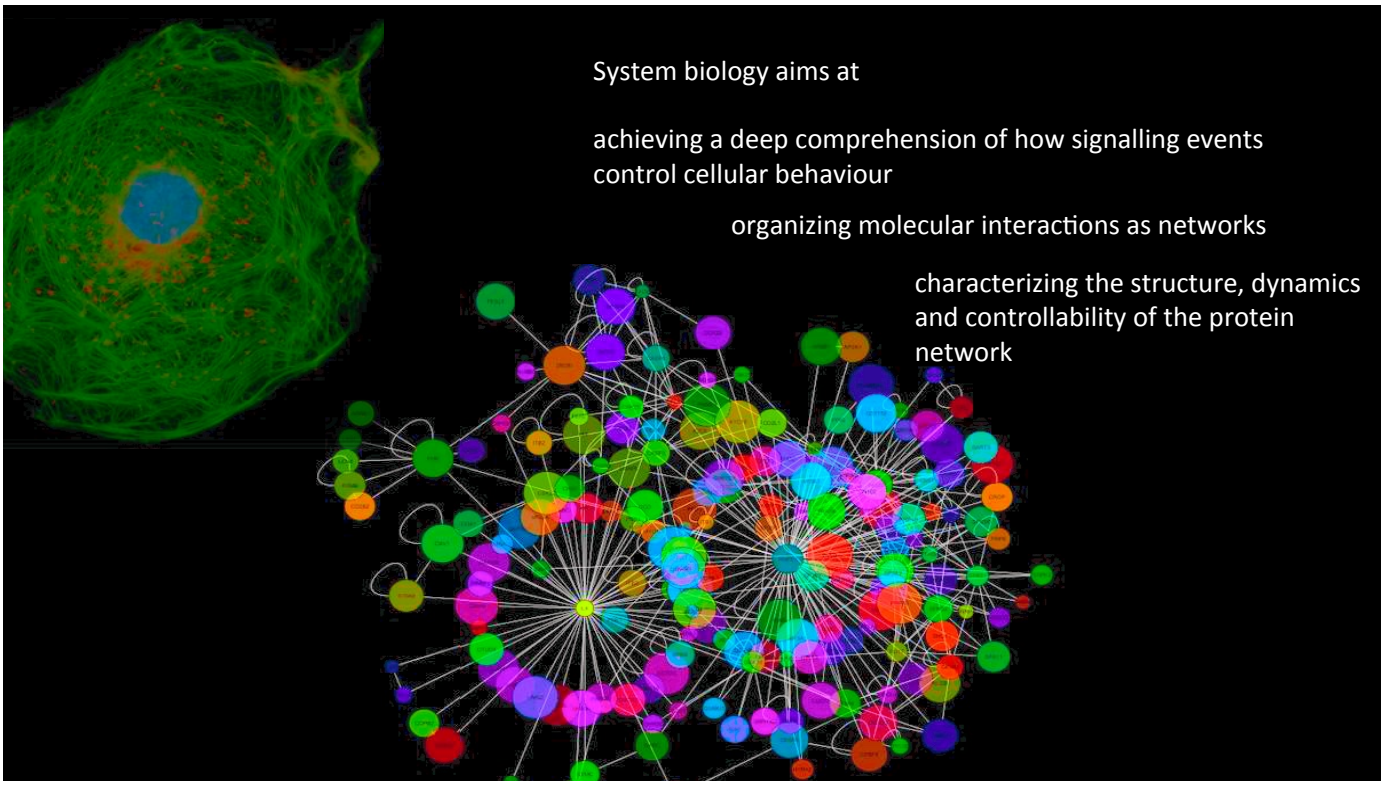
University of Rome Tor Vergata
Department of Biology

BioNetVisA
Biological
Network
Visualisation
Analysis

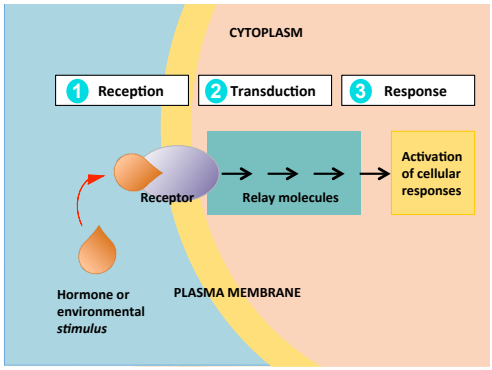
Signor

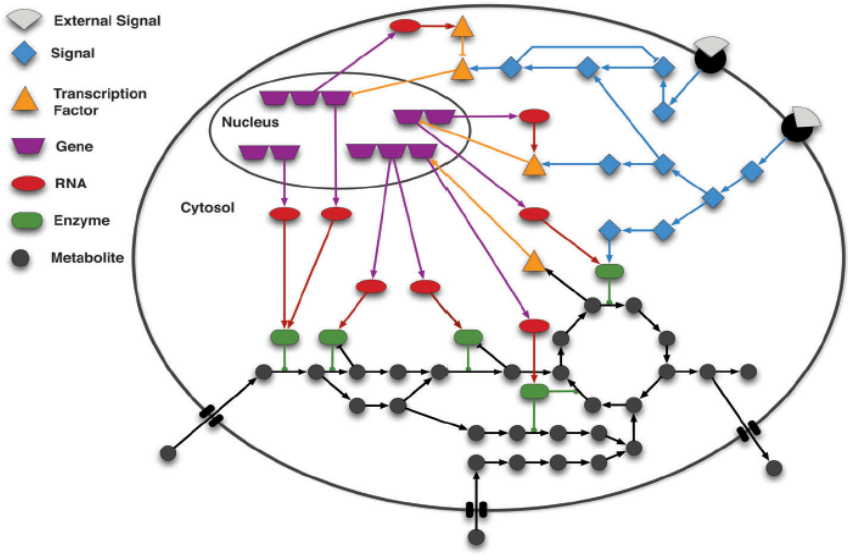
SIGNOR: a new signaling resource

Developed by **Livia Perfetto, Leonardo Briganti and Alberto Calderone**
Group Leader: **Gianni Cesareni and Luisa Castagnoli**



Signal Transduction





Conçalves *et al*., 2012 Mol. BioSyst.

The cell logic model

"a cellular phenotype results from interactions between various gene products, signalling molecules, metabolites, etc..."

integrate data from different sources (pathways, PPI, metabolism, transcriptional regulation, miRNA)

model or predict the cellular response to a stimulus

the prior Knowledge model is trained and tailored to any specific cell context by confronting with experimental data

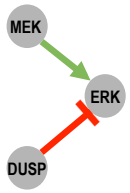
SIGNOR a new of causal relationships between biological entities available at http://signor.uniroma2.it

Signor

(SIGnaling Network Open Resource)

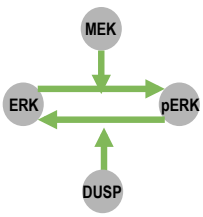
Signor adopts a boolean representation of signaling interactions

LOGIC — Boolean/Fuzzy logic, truth tables



DUSP	MEK	ERK
0	0	0
0	1	1
1	0	0
1	1	1

REACTION BASED — Ordinary Differential Equations (ODEs)



$$\frac{d[pERK]}{dt} = k[MEK][ERK]-k1[DUSP][pERK]$$

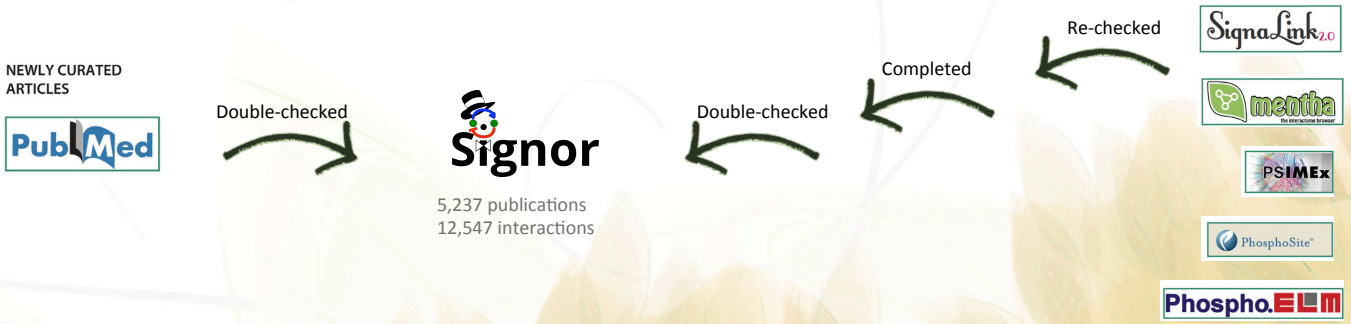
PRO ✔
- Easy to be computed;
- doesn't require a detailed mechanistic understanding of interactions;

CONS ✖
- requires normalization of experimental data;
- extreme simplification of biological complexity.

PRO ✔
- represent biochemical processes in time and space dimension;
- more realistic representations of biological mechanisms.

Cons ✖
- require knowledge of many parameters;
- impractical for large networks.

Signor is a manually-curated database



ENTITIES
- Molecule Type (*e.g.* Chemical, Proteins)
- Molecule identifiers (*e.g.*UniprotKB id)

RELATIONSHIPS
- Effect (up/down- regulates);
- Mechanism (*e.g.* phosphorylation);
- Modified residue (*i.e.* Ser36)
- Cell lines/tissues

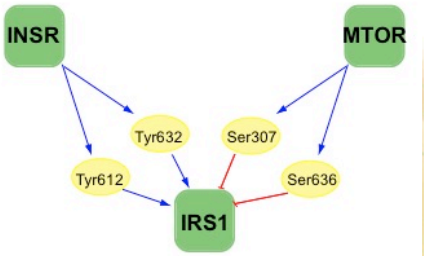
REFERENCE
- PubMedID;
- Short sentence.

SIGNOR Controlled Vocabulary

Entity Types	Mechanisms	Effects	Direct
PROTEIN	phosphorylation	UP-REGULATES QUANTITY	YES
COMPLEX	dephosphorylation	UP-REGULATES QUANTITY BY EXPRESSION	NO
SMALL MOLECULES	ubiquitination	UP-REGULATES QUANTITY BY STABILIZATION	UNKNOWN
CHEMICAL	deubiquitination	DOWN-REGULATES	
PHENOTYPE	acetylation	DOWN-REGULATES ACTIVITY	
STIMULUS	deacetylation	DOWN-REGULATES QUANTITY	
PROTEIN FAMILY	binding	DOWN-REGULATES QUANTITY BY REPRESSION	
	transcriptional activation	DOWN-REGULATES QUANTITY BY DESTABILIZATION	
	transcriptional repression	FORM COMPLEX	
	relocalization	UNKNOWN	
	cleveage		
	sumoylation		
	methylation		
	glycosilation		
	Chemical activation		

PhosphoSIGNOR

Gene A	GeneB	effect	effect_mechanism	modified_residue
INSR1	IRS1	activates	phosphorylation	Tyr612
INSR1	IRS1	activates	phosphorylation	Tyr632
PDPK1	AKT1	activates	phosphorylation	Thr308
AKT1	TSC1	inactivates	phosphorylation	Ser939
AKT1	MTOR	activates	phosphorylation	Thr450
MTOR	IRS1	inactivates	phosphorylation	Ser307

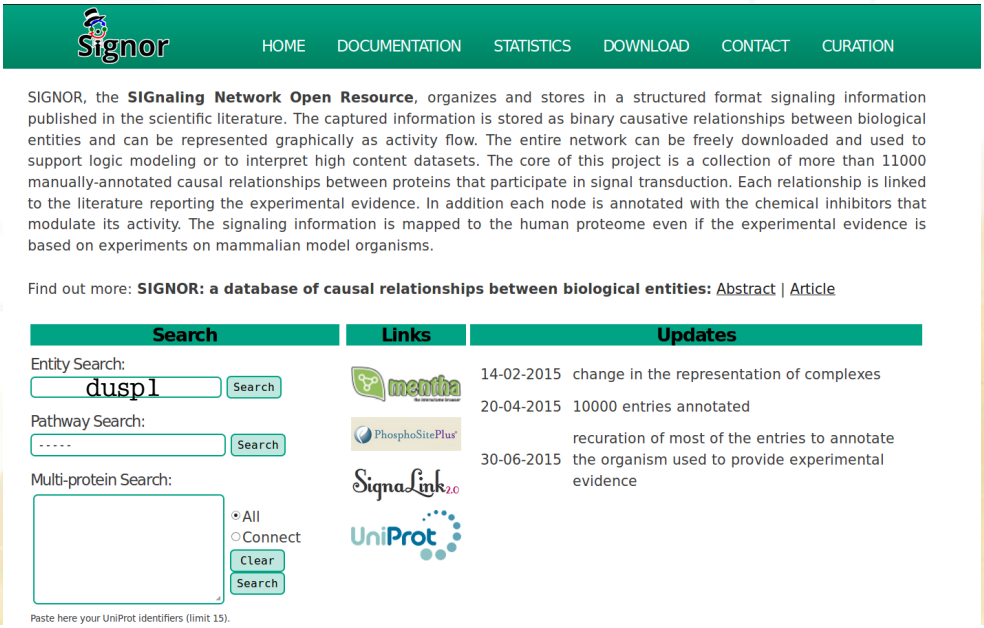


PHOSPHO Signor

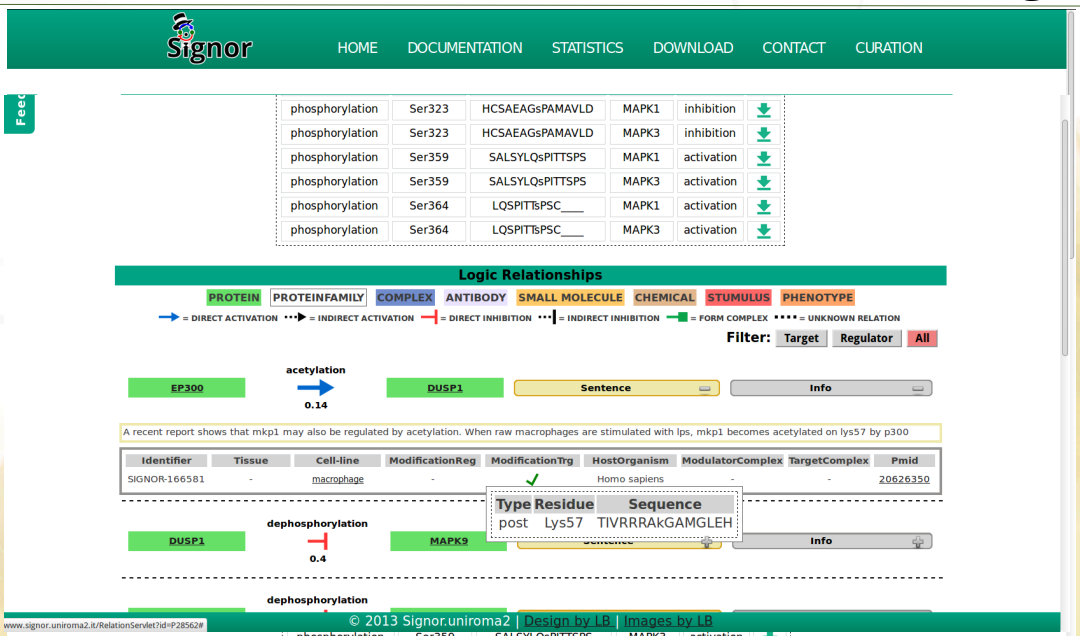
Gene A	GeneB	effect	effect_mechanism
INSR1	IRS1_Tyr612	activates	phosphorylation
IRS1_Tyr612	IRS1	activates	-
INSR1	IRS1_Tyr632	activates	phosphorylation
IRS1_Tyr632	IRS1	activates	-
PDPK1	AKT1_Thr308	activates	phosphorylation
AKT1_Thr308	AKT1	activates	-
AKT1	TSC1_Ser939	activates	phosphorylation
TSC1_Ser939	TSC1	inactivates	-
AKT1	MTOR_Thr450	activates	phosphorylation
MTOR_Thr450	MTOR	activates	-
MTOR	IRS1_Ser307	activates	phosphorylation
IRS1_Ser307	IRS1	inactivates	-

- Approx. 4900 phosphorylation reactions;
- Approx. 250 dephosphorylation reactions

SIGNOR implementation: the web site

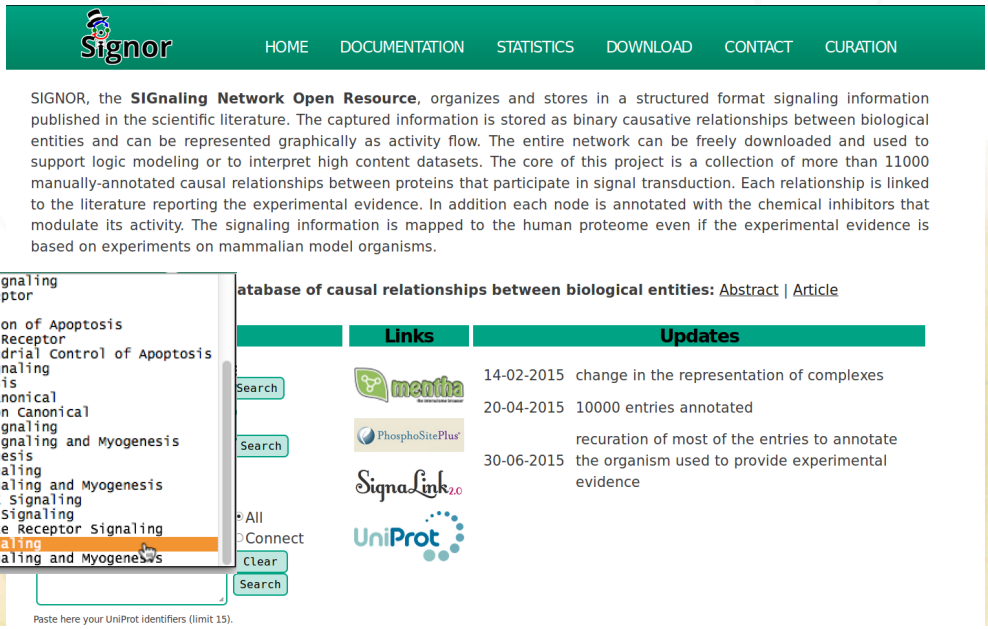


“entity” search

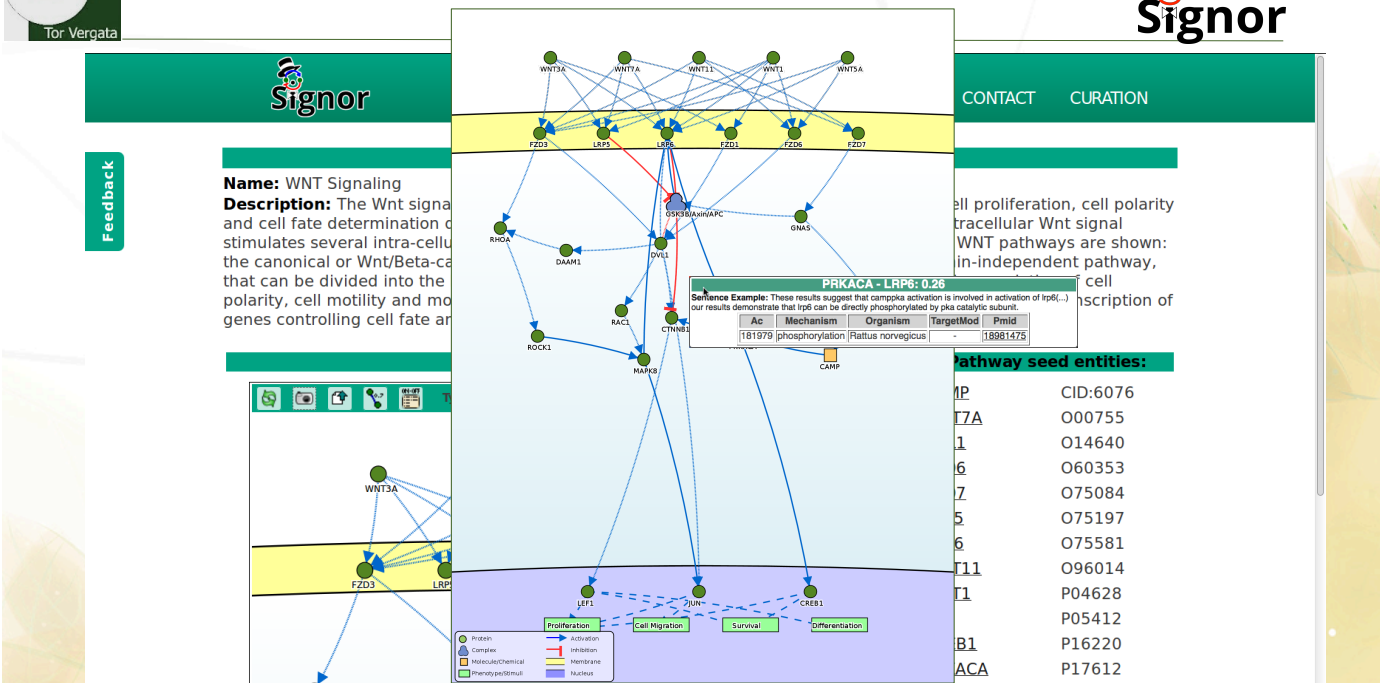


Graphical visualizer By Alberto Calderone

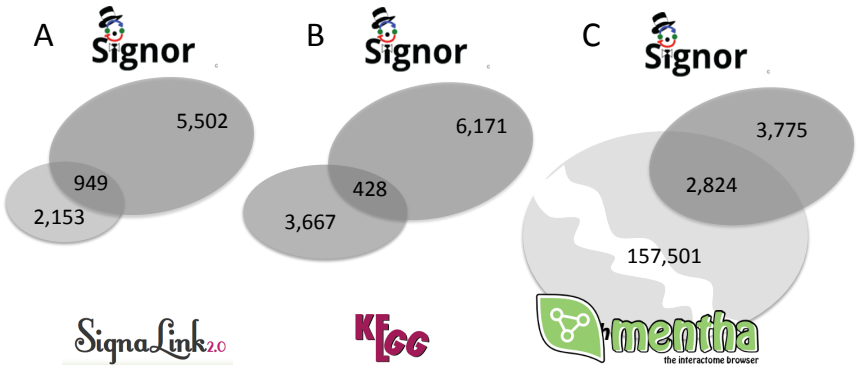
pathways in SIGNOR



SIGNOR: Pathway Search



SIGNOR vs SignaLink2.0, KEGG and mentha a quantitative analysis



conclusions

Nucleic Acids Research Advance Access published October 13, 2015

Nucleic Acids Research, 2015 **1**
doi: 10.1093/nar/gkv1048

SIGNOR: a database of causal relationships between biological entities

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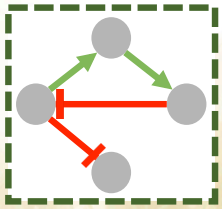
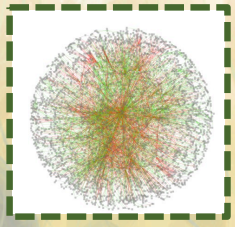
http://signor.uniroma2.it

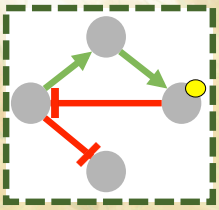


LOGIC RELATIONSHIPS

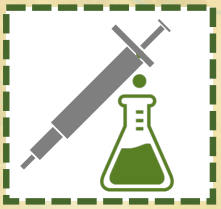
MANUALLY CURATED



VALUABLE COVERAGE (12,547 INTERACTIONS 5,237 PUBLICATIONS)



PHOSPHO-MAPPING approx. 6,000 MODIFIED RESIDUES



TOOL FOR EXPERIMENTAL SETUP

Aknowledgments

Gianni Cesareni
Luisa Castagnoli
Leonardo Briganti
Alberto Calderone
Daniele Peluso
The SIGNOR curation team
The MINT curation team

THANK YOU!