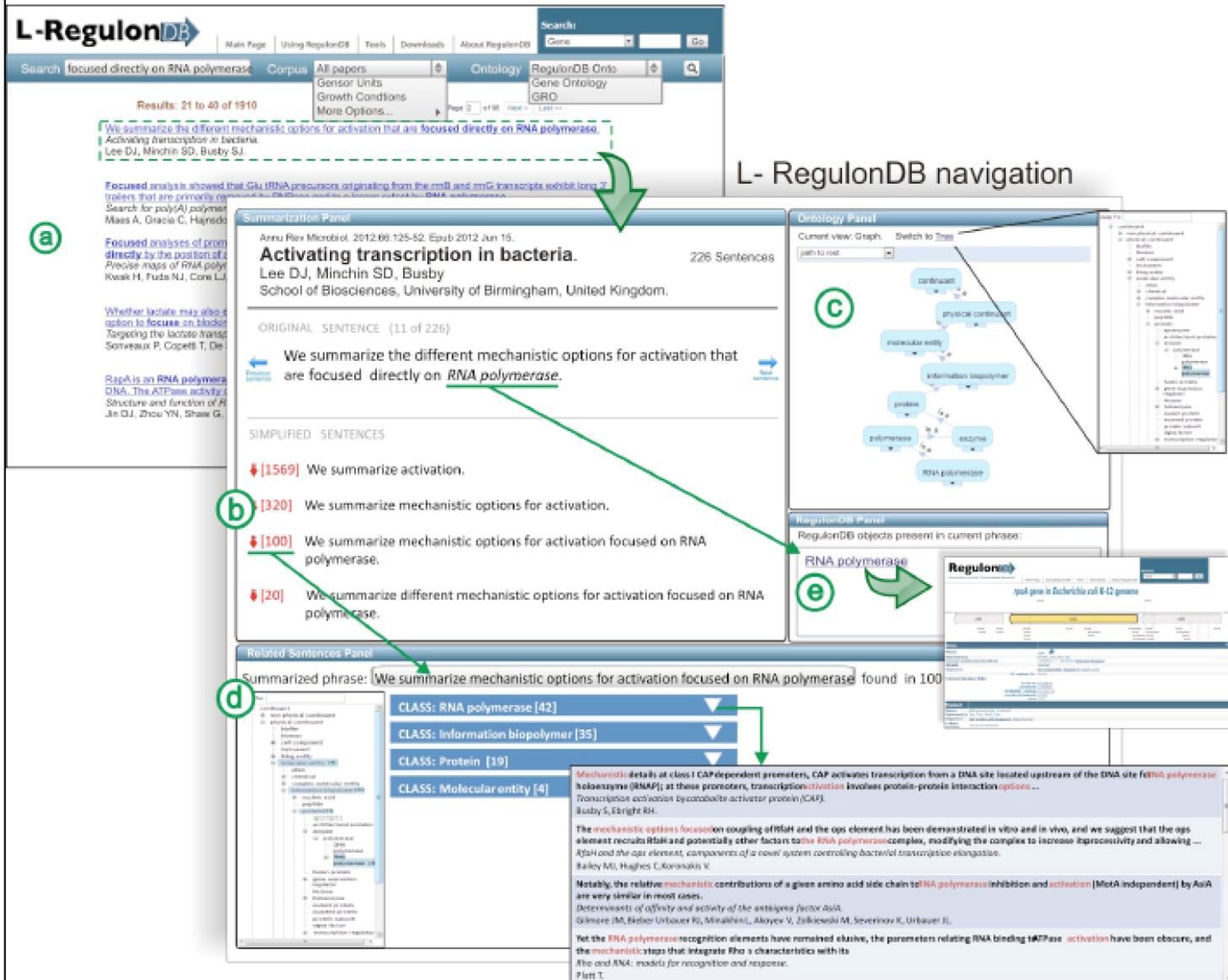
Transcription Factor Mat

The consensus and patterns
Transcription Factor Name
Total of unique binding sites

Matrix
A 2 3 1 1 1 3 2 3
C 1 0 0 1 0 1 0
G 0 0 1 0 0 0 0
T 0 0 1 1 0 0 0

AlignmentScore
AAGCAAAGCGCAGCG
AAAAAATTAAAGCGC
CATTACATTGCTGAT

Phrase search results



L-RegulonDB Search: **focused directly on RNA polymerase** Corpus: All papers | Ontology: RegulonDB Onto

Results: 21 to 40 of 1910

Summary Panel:
Annu Rev Microbiol. 2012;66:125-52. Epub 2012 Jun 16.
Activating transcription in bacteria. 226 Sentences
Lee DJ, Minchin SD, Busby SJ
School of Biosciences, University of Birmingham, United Kingdom.

ORIGINAL SENTENCE (11 of 226)
We summarize the different mechanistic options for activation that are focused directly on RNA polymerase.

SIMPLIFIED SENTENCES
 [1569] We summarize activation.
 [320] We summarize mechanistic options for activation.
 [100] We summarize mechanistic options for activation focused on RNA polymerase.
 [20] We summarize different mechanistic options for activation focused on RNA polymerase.

Related Sentences Panel:
Summarized phrase: We summarize mechanistic options for activation focused on RNA polymerase found in 100

Ontology Panel:
Current view: Graph. Switch to Tree.
path to root: RNA polymerase

RegulonDB Panel:
RegulonDB objects present in current phrase:
RNA polymerase

CLASS: RNA polymerase [42]
CLASS: Information biopolymer [35]
CLASS: Protein [19]
CLASS: Molecular entity [4]

Mechanistic details at class I CAP-dependent promoters, CAP activates transcription from a DNA site located upstream of the DNA site for RNA polymerase holoenzyme (RNAP); at these promoters, transcription activation involves protein-protein interaction options ...
Transcription activation by *cro* and *lambda* activator protein (CAP).
Busby SJ, Ebright RH.

The mechanistic options focus on coupling of RNA and the *ops* element has been demonstrated in vitro and in vivo, and we suggest that the *ops* element recruits Rho and potentially other factors to the RNA polymerase complex, modifying the complex to increase processivity and allowing ...
AraC and the *ops* element, components of a novel system controlling bacterial transcription elongation.
Bailey MJ, Hughes C, Koronakis K.

Notably, the relative mechanistic contributions of a given amino acid side chain to RNA polymerase inhibition and activation (MecA independent) by AraC are very similar in most cases.
Determinants of affinity and activity of the enteric factor AraC.
Sikness JM, Beyer Urbauer R, Minakami I, Aloyev V, Zalkiewski M, Severinov K, Urbauer JL.

Yet the RNA polymerase recognition elements have remained elusive, the parameters relating RNA binding to Rho activation have been obscure, and the mechanistic steps that integrate Rho characteristics with its Rho and RNA: models for recognition and response.
Platt T.

L-RegulonDB navigation



Article metadata (title, author, journal, year)

Posttranscriptional activation of the transcriptional activator Rob by dipyriddy in Escherichia coli.

Rosner JL(1), Dangi B, Gronenborn AM, Martin RG.

AA Frase de mayor coincidencia

AA Frases con relaciones

Mapa

Abstract

(NTD)(CTD)The transcriptional activator Rob consists of an N-terminal domain of DNA binding and promoter activation and a C-terminal domain of 169 amino acid. Although several thousand molecules of are normally present per Escherichia promoters of the rob regulon poorly.(the latter is not a metal chelator) We report either 2,2"- or 4,4"-dipyridyl, Rob-mediated transcription of various rob regulon promoters was increased substantially. A small, growth-phase-dependent effect of dipyriddy on the rob promoter was observed.(lac) However, dipyriddy enhanced Rob's activity even when rob was regulated by a heterologous promoter showing that the action of dipyriddy is mainly posttranscriptional. Mutants lacking from 30 to 166 of the C-terminal amino acids of Rob had basal levels of activity similar to that of wild-type cells, but dipyriddy treatment did not enhance this activity. Thus, the CTD is not an inhibitor of but is required for activation of by dipyriddy. In contrast to its relatively low activity in vivo, binding to cognate DNA and activation of transcription in vitro is similar to that of MarA, which has a homologous NTD but no CTD. In vitro nuclear magnetic resonance studies demonstrated that 2,2"-dipyridyl binds to Rob but not to the CTD-truncated Rob or to MarA, suggesting that the effect of dipyriddy on Rob is direct. Thus, it appears that Rob can be converted from a low activity state to a high-activity state by a CTD-mediated mechanism in vivo or by purification in vitro.

(pri)C)Rob is an abundant 289-amino-acid protein originally discovered by virtue of the ?right side? of the origin of replication in Escherichia coli.(NTD) Subsequently, has an N-terminal domain of 120 amino acids that is highly homologous to the s and SoxS, is also a transcriptional activator when overexpressed and has D promoter specificities in vitro that are similar to those of and SoxS. For convenience, the dozen or more promoters activated by these proteins are collectively referred to here as the mar/sox/rob regulon even though

Selected phrase

Biological objects in RegulonDB

Frases relacionadas en este artículo

SCORE	SECCIÓN
50%	Abstract
27%	
38%	MATERIALS AND METHODS

Abstract

50%

27%

MATERIALS AND METHODS

38%

Related phrases in the same publication

FRASE SELECCIONADA:

* Mutants lacking from 30 to 166 of the C-terminal amino acids of Rob had basal levels of activity similar to that of wild-type cells, but dipyriddy treatment did not enhance this activity.*

Relaciones en este artículo

Orden article by Relevancia (score) ▾

1 ... Rob binds more tightly to many of its cognate sites in vitro than does MarA or SoxS, and yet basal levels of Rob activate the mar/sox/rob regulon promoters to a rather low extent in vivo...

SCORE:50.71%

2 ... The transcriptional activator Rob consists of an N-terminal domain of 120 amino acids responsible for DNA binding and promoter activation and a C-terminal domain of 169 amino acids

Relaciones en otros artículos

Orden article by Relevancia (score) ▾

Publication content (reading panel)

Map of sections & related phrases

Related phrases in other publications

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Release: 6.4 Date: 10-AUG-09

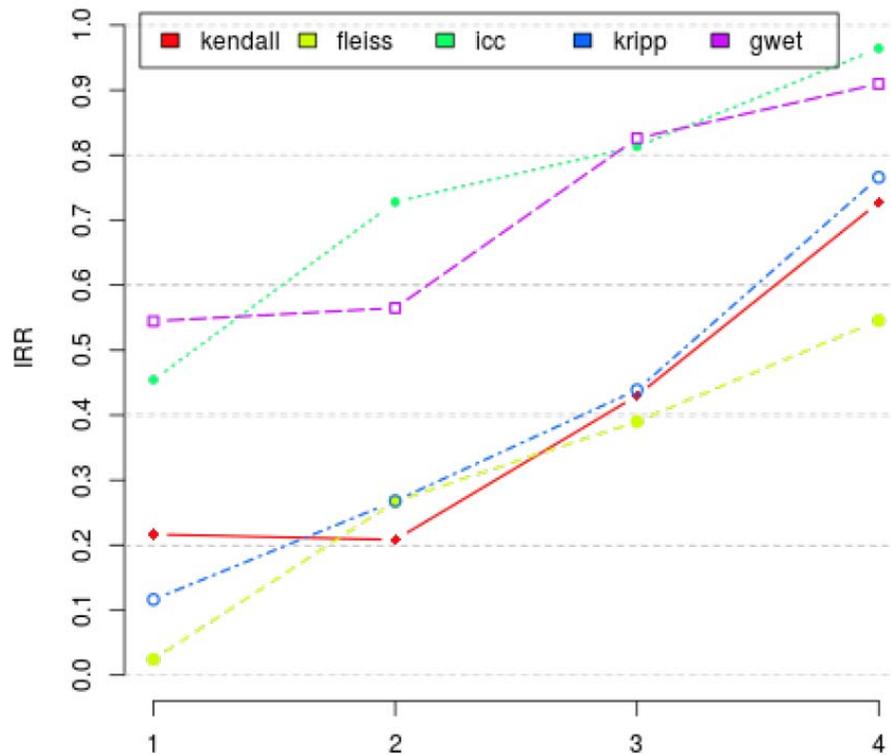
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Matrix
A 2 3 1 1 3 2 3 0 0 1 1 2 0 0 1 0 2 2 0
C 1 0 0 1 0 1 0 0 1 0 2 0 0 2 0 4 1 0 0
G 0 0 1 0 0 0 0 1 0 2 0 0 3 1 2 0 0 0 3
T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0 2 0 1 0

AlignmentScore
AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
AAAAAATTAAGCGCAAGATTGTTGGTT21.42
CATTACATTGCTGGATAAGAATGTTTAG19.78

Evolution of IRR in consensus sessions



Inter-rating reliability (IRR) through agreement sessions

Three young friends

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Photos



Xochicalco, 1994





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Matrix
A 2 3 1 1 3 2 3 0 0 1 1 2 0 0 1 0 2 2 0 3 2 0 1 1 0 0 0 1 0
C 1 0 0 1 0 1 0 0 1 0 2 0 0 2 0 4 1 0 0 0 0 0 0 0 1 0 0 0 0
G 0 0 1 0 0 0 0 1 0 2 0 0 3 1 2 0 0 0 3 0 0 0 2 0 0 2 1 0 1
T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0 2 0 1 0 0 1 3 0 2 2 1 2 2 2

AlignmentScore
AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
AAAAAATTAAAGCGCAAGATTGTTGGTT21.42
CATTACATTGCTGGATAAGAATGTTTAG19.78

Xochicalco, 1994





And an old friend with great vision ! Congratulations Edgar !!



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Citation

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Release: 6.4.0

Transcription Factor

The consensus sequence for the transcription factor is:
Transcription Factor
Total of unique binding sites: 1

Matrix
A 2 3 1 0 0
C 1 0 0 0 0
G 0 0 1 0 0
T 0 0 1 0 0

AlignmentScore
AAGCAAAGC
AAAAAATTA
CATTACATTG





Acknowledgements

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Nucleic Acids Research, 2008, vol 36, D120-D124

Release: 6.4 Date: 10-AUG-09

To all in the lab



Thank you for your remote attention

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Transcription Factor Name:Ada
Total of uniq binding sites:3

Matrix
A 2 3 1 1 3 2 3 0 0 1 1 2 0 0 1 0 2 2 0 3 2 0 1 1 0 0 0 1 0
C 1 0 0 1 0 1 0 0 1 0 2 0 0 2 0 1 1 0 0 0 0 0 0 0 1 0 0 0 0
G 0 0 1 0 0 0 0 1 0 2 0 0 3 1 2 0 0 0 3 0 0 0 2 0 0 2 1 0 1
T 0 0 1 1 0 0 0 2 2 0 0 1 0 0 0 2 0 1 0 0 1 3 0 2 2 1 2 2 2

AlignmentScore
AAGCAAAGCGCAGCGTCTGAATAACGTTT20.66
AAAAAATTAAGCGCAAGATTGTTGGTT21.42
CATTACATTGCTGGATAAGAATGTTTAG19.78

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