



UNIVERSIDAD  
DE MÁLAGA



Bases Moleculares de la  
**Proliferación Celular**  
Departamento de Biología Molecular y Bioquímica



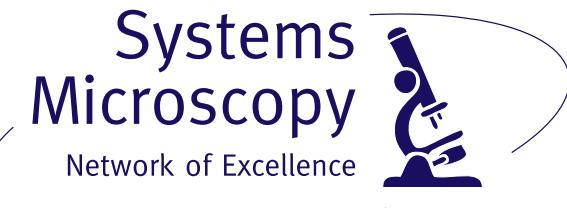
GOBIERNO  
DE ESPAÑA

MINISTERIO  
DE ECONOMÍA  
Y COMPETITIVIDAD

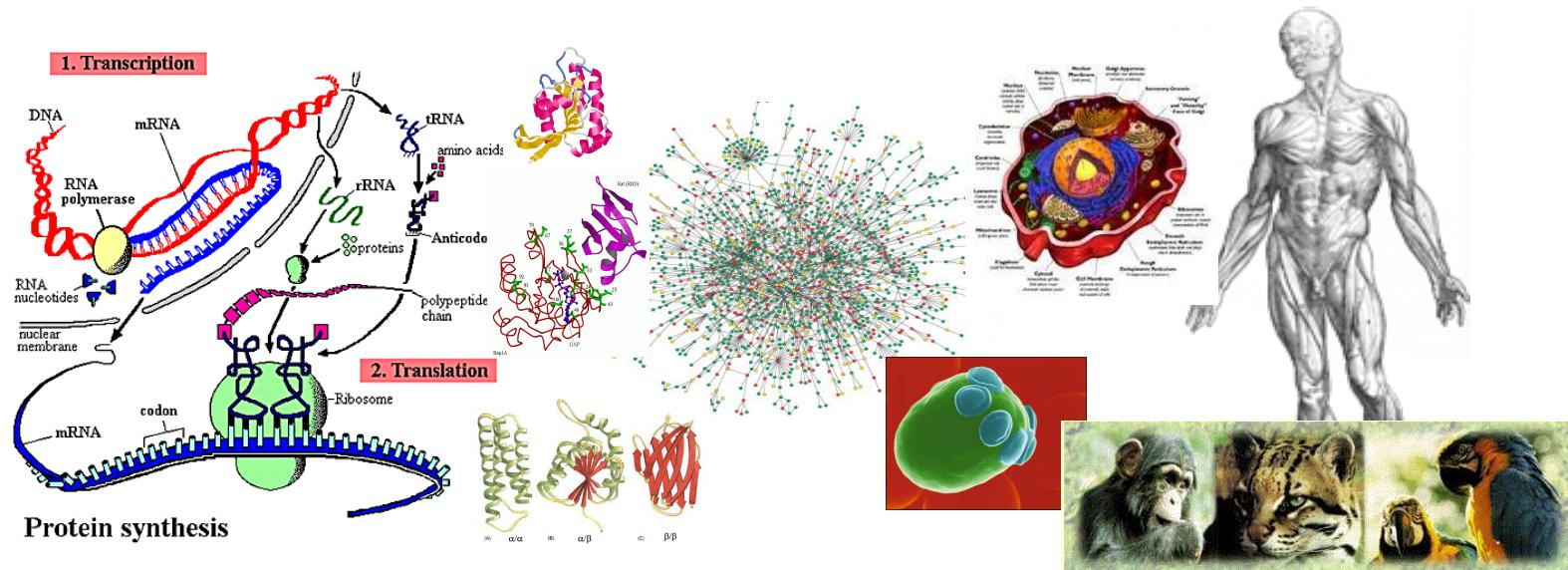
# ***Modelado de redes de interacción molecular y su aplicación en la predicción funcional de nuevas dianas.***

Juan A. G. Ranea

13 Junio 2013, Málaga.



*Organism's complexity arises in part from the intricate and dynamic networks of protein associations.*

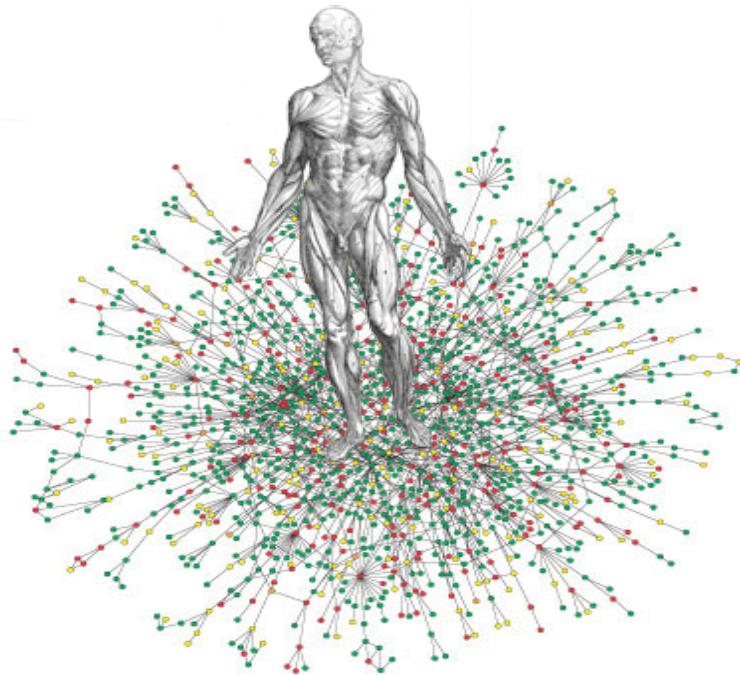


We come from here

We're going to ...

Complexity

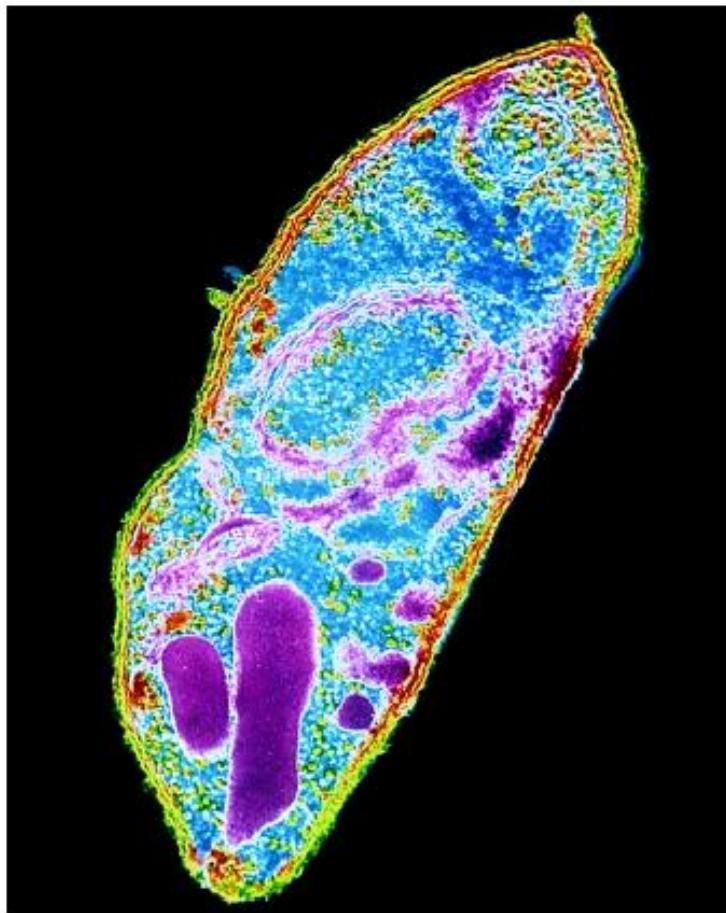
*<10% of PPI interactions in humans have been experimentally characterized.*



*Despite the main resources providing experimental information on protein associations: Intact, MINT, DIP, BIOGRID, HPRD, REACTOME, etc.*

Outside the model organisms the number of known interactions drops rapidly.

For example medically important pathogens have been screened such as malaria, but these isolated data sets are relatively small.



# Emergent property: the black box

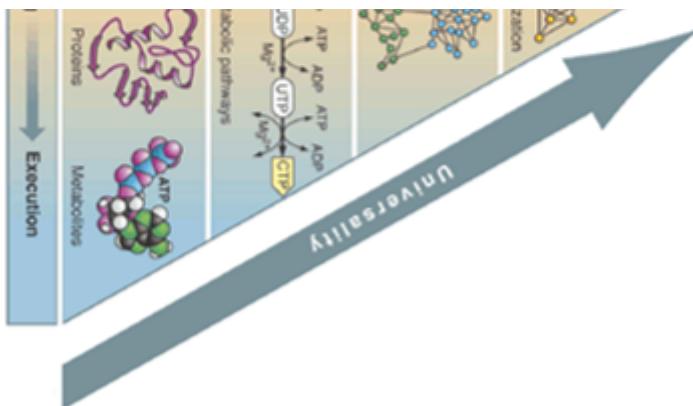
1 gene -> 1 function ?



Mutat

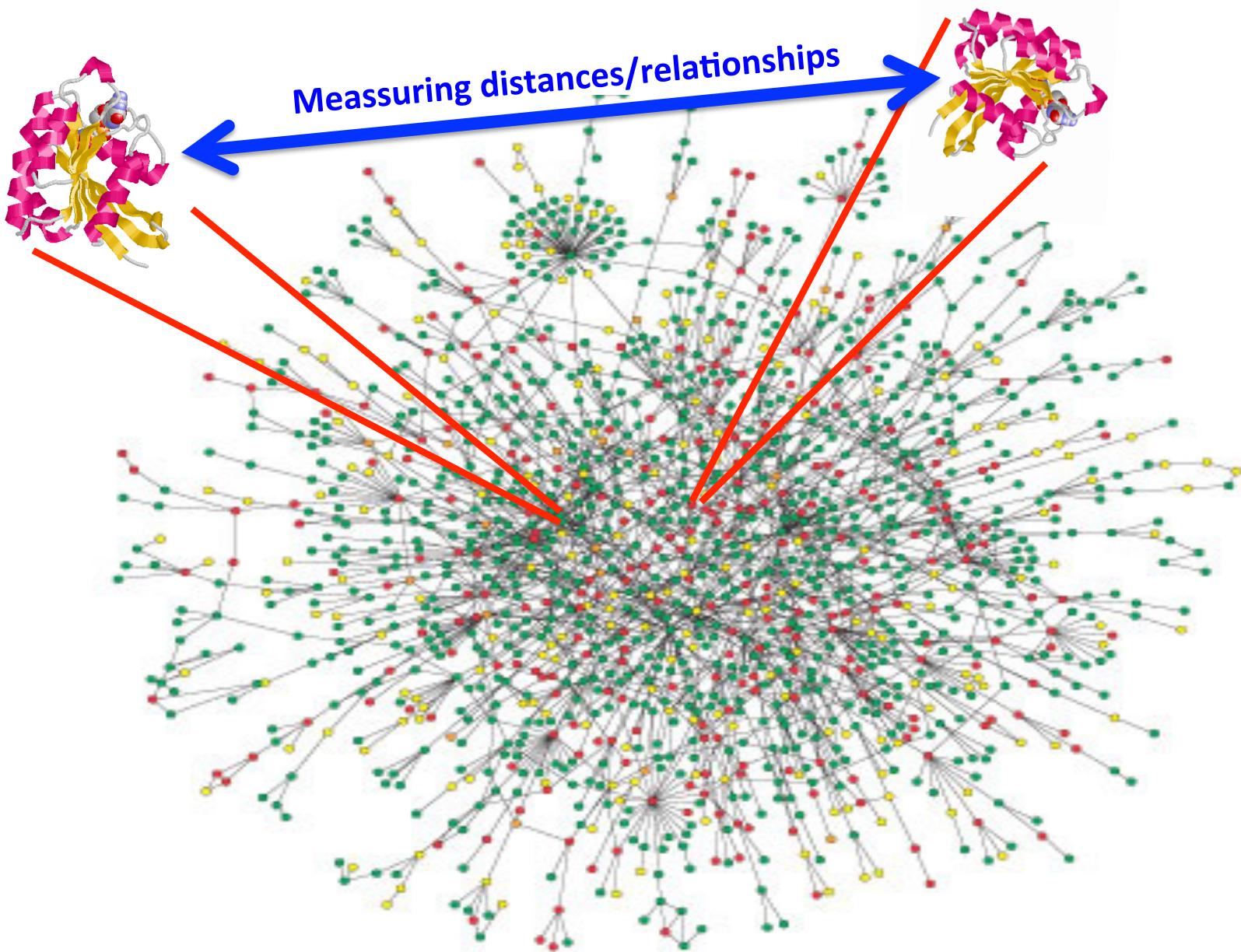
*“Some mice should, by rights, be dead. At the very least, Teyumuras Kurzchalia expected his to be critically ill. But the most prominent symptom of his genetically engineered mice was a persistent erection”*

Pearson, H. (2002) Surviving a knockout blow. *Nature*, **415**, 8-9.



Oltvai, Z.N. and Barabási, A.-L. (2002)  
Life's complexity pyramid. *Science*, **298**, 763–764.

## Exploiting the network structure



## Functional association predictions based on context information

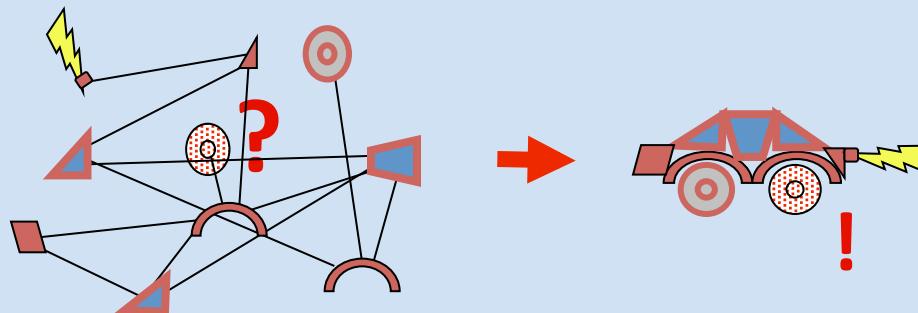
Matriz de la red de interacciones

	1	2	3	4	5	6	7	8	9	...
1						X	X		X	
2						X	X		X	
3	X	X			X					
4	X	X			X					
...										

Cell cycle

Functional prediction

## Searching the function in the network context



Novel Nodes

Prot. 8 – Prot. 10

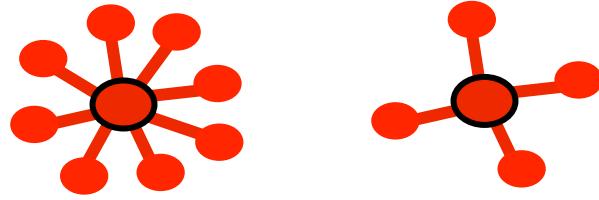
Associated pairs



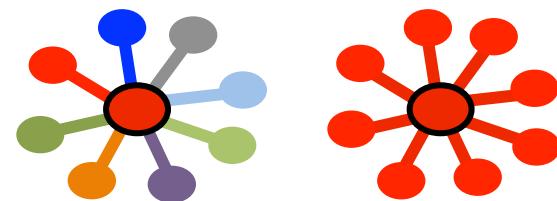
## ¿POR QUÉ UTILIZAR MODELOS DE REDES?

El estudio topológico y modular en la red de los genes puede ayudar a optimizar la generación de hipótesis así como a interpretar su función:

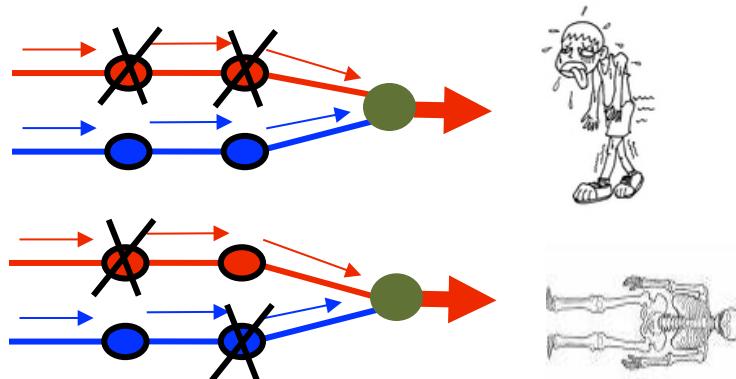
**Esencialidad (hubs) / No esencialidad**



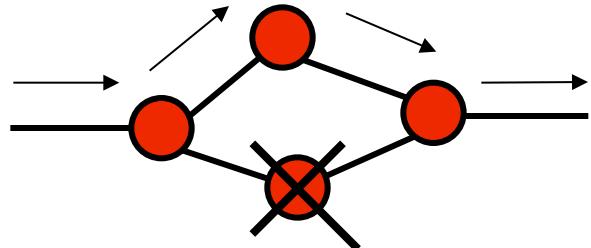
**Pleiotropía / Especificidad fenotípica**



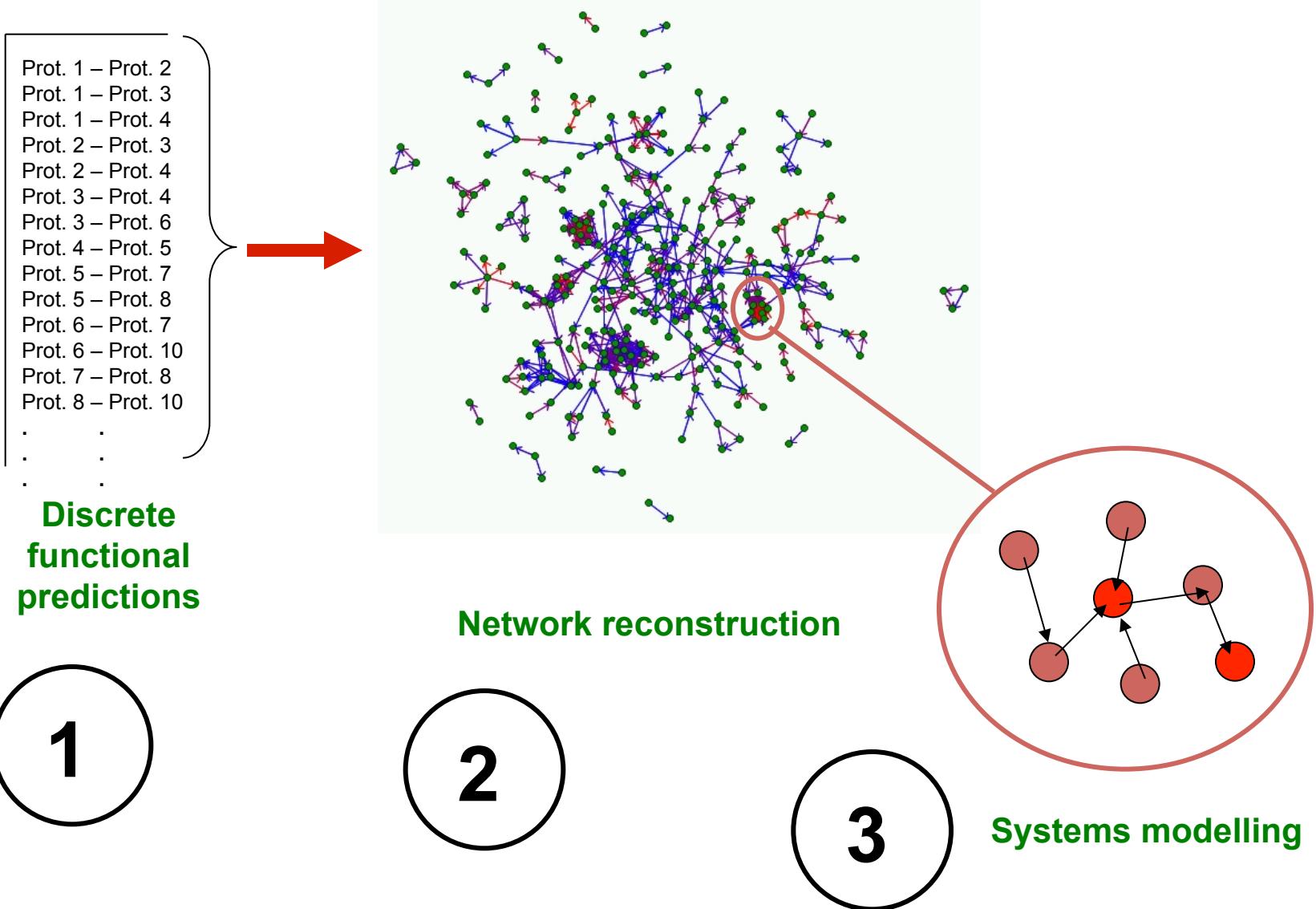
**Letalidad sintética/ Sinergia**



**Mutation Buffering**



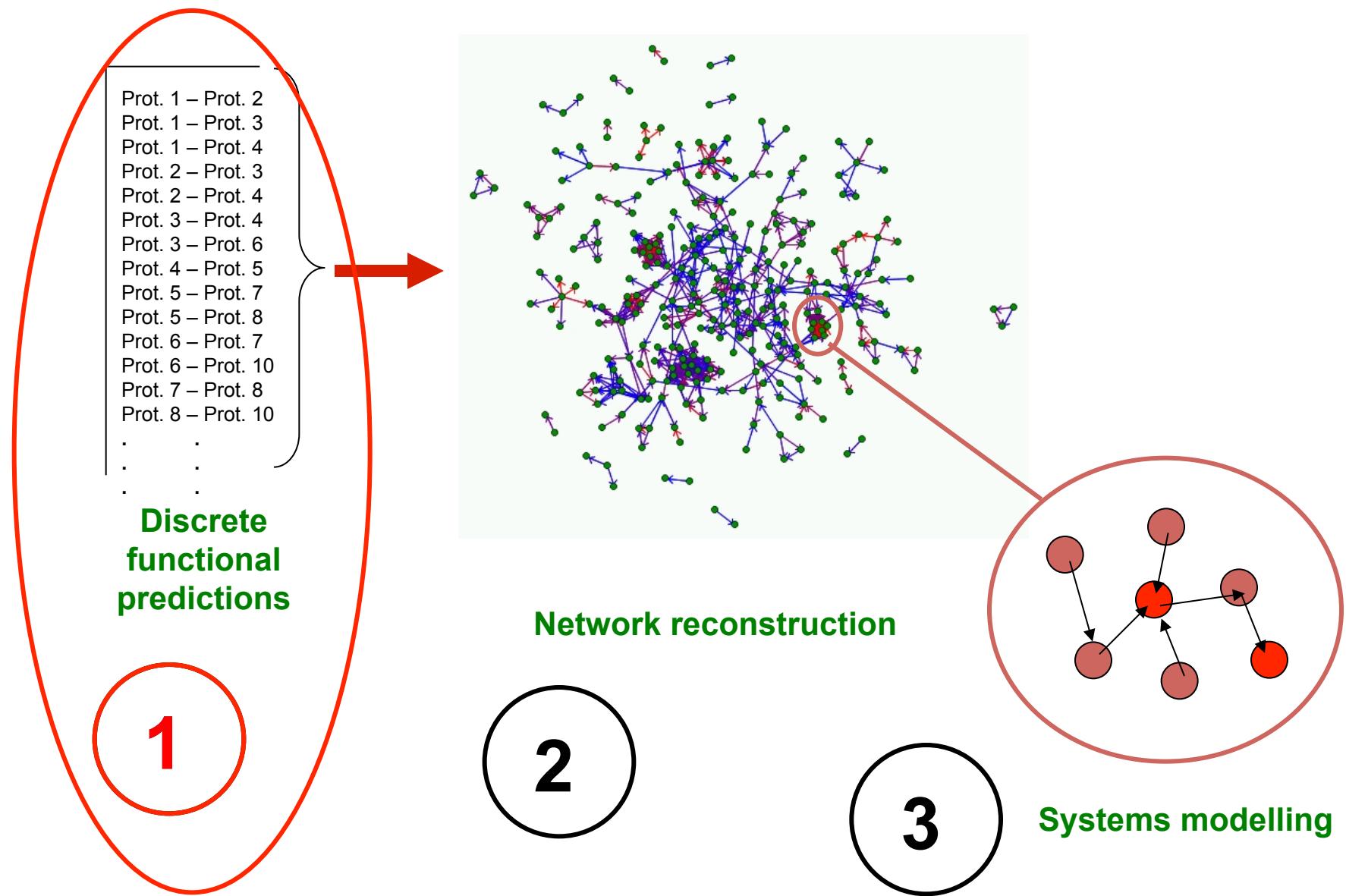
# SYSTEM MODELLING: building up step by step



# **Systematic computational prediction of protein interaction networks**

- (i) Protein association prediction methods:** the principles behind the different computational methods available to predict pairwise protein–protein interactions (PPIs)
- (ii) Integrating prediction methods:** ways of combining these individual methods in order to increase accuracy and coverage while reducing noise in predicting PPIs.
- (iii) Exploiting the network structure:** some successful applications of computational and mathematical methods that exploit network context to predict novel interactions or novel members of different biological processes.

# SYSTEM MODELLING: building up step by step



# **1. Protein association prediction methods:**

## **Physical / Functional Association**

### *1.1. Genomic context methods*

- 1.1.1 Co-occurrence profiles*
- 1.1.2. Gene/Domain fusion.*
- 1.1.3. Genomic neighborhood.*

### *1.2. Sequence-based prediction*

- 1.2.1. Sequence co-evolution: mirror trees.*
- 1.2.2. Sequence co-evolution: Correlated mutations.*
- 1.2.3. Inheriting protein interactions from sequence.*

### *1.4. Exploiting experimental data*

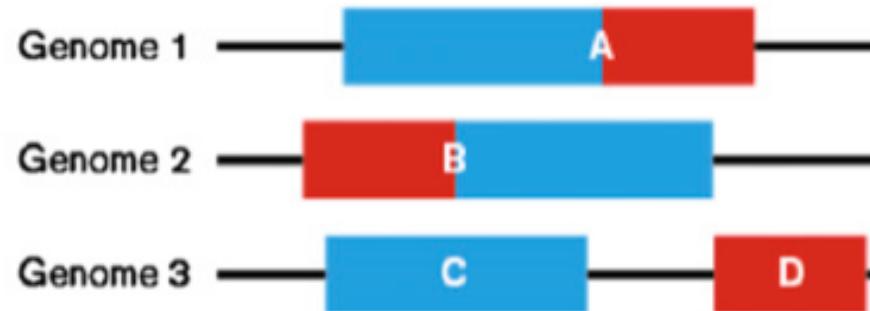
- 1.3.1. mRNA expression.*
- 1.3.2. Other experimental screens of PPIs.*
- 1.3.3. Phenotypic vectors comparison*

### *1.5. Literature-derived associations*

- 1.4.1. Text mining.*
- 1.4.2. Functional semantic similarity.*

# *Gene/domain fusion*

## *Gene fusion*

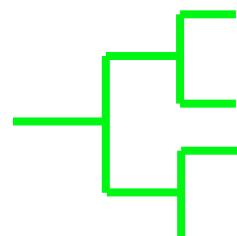


## *Protein domain fusion*

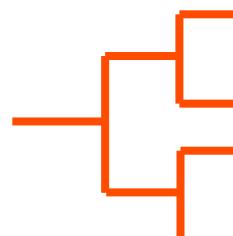


## ***Sequence co-evolution: Mirror trees***

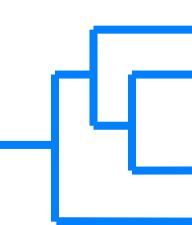
Fam. Prot. A



Fam. Prot. B



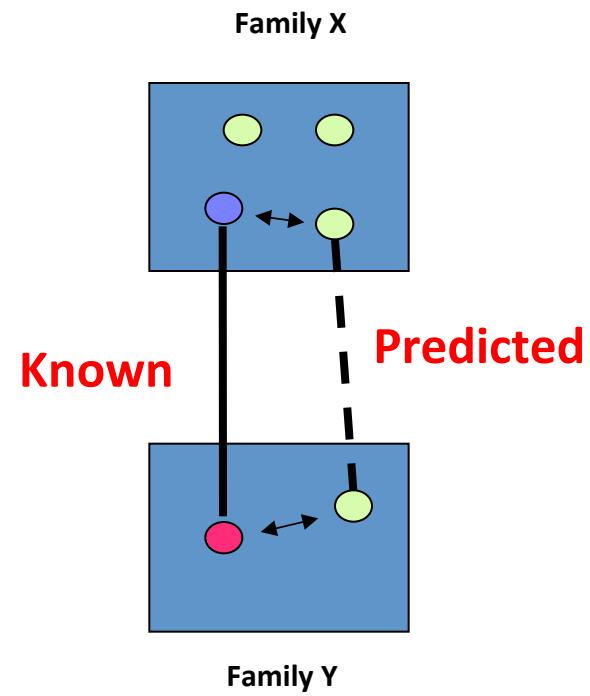
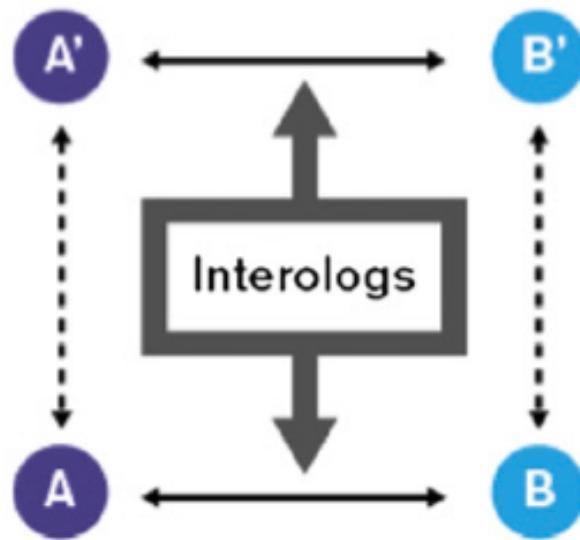
Fam. Prot. C



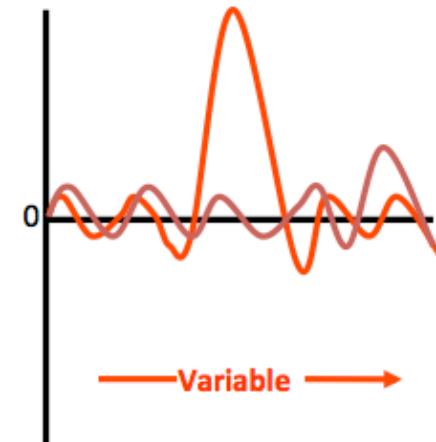
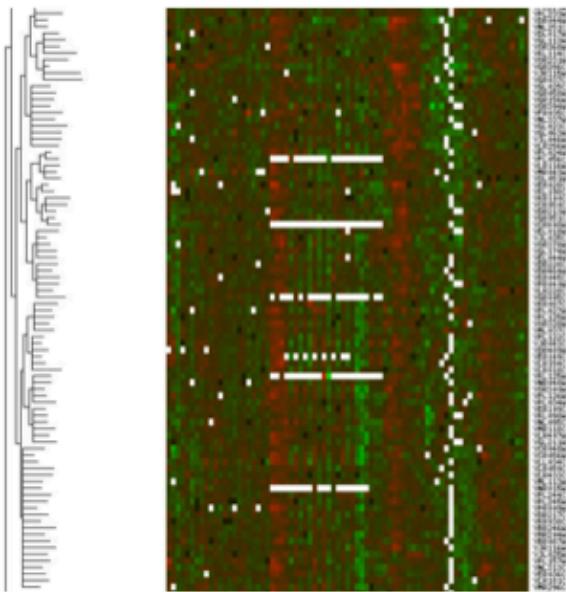
## Co-evolution: A-B

## No co-evolution: B-C

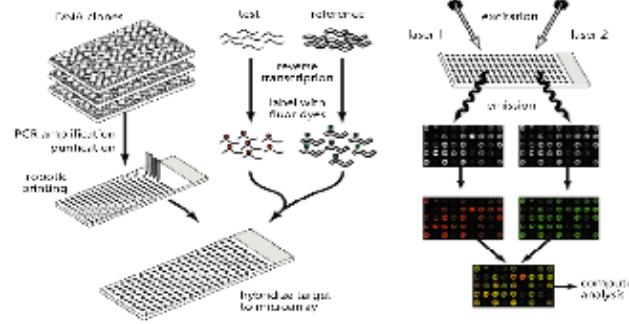
## *Inheriting protein interactions from sequence*



## *Exploiting experimental data: RNA-seq / Microarray.*



### *Microarray*

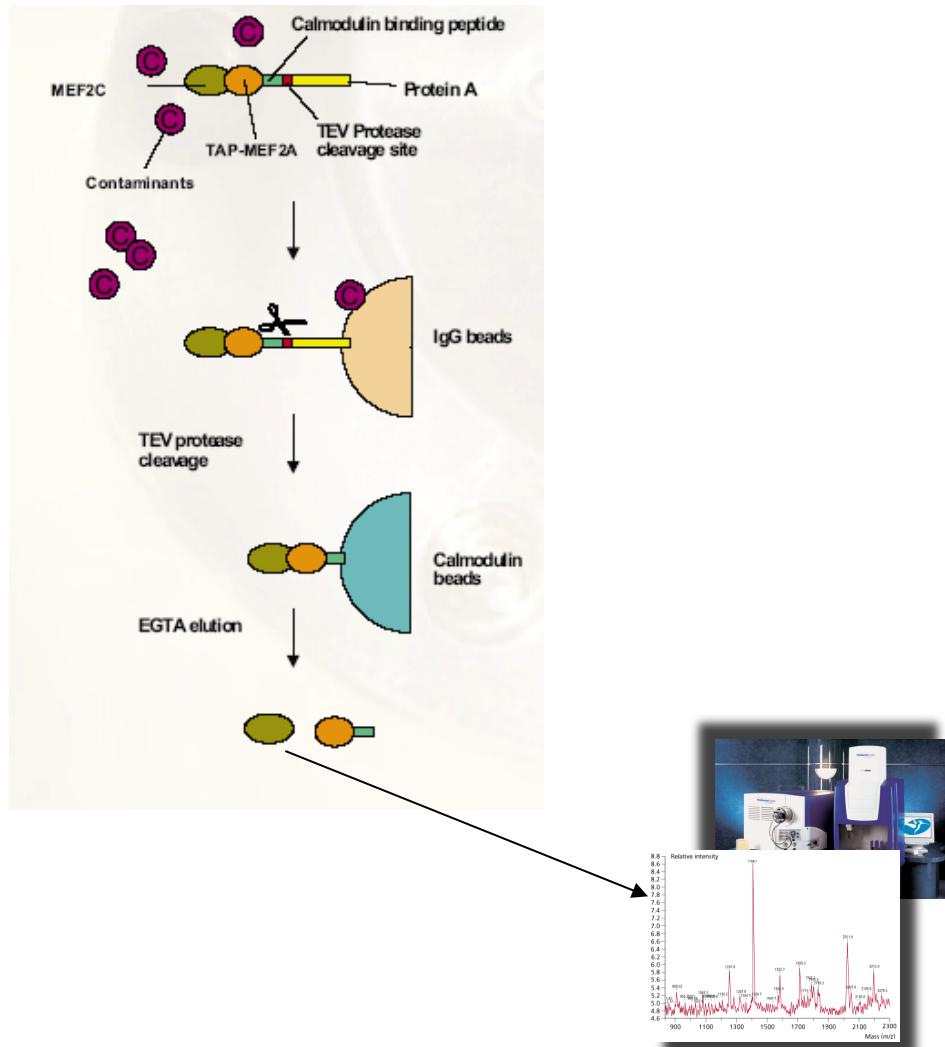


### *RNA-seq*

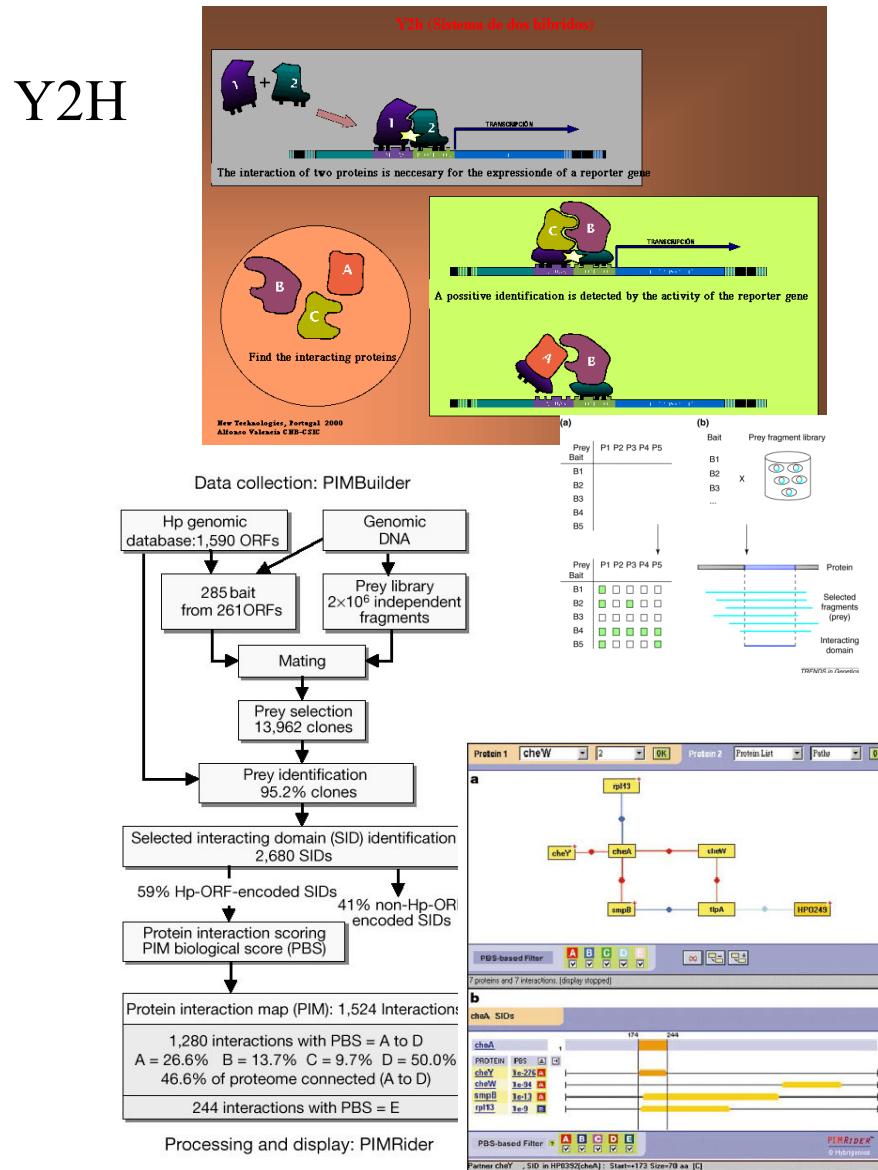


# Exploiting experimental data: Other experimental screens of PPIs

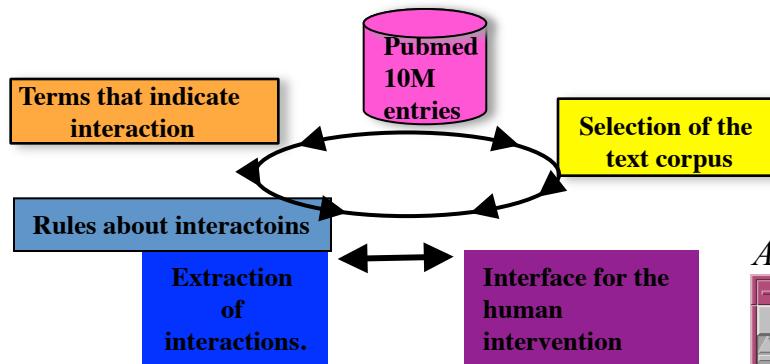
## Tandem Affinity Purification TAP/MS



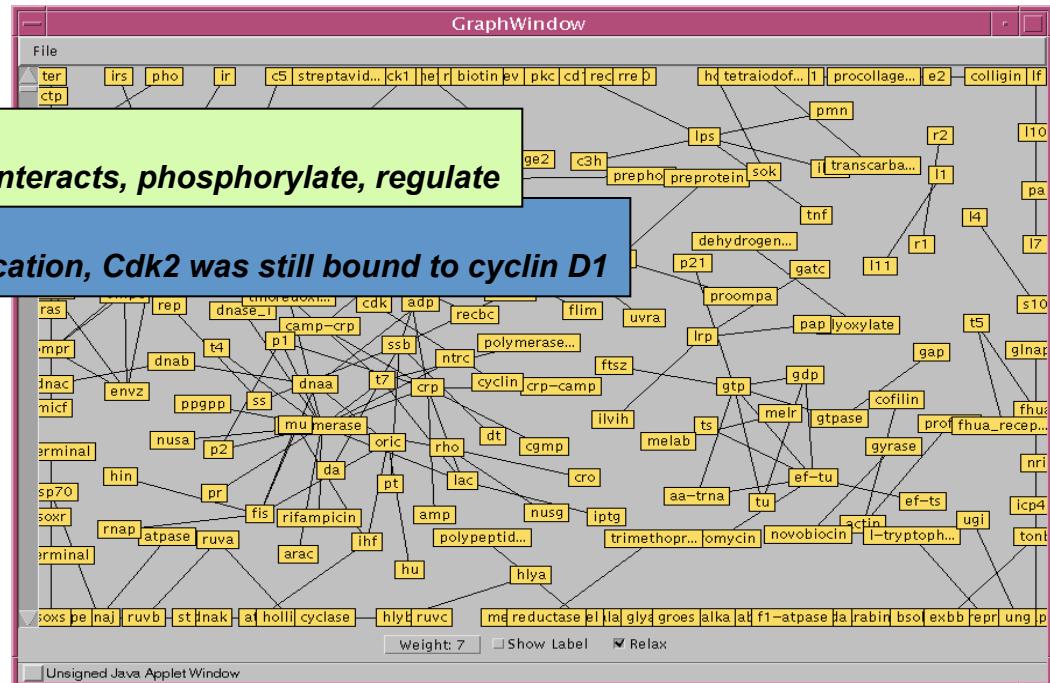
## Y2H



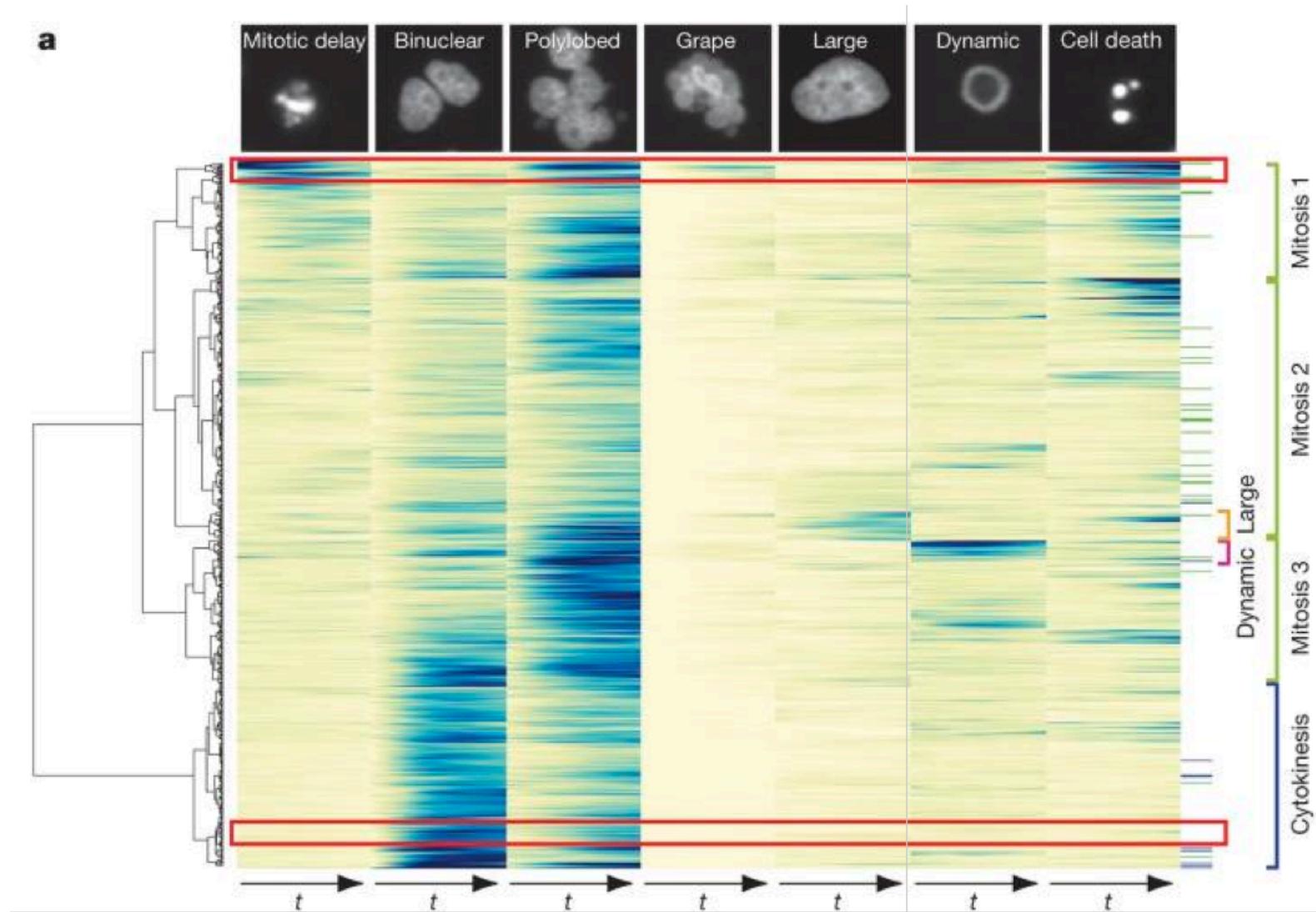
# Literature-derived associations: Text mining.



A. Valencia



# Exploiting experimental data: Phenotypic vectors comparison



Neumann et al. (2010). Phenotypic profiling of the human genome by time-lapse microscopy reveals cell division genes. Nature. 464(7289): 721-7.

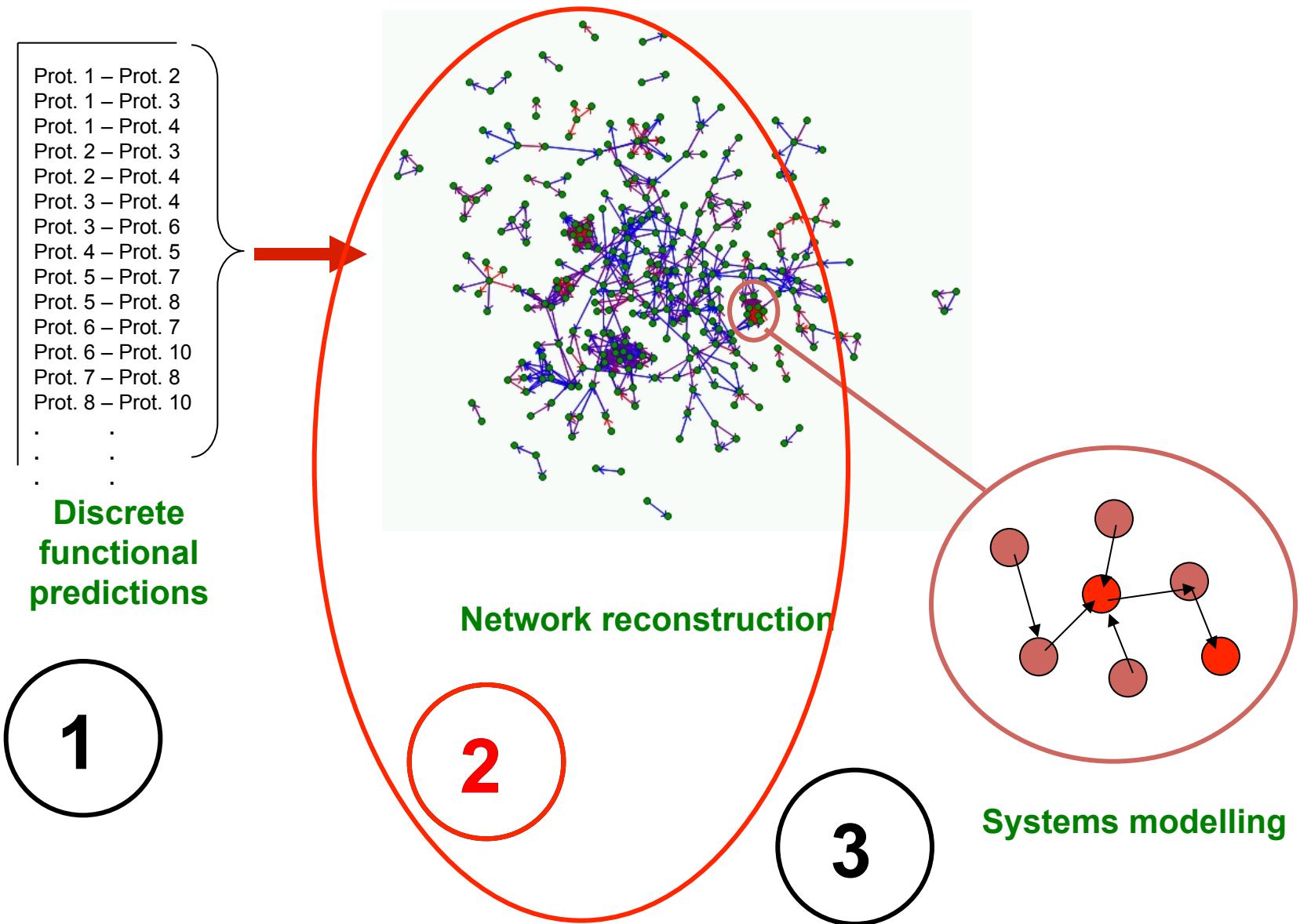
## Systematic computational prediction of protein interaction networks

(i) Protein association prediction methods: the principles behind the different computational methods available to predict pairwise protein–protein interactions (PPIs)

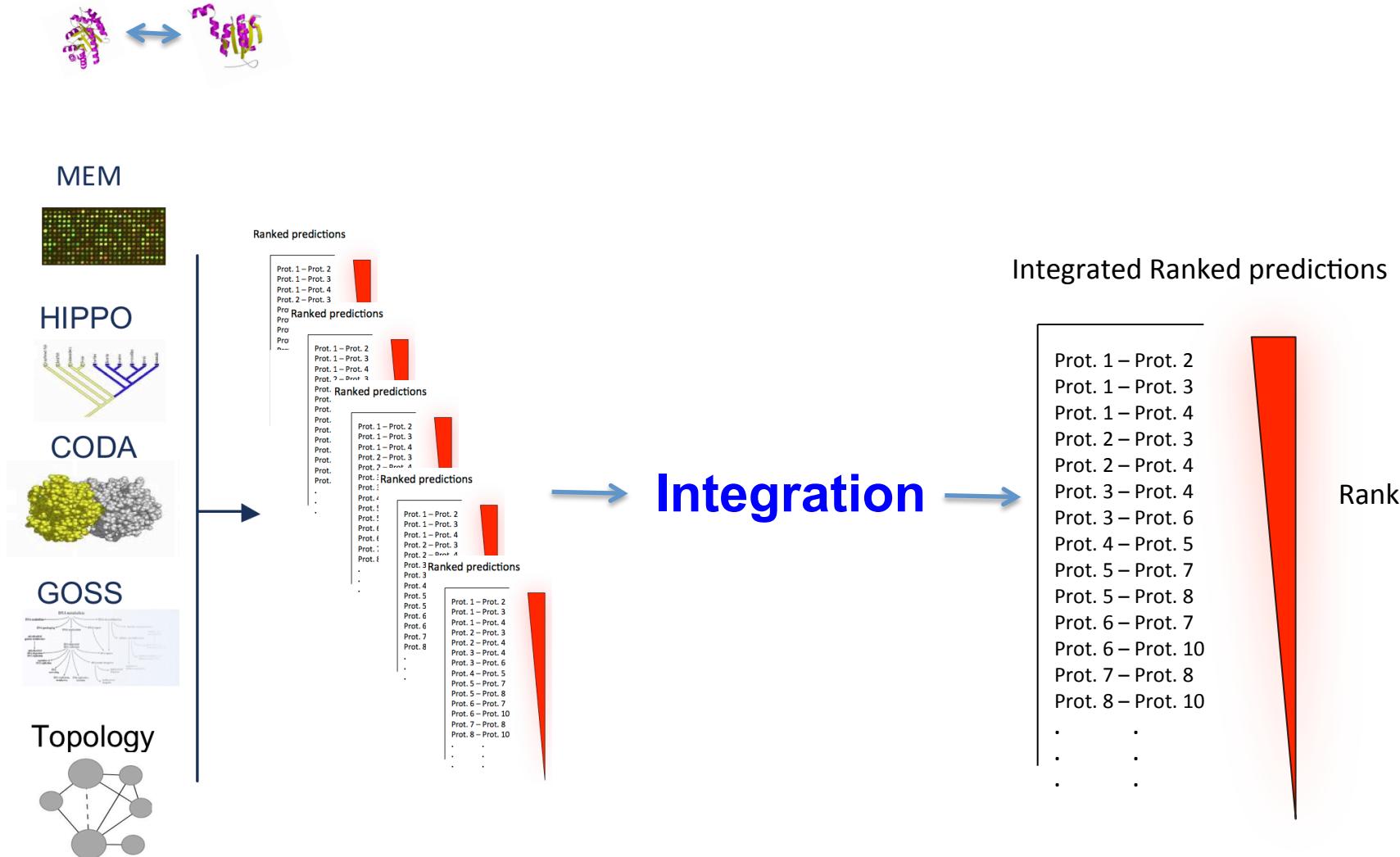
**(ii) Integrating prediction methods:** ways of combining these individual methods in order to increase accuracy and coverage while reducing noise in predicting PPIs.

(iii) Exploiting the network structure: some successful applications of computational and mathematical methods that exploit network context to predict novel interactions or novel members of different biological processes.

# Modelling networks and exploiting functional context



# Predicting PPIs



## **2. Integrating prediction methods:**

*2.1. Fisher*

*2.2. Bayes*

*2.3. Kernels*

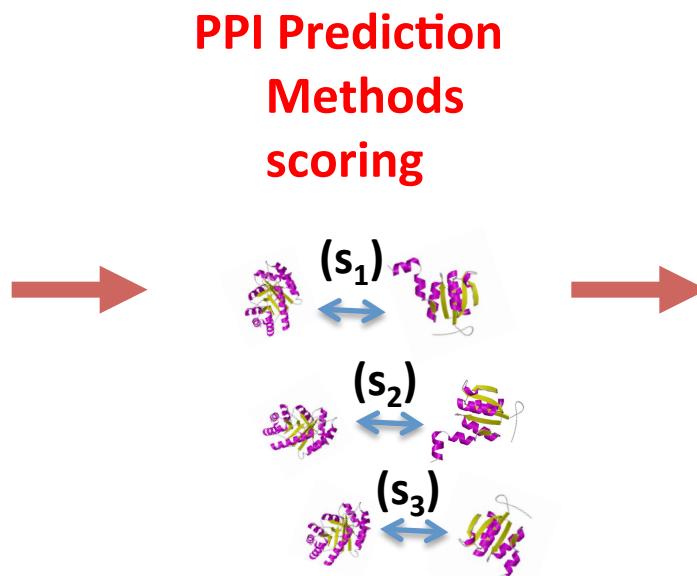
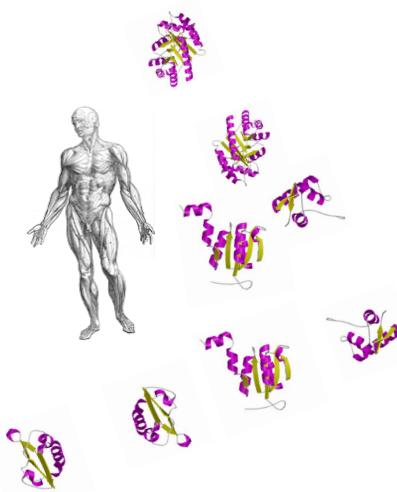
*2.n Others ..*

# Integration methods comparison

Advantageous property	Integration method/example reference			
	Naïve Bayes [80, 90]	Fisher's [85, 91]	SVM [92, 93]	Graph kernel + SVM [46, 88]
Copes well with missing values	1	1	0	0
Importance of input features can be readily obtained	1	0	0	0
Copes well with high-dimensional data	0	0	1	1
Complex relationships between input variables can be learned	0	0	1	1
Probability estimate readily obtained from output	1	0	0	0
No parameter optimization required	0	1	0	0
No requirement for independence between input data	0	0	1	1
No training data required	0	1	0	0

# Fisher's method application and Scores' p\_value calculation:

Human genome/  
proteome



Ranked predictions

Rank
Prot. 1 – Prot. 2
Prot. 1 – Prot. 3
Prot. 1 – Prot. 4
Prot. 2 – Prot. 3
Prot. 2 – Prot. 4
Prot. 3 – Prot. 4
Prot. 3 – Prot. 6
Prot. 4 – Prot. 5
Prot. 5 – Prot. 7
Prot. 5 – Prot. 8
Prot. 6 – Prot. 7
Prot. 6 – Prot. 10
Prot. 7 – Prot. 8
Prot. 8 – Prot. 10
.
.
.



## Fisher Integration Method:

Prot. 1	Prot. 2	Method's predicts. 1	Method's predicts. 2	Method's predicts. 3	Method's predicts. 4
1	2	P_val(1,2)	-	P_val(1,2)	-
1	3	-	P_val(1,3)	P_val(1,3)	-
1	4	-	P_val(1,4)	-	-
2	3	P_val(2,3)	P_val(2,3)	P_val(2,3)	P_val(2,3)
2	4	-	P_val(2,4)	-	P_val(2,4)
3	4	P_val(3,4)	-	-	-
...	...	...	...	...	...

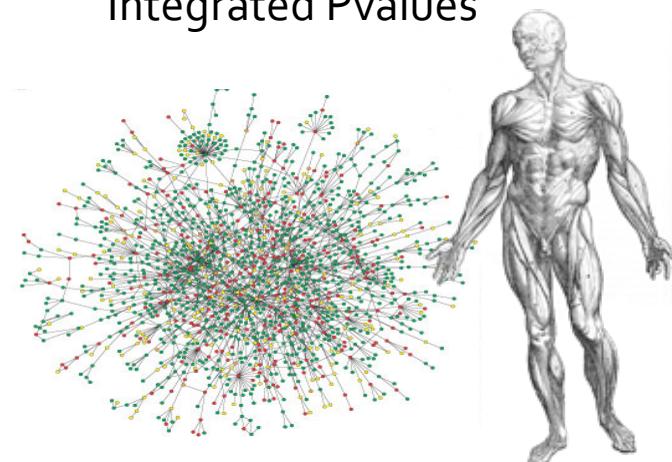
P-values of the Single Methods Matrix



For each pair (prot 1 – prot 2):  
 - Fisher (W) =  $-2 \sum_{(1-i)} w_i \log(p_i)$



Integrated Pvalues



Hwang D. et al.(2005) "A data integration methodology for systems biology".  
*PNAS* 102(48), 17296–17301.

Shannon C. (1948) "A Mathematical Theory of Communication". *The Bell System Technical Journal*, Vol. 27, pp. 379–423, 623–656.

# 1. Construcción del modelo: datos experimentales

Bases de datos de pares de proteínas interaccionantes

HRPD

Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 3 – Prot. 6  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 7  
Prot. 5 – Prot. 8  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
.  
.  
.

MINT

Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 3 – Prot. 6  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 7  
Prot. 5 – Prot. 8  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
.  
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.

Reactome

Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 3 – Prot. 6  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 7  
Prot. 5 – Prot. 8  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
.  
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.

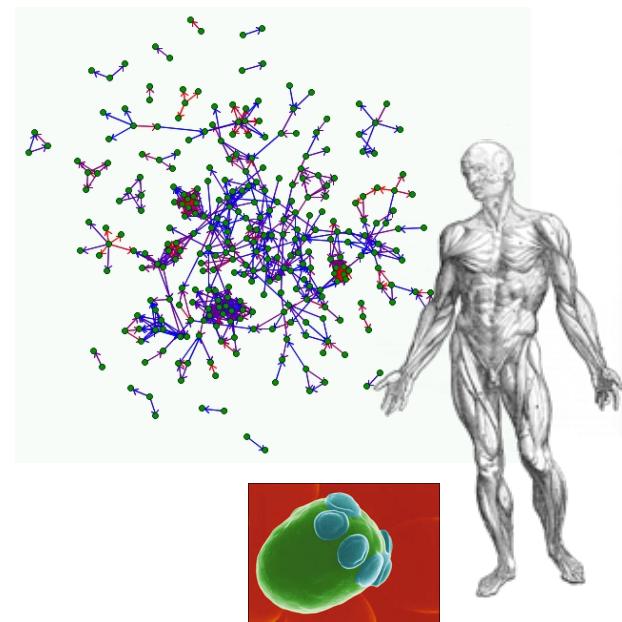
Intact

Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 3 – Prot. 6  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 7  
Prot. 5 – Prot. 8  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
.  
.  
.

Combinación de todas las bases de datos

Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 3 – Prot. 6  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 7  
Prot. 5 – Prot. 8  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
.  
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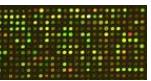
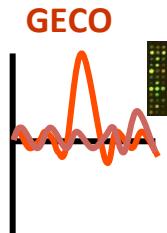
Reconstrucción de la red: KnowledgeGram (KG)



# 1. Construcción del modelo: predicciones

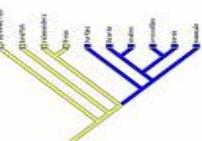
## Predicciones de interactomas completos

GECO



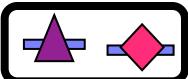
Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 6  
Prot. 5 – Prot. 7  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
⋮ ⋮

hiPPI

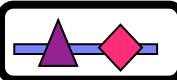


Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 3 – Prot. 6  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 7  
Prot. 5 – Prot. 8  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
⋮ ⋮

CODA



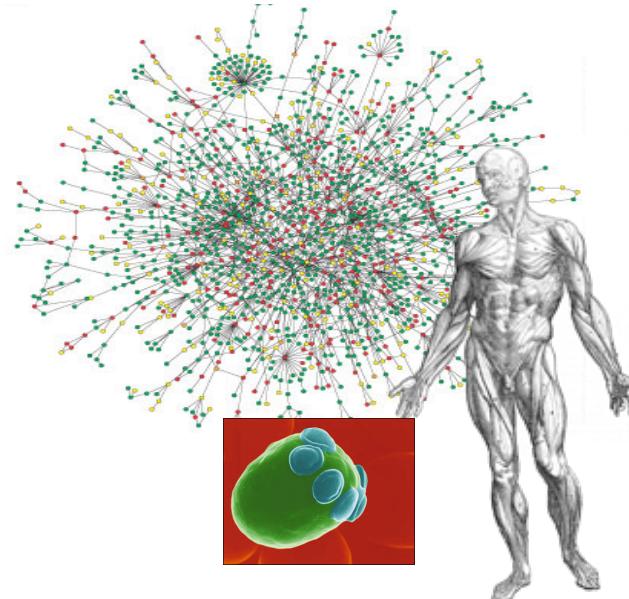
Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 3 – Prot. 6  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 7  
Prot. 5 – Prot. 8  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
⋮ ⋮



## Integración por: Fisher, Bayes, Kernels, etc.

Prot. 1 – Prot. 2  
Prot. 1 – Prot. 3  
Prot. 1 – Prot. 4  
Prot. 2 – Prot. 3  
Prot. 2 – Prot. 4  
Prot. 3 – Prot. 4  
Prot. 3 – Prot. 6  
Prot. 4 – Prot. 5  
Prot. 5 – Prot. 7  
Prot. 5 – Prot. 8  
Prot. 6 – Prot. 7  
Prot. 6 – Prot. 10  
Prot. 7 – Prot. 8  
Prot. 8 – Prot. 10  
⋮ ⋮

## Reconstrucción de la red: PredictioGram (PG)



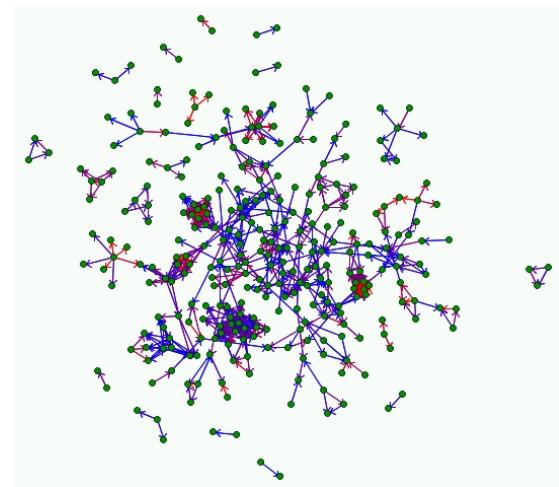
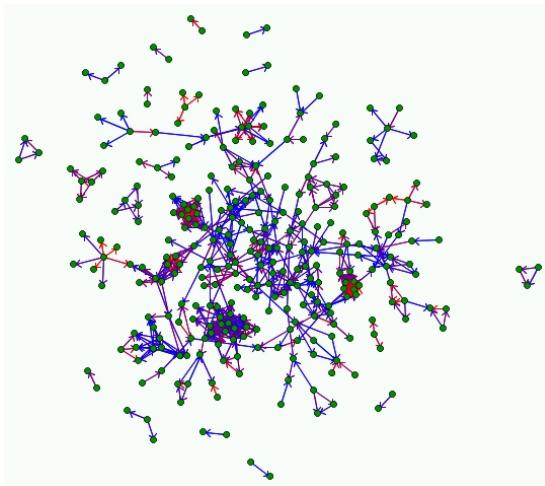
# Predictogram (PG) / Knowledgegram (KG)

## Predictogram:

Integrated PPIs datasets form CODA, GECO  
and hiPPI predictions

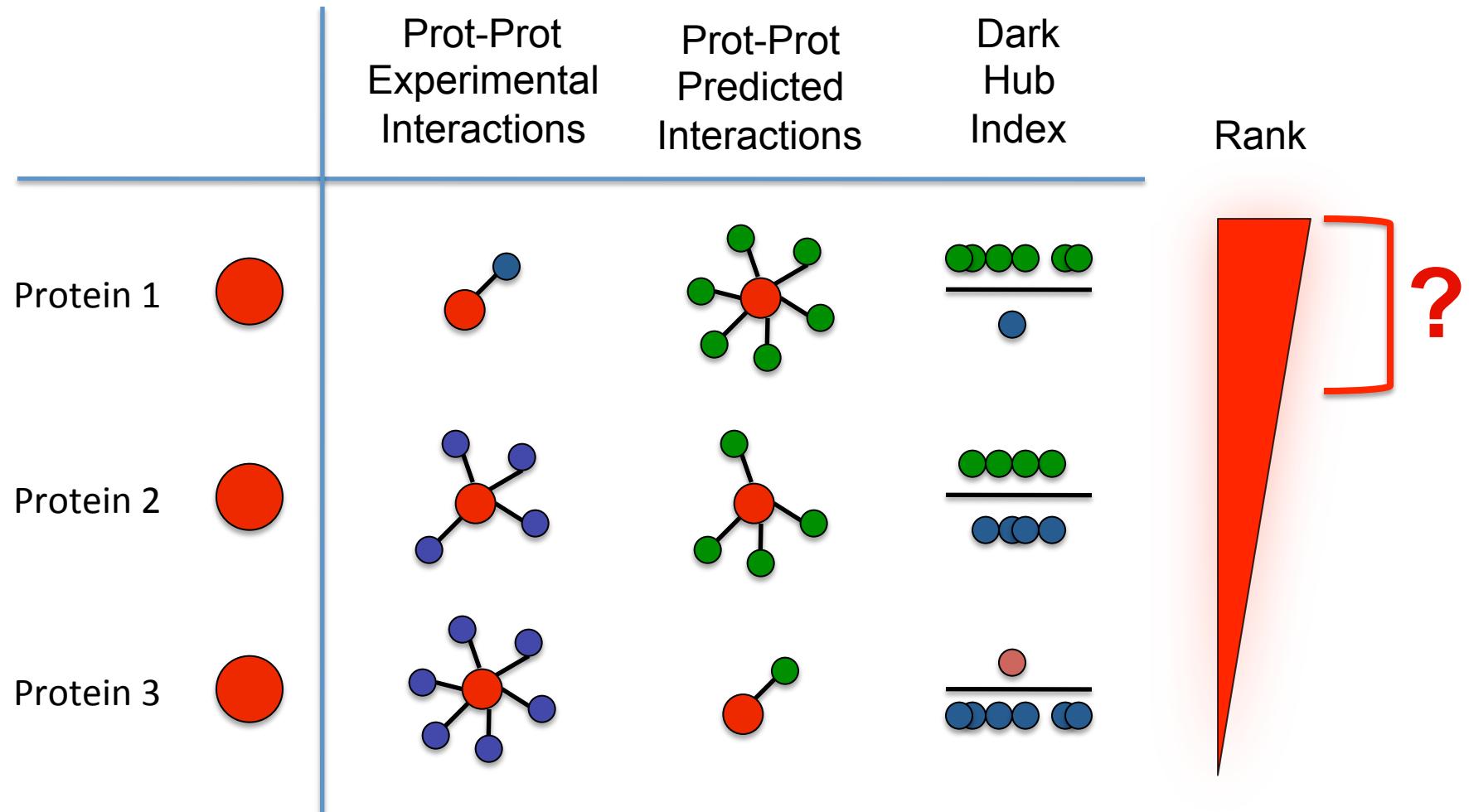
## Knowledgegram:

Combination of all PPIs in HRPD, MINT, Intact,  
Reactome, Kegg, FunCat and GO databases



PG/KG network models comparison at  
different reliability levels

## *Analysing the ‘dark matter’ in the Predicted PPI network models*



# Analysing the ‘dark matter’ in the Predicted PPI models: Membrane proteins / Extracellular proteins

	GO term	GO cat.	Top 10 %	Bot. 10 %	Tot. %	P-val	GO: number Ids	GO definition
Yeast	Intrinsic to membrane	cc	111		23	9,10 E-06	0031224	Located in a membrane such that some covalently attached portion of the gene product, for example part of a peptide sequence or some other covalently attached moiety such as a GPI anchor, spans or is embedded in one or both leaflets of the membrane.
	Integral to membrane	cc	106		22	1,80 E-05	0016021	Penetrating at least one phospholipid bilayer of a membrane. May also refer to the state of being buried in the bilayer with no exposure outside the bilayer. When used to describe a protein, indicates that all or part of the peptide sequence is embedded in the membrane.
	Regulation of transcription	bp		110	21	1,20 E-08	0045449	Any process that modulates the frequency, rate or extent of the synthesis of either RNA on a template of DNA or DNA on a template of RNA.
	Non-membrane-bounded organelle	cc		132	25	2,60 E-03	0043228	Organized structure of distinctive morphology and function, not bounded by a lipid bilayer membrane. Includes ribosomes, the cytoskeleton and chromosomes.
	Intracellular non-membrane-bounded organelle	cc		132	25	2,60 E-03	0043232	Organized structure of distinctive morphology and function, not bounded by a lipid bilayer membrane and occurring within the cell. Includes ribosomes, the cytoskeleton and chromosomes.
human	Extracellular region	cc		423	21	2,00 E-24	0005576	The space external to the outermost structure of a cell. For cells without external protective or external encapsulating structures this refers to space outside of the plasma membrane. This term covers the host cell environment outside an intracellular parasite

## Analysing the ‘dark matter’ in the Predicted PPI models: Transient interactions

	<b>GO term name</b>	<b>GO code</b>	<b>P-value</b>	<b>N</b>	<b>B</b>	<b>n</b>	<b>b</b>	<b>E.</b>
<b>Biol. proc.</b>	Protein amino acid phosphorylation	GO:0006468	7.63E-22	12769	508	991	111	3
	Regulation of small GTPase mediated signal transduction	GO:0051056	1.64E-13	12769	124	982	39	4
	└ Regulation of Ras protein signal transduction	GO:0046578	2.27E-10	12769	85	982	28	4
<b>Molecular function</b>	Protein kinase activity	GO:0004672	3.62E-21	12769	480	991	106	3
	└ Protein serine/threonine kinase activity	GO:0004674	4.83E-14	12769	349	984	75	3
	└ Protein tyrosine kinase activity	GO:0004713	2.73E-10	12769	146	972	37	3
	GTPase regulator activity	GO:0030695	7.06E-13	12769	319	908	63	3
	└ Guanyl-nucleotide exchange factor activity	GO:0005085	1.92E-11	12769	123	982	36	4
	└ Small GTPase regulator activity	GO:0005083	1.59E-10	12769	211	982	47	3
	ATP binding	GO:0005524	4.61E-25	12769	1097	991	190	2

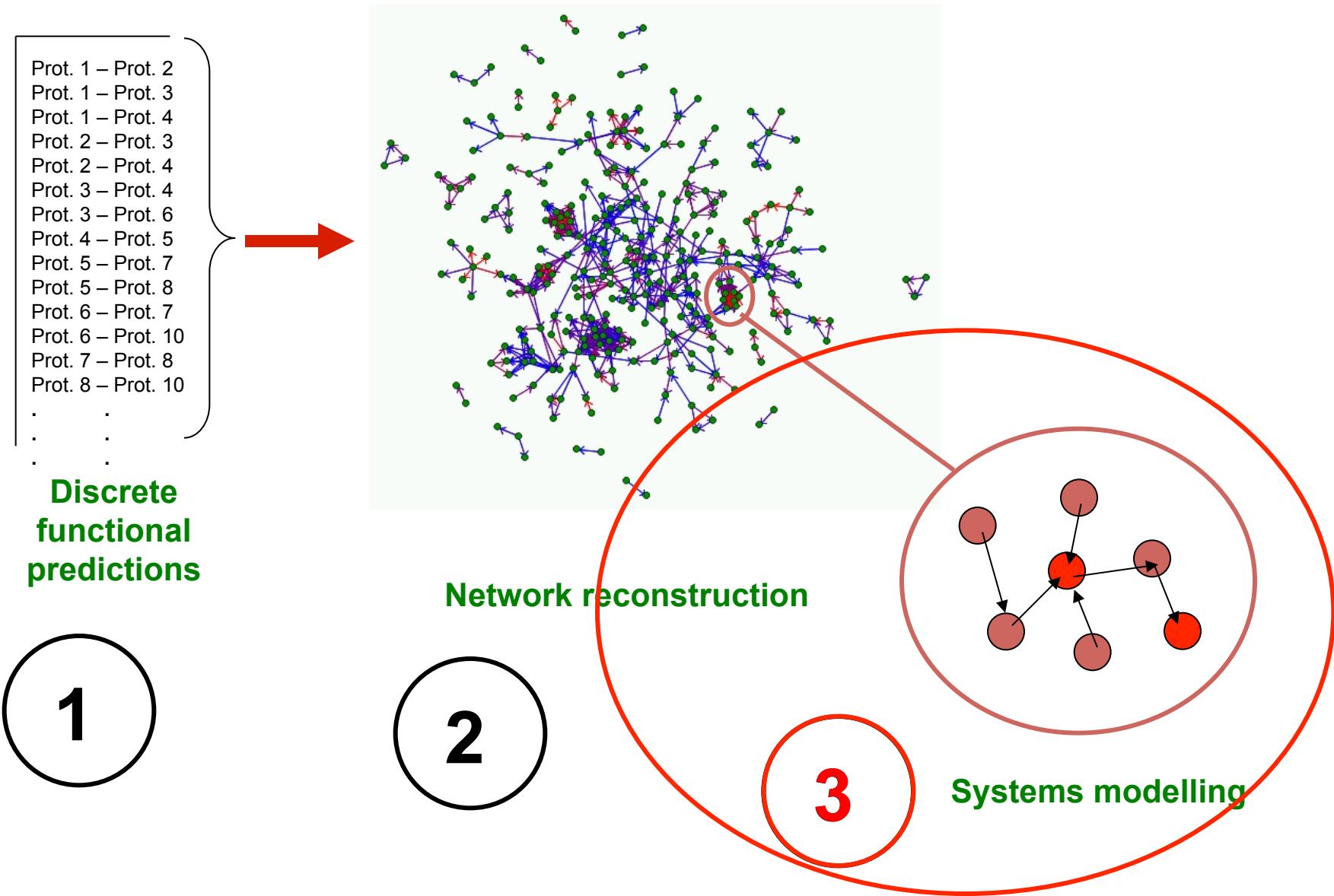
## Systematic computational prediction of protein interaction networks

(i) Protein association prediction methods: the principles behind the different computational methods available to predict pairwise protein–protein interactions (PPIs)

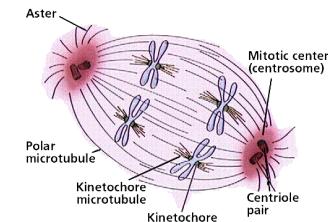
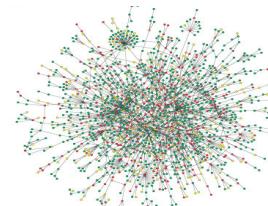
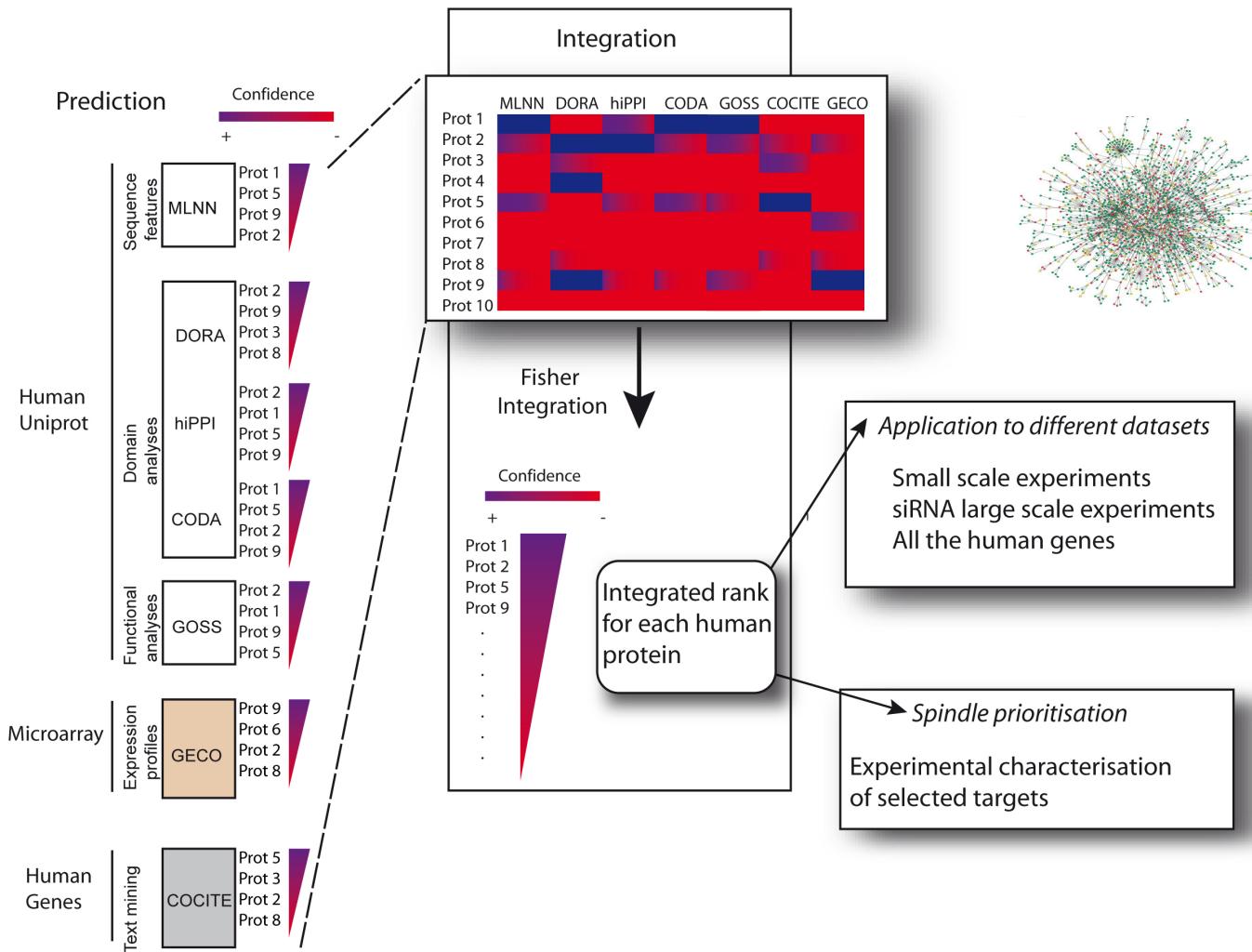
(ii) Integrating prediction methods: ways of combining these individual methods in order to increase accuracy and coverage while reducing noise in predicting PPIs.

(iii) Exploiting the network structure: some successful applications of computational and mathematical methods that exploit network context to predict novel interactions or novel members of different biological processes.

# Modelling networks and exploiting functional context



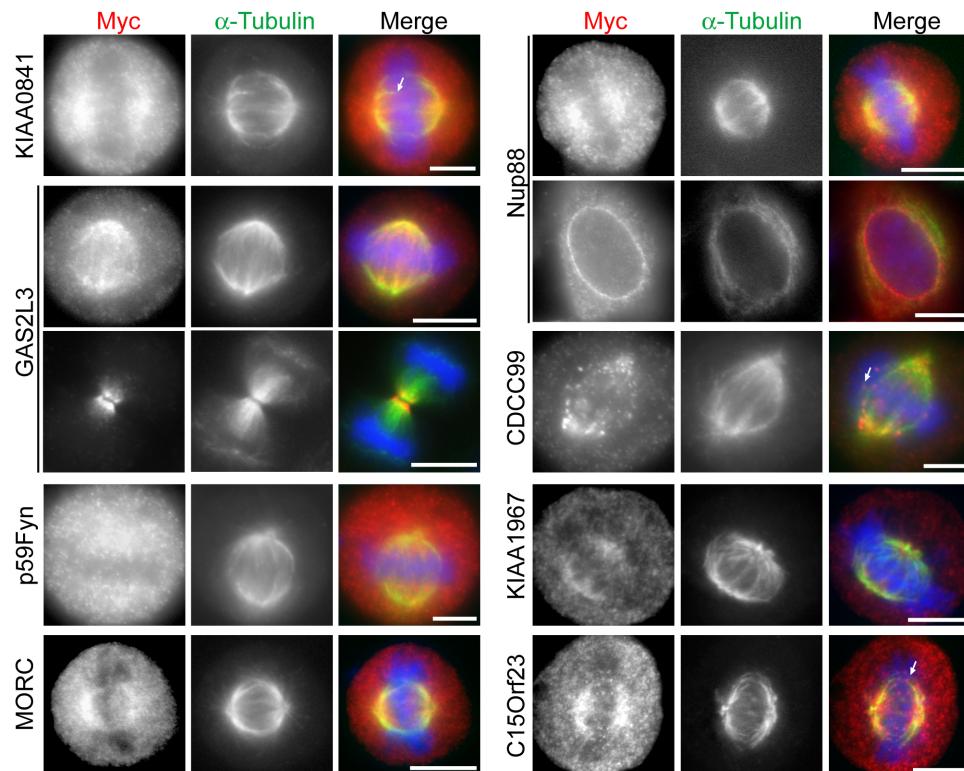
# Spindle Prediction Integrated Platform (SPIP)



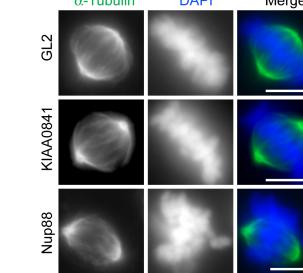
# Validación experimental de la plataforma SPIP :

Más de un 70% de éxito encontrando nuevas proteínas del huso mitótico

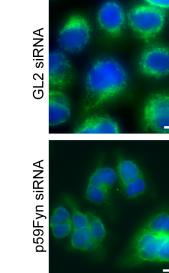
A



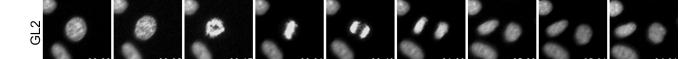
A



B



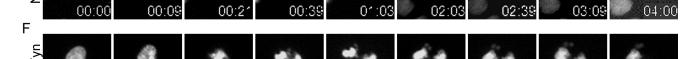
C



D



E



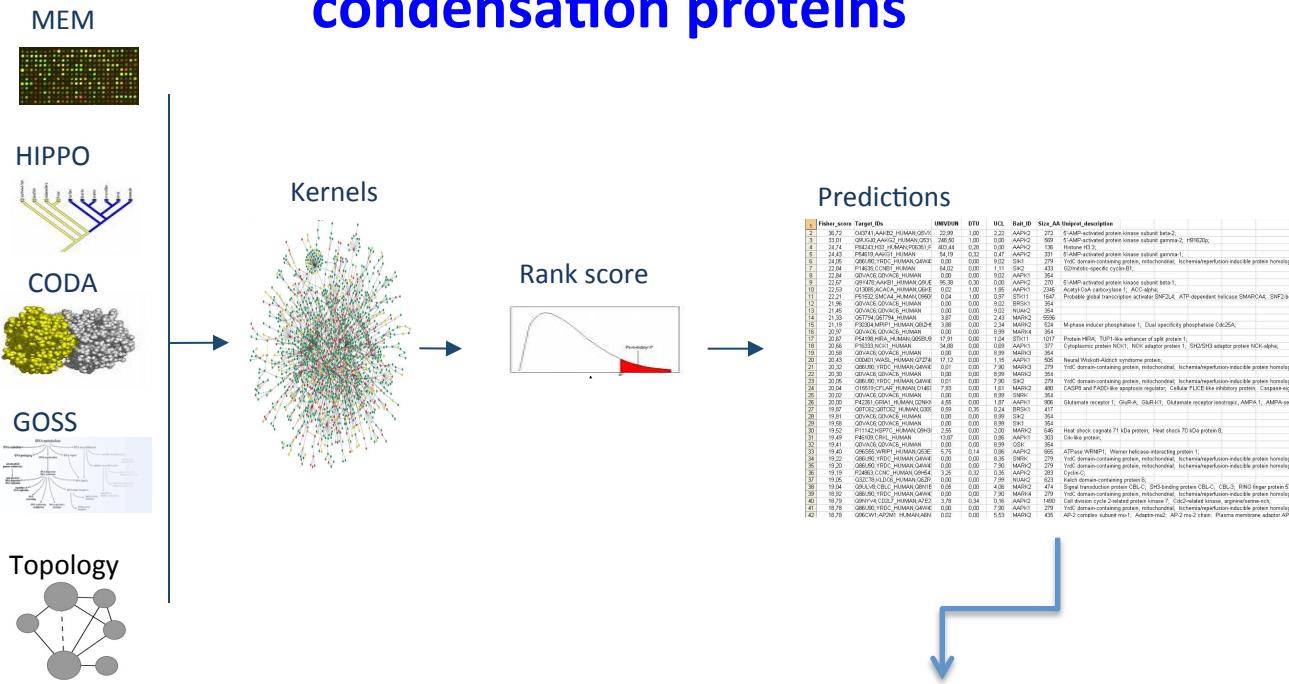
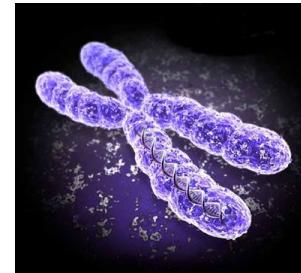
F



G



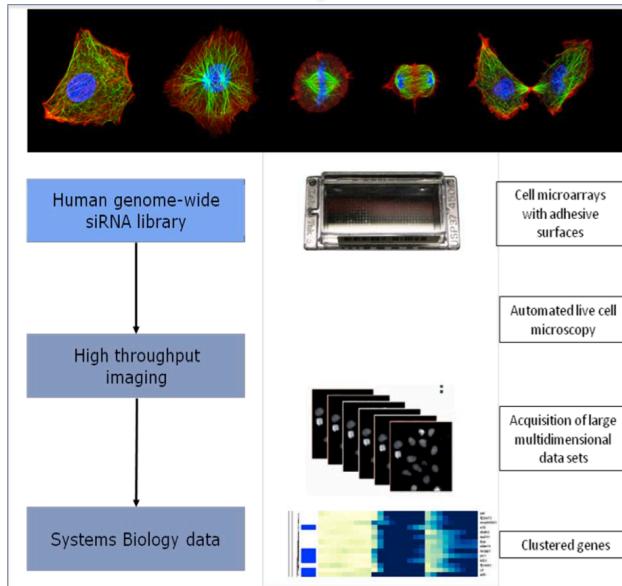
# Prediction of novel mitotic chromosome condensation proteins



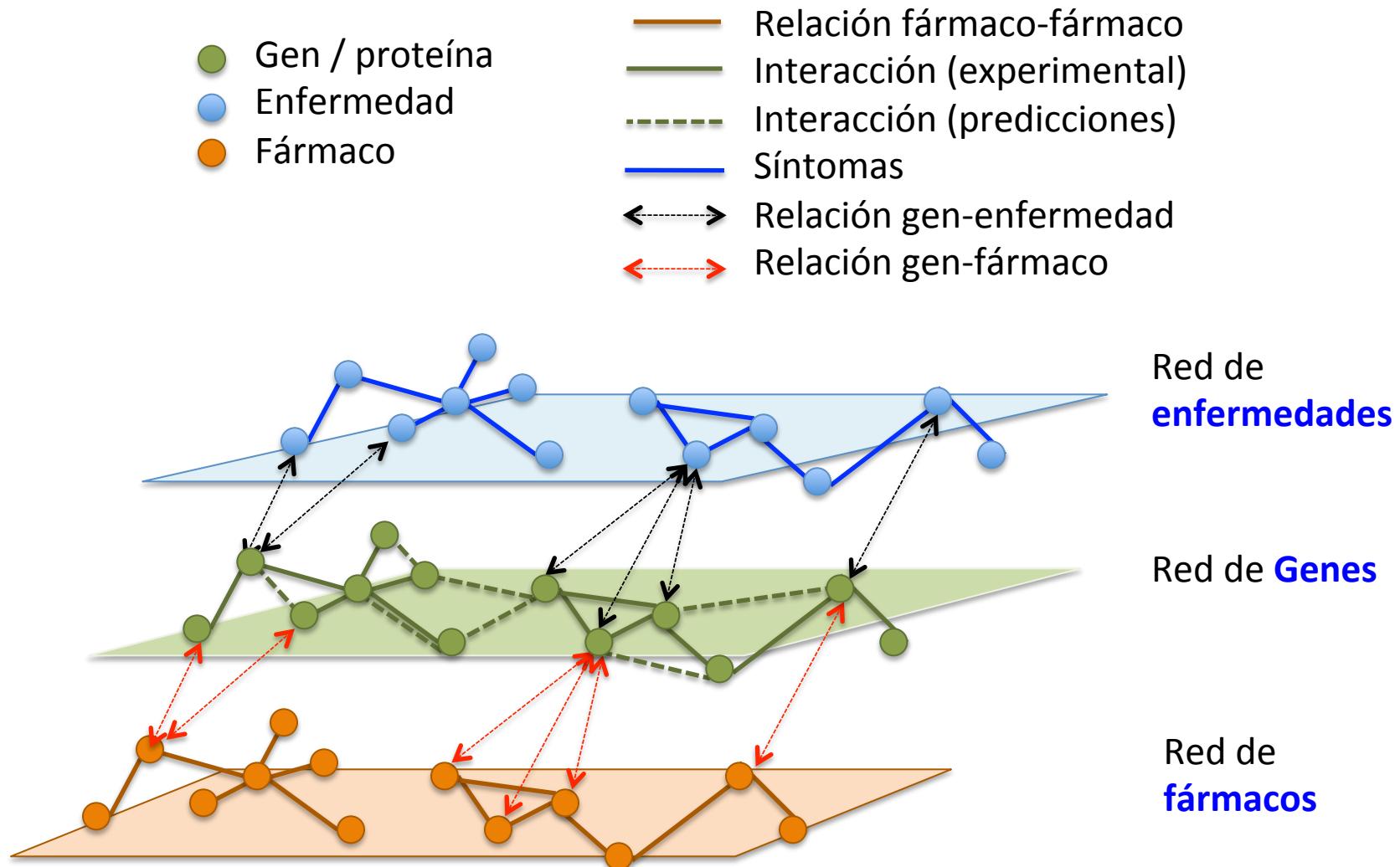
# *RNAi cell screening system*

**Integration of biological data by kernels on graph nodes allows prediction of genes involved in mitotic chromosome condensation**

Jean-Karim Hériché, Jon G. Lees, Ian Morilla, Thomas Walter, Boryana Petrova, Priti Adler, José M. Fernández, Christian Haering, Jaak Vilo, Alfonso Valencia, Juan A. Ranea, Christine Orengo and Jan Ellenberg. (**ENVIADO**)



# Construcción de redes heterogéneas de genes, enfermedades raras y fármacos



- Moya-García AA, Ranea JA. Insights into Polypharmacology from Drug-Domain Associations. *Bioinformatics*. 2013 Jun 5. [Epub ahead of print]

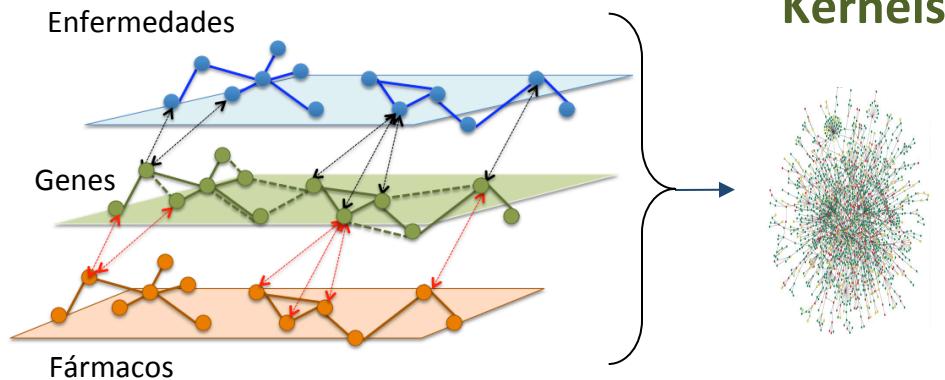
- Reyes-Palomares A, Rodríguez-López R, Ranea JA, Sánchez Jiménez F, Medina MA. Global analysis of the human pathophenotypic similarity gene network merges disease module components. *PLoS One*. 2013;8(2):e56653.

- Moya-García AA, Rodriguez CE, Morilla I, Sanchez-Jimenez F, Ranea JA.. The function of histamine receptor H4R in the brain revealed by interaction partners. *Front Biosci (Schol Ed)*. 2011 Jun 1;3:1058-66.

- Lees JG, Heriche JK, Morilla I, Ranea JA, Orengo CA. . Systematic computational prediction of protein interaction networks. *Phys Biol*. 2011 Jun;8(3):035008.

# Explotación de redes heterogéneas de genes, enfermedades raras y fármacos Para predecir nuevos genes y fármacos

## Redes heterogéneas



## Predicciones priorizadas

Rank	Filter	Target IDs	Interaction	DTU	ECL	Rank ID	Score	AA	Interact description
2	36.32	04274:AAA-R2L_HUMAN_0526	22.09	1.00	2.22	AAPK2	275	5	cAMP-activated protein kinase subunit gamma-2.
3	33.01	09130:AAA-G02_HUMAN_053	246.60	1.00	0.00	AAPK2	369	5	cAMP-activated protein kinase subunit gamma-2, HPI620;
4	32.80	04274:AAA-R2L_HUMAN_052617	22.09	1.00	0.00	AAPK2	369	5	cAMP-activated protein kinase subunit gamma-2.
5	24.43	PSA619:AC02_HUMAN	54.49	0.32	0.47	AAPK2	321	5	cAMP-activated protein kinase subunit gamma-2; Y6C domain-containing protein, mitochondrial, teneurin/reperfusion-inducible protein homolog;
6	08839:Y3ZC_HUMAN	0.00	0.00	9.02	SRI1	123	5	Y6C domain-containing protein, mitochondrial, teneurin/reperfusion-inducible protein homolog;	
7	23.09	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	AAPK1	354	5	cAMP-activated protein kinase subunit beta-1.
8	22.84	04274:AAA-G02_HUMAN_054	22.09	1.00	0.00	AAPK1	354	5	cAMP-activated protein kinase subunit beta-1.
9	22.62	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	AAPK1	354	5	cAMP-activated protein kinase subunit beta-1.
10	22.53	01308:AC04_A_HUMAN_0526	0.02	1.00	1.85	AAPK1	2345	5	Acetyl-CoA carboxylase 1, ACC-aph;
11	22.42	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
12	21.36	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
13	21.45	04274:AAA-G02_HUMAN	0.00	0.00	9.02	MAN2B	354	5	Mannosidase inducer phosphatase 1; Dual-specificity phosphatase Cd25A;
14	21.33	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	MAN2B	354	5	Mannosidase inducer phosphatase 1; Dual-specificity phosphatase Cd25A;
15	21.19	P20204:MP1_HUMAN_0526	3.88	0.00	2.34	MAR2	124	5	Mannose 6-phosphate isomerase; Mannose 6-phosphate isomerase;
16	20.90	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	MAR2	124	5	Mannose 6-phosphate isomerase; Mannose 6-phosphate isomerase;
17	20.67	PSA19:HR2L_HUMAN_052609	17.91	0.00	1.04	STC11	1617	5	Protein HPA; TUP1-like enhancer of split protein 1;
18	20.58	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	SH3D9C	354	5	Cytosolic protein NCK1; NCK-adapter protein 1; SH3D9C adapter protein NCK-aph;
19	20.58	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	SH3D9C	354	5	Cytosolic protein NCK1; NCK-adapter protein 1; SH3D9C adapter protein NCK-aph;
20	20.43	00061:WASH1_HUMAN_0727	17.12	0.00	1.15	AAPK1	305	5	Neuro Wiskott-Aldrich syndrome protein;
21	19.58	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
22	20.30	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
23	20.20	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
24	20.04	01569:FLJ148_HUMAN_0146	7.93	0.00	1.61	MAR2	480	5	Y6C domain-containing protein, mitochondrial, teneurin/reperfusion-inducible protein homolog CAP38 and FAO-like apoptosis regulator; Cellular FLEx-like inhibitor protein; Caspase-regulating protein 5;
25	20.03	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	SNR1	94	5	Y6C domain-containing protein, mitochondrial, teneurin/reperfusion-inducible protein homolog CAP38 and FAO-like apoptosis regulator; Cellular FLEx-like inhibitor protein; Caspase-regulating protein 5;
26	19.97	04274:G0252_HUMAN	0.00	0.00	0.00	BRSK1	417	5	Glutamate receptor 1, GABA-A, GluR-K1; Glutamate receptor ionotropic, AMPA-1; AMPA-1; Glutamate receptor 1, GABA-A, GluR-K1; Glutamate receptor ionotropic, AMPA-1; AMPA-1;
27	19.97	04274:G0252_HUMAN_0526	0.00	0.00	0.00	BRSK1	417	5	Glutamate receptor 1, GABA-A, GluR-K1; Glutamate receptor ionotropic, AMPA-1; AMPA-1;
28	19.96	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	BRSK1	417	5	Glutamate receptor 1, GABA-A, GluR-K1; Glutamate receptor ionotropic, AMPA-1; AMPA-1;
29	19.95	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	BRSK1	417	5	Glutamate receptor 1, GABA-A, GluR-K1; Glutamate receptor ionotropic, AMPA-1; AMPA-1;
30	19.94	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	BRSK1	417	5	Glutamate receptor 1, GABA-A, GluR-K1; Glutamate receptor ionotropic, AMPA-1; AMPA-1;
31	19.49	P46109:CHL1_HUMAN	13.87	0.00	0.00	AAPK1	303	5	Heat shock cognate 71 kDa protein; Heat shock 70 kDa protein; Cdc-like protein;
32	19.48	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
33	19.40	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
34	19.22	08919:Y3ZC_HUMAN_0526	0.00	0.00	0.00	SNR1	94	5	ATPase WRNIP1; Werner helicase-interacting protein 1;
35	19.19	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
36	19.19	P20830:CNC_HUMAN_0526	3.25	0.32	0.35	AAPK2	383	5	Y6C domain-containing protein, mitochondrial, teneurin/reperfusion-inducible protein homolog;
37	19.19	04274:AAA-R2L_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
38	19.04	05116:CEBL_HUMAN_0526	0.00	0.00	4.06	MAR2	474	5	Signal transduction protein CEBL; SH3-binding protein CEBL-C; PMS finger protein 1;
39	18.92	08919:Y3ZC_HUMAN_0526	0.00	0.00	7.00	MAR2	474	5	Y6C domain-containing protein, mitochondrial, teneurin/reperfusion-inducible protein homolog;
40	18.79	04274:AAA-G02_HUMAN_0526	22.09	1.00	0.00	STC11	1647	5	Probable global transcription activator SNF2L4; ATP-dependent helicase SNF2L4; SNF2-like;
41	18.78	08919:Y3ZC_HUMAN_0526	0.00	0.00	7.90	AAPK1	279	5	ATPase WRNIP1; Werner helicase-interacting protein 1;
42	18.78	08919:Y3ZC_HUMAN_0526	0.00	0.00	5.53	MAR2	475	5	ATPase WRNIP1; Werner helicase-interacting protein 1;

Inmenso Espacio de exploración

Pequeño Espacio a explorar  
Enriquecido en Verdaderos Positivos

- Predecir nuevos genes implicados en enfermedad
- Predecir nuevas relaciones/aplicaciones entre fármacos-proteínas-ERs
- Estudiar los contextos funcionales y moleculares donde antúan los fármacos y las proteínas, o donde se originan las enfermedades

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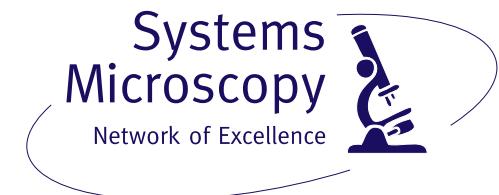
Department of Cell Biology, Max Plank (Munich)

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Ana Santamaría

Rainer Malik



Projects: SAF2009-09839 and ECO2010-14749; Ministerio de Ciencia e Innovación, Spain)



Gobierno de España  
Ministerio de Ciencia e Innovación

CATH  
Gene3D  
Domain Architecture Classification

# *La tripulación...*



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