

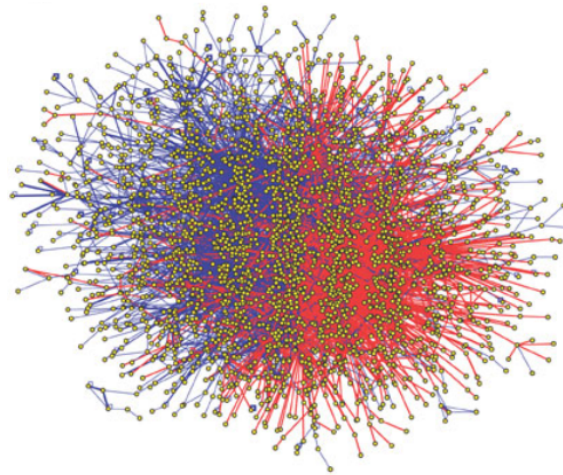
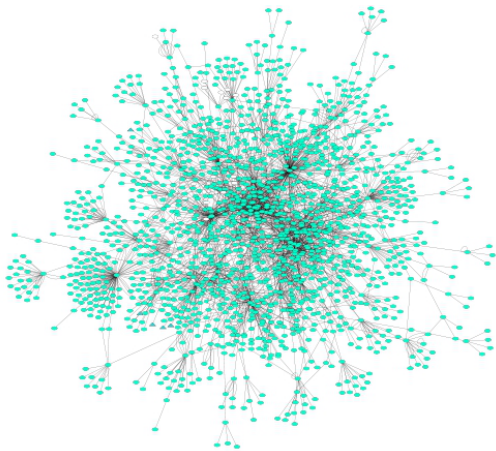
Introduction to protein-protein interactions (PPIs)

Some definitions...

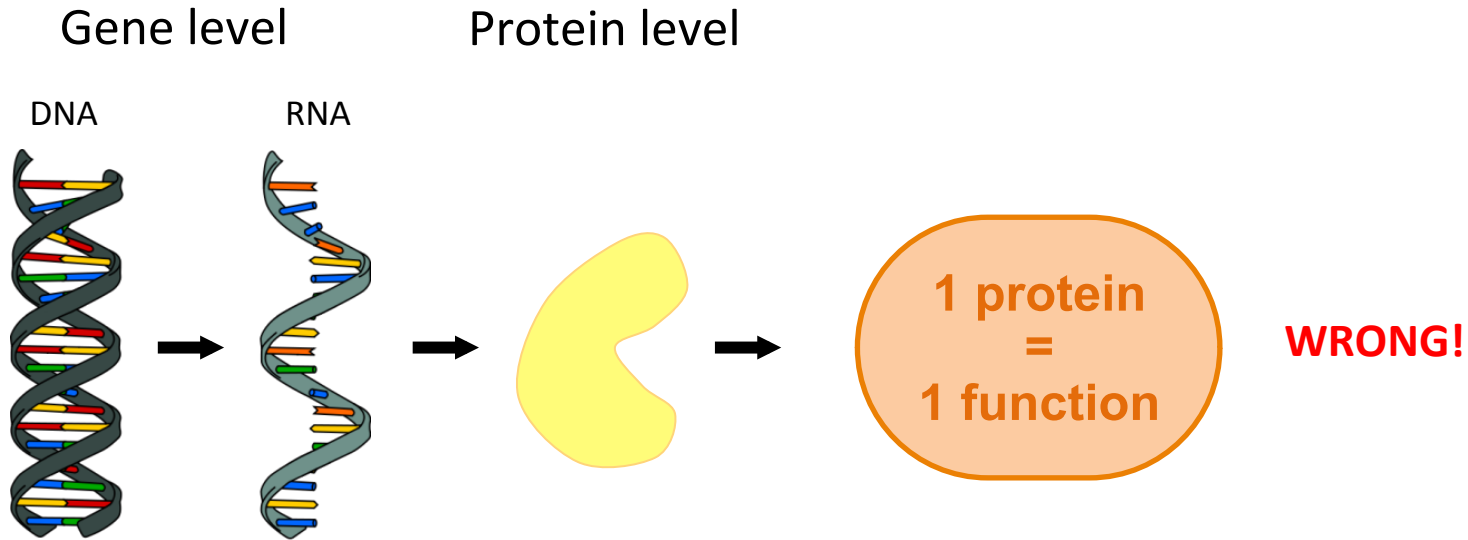
Protein-protein interactions (PPIs): **physical** and **selective** contacts that happen between pairs of proteins, in **certain molecular regions** and in a **defined biological context**.

Interactome: the **totality** of PPIs that happen in a cell / in an organism / in a specific biological context...

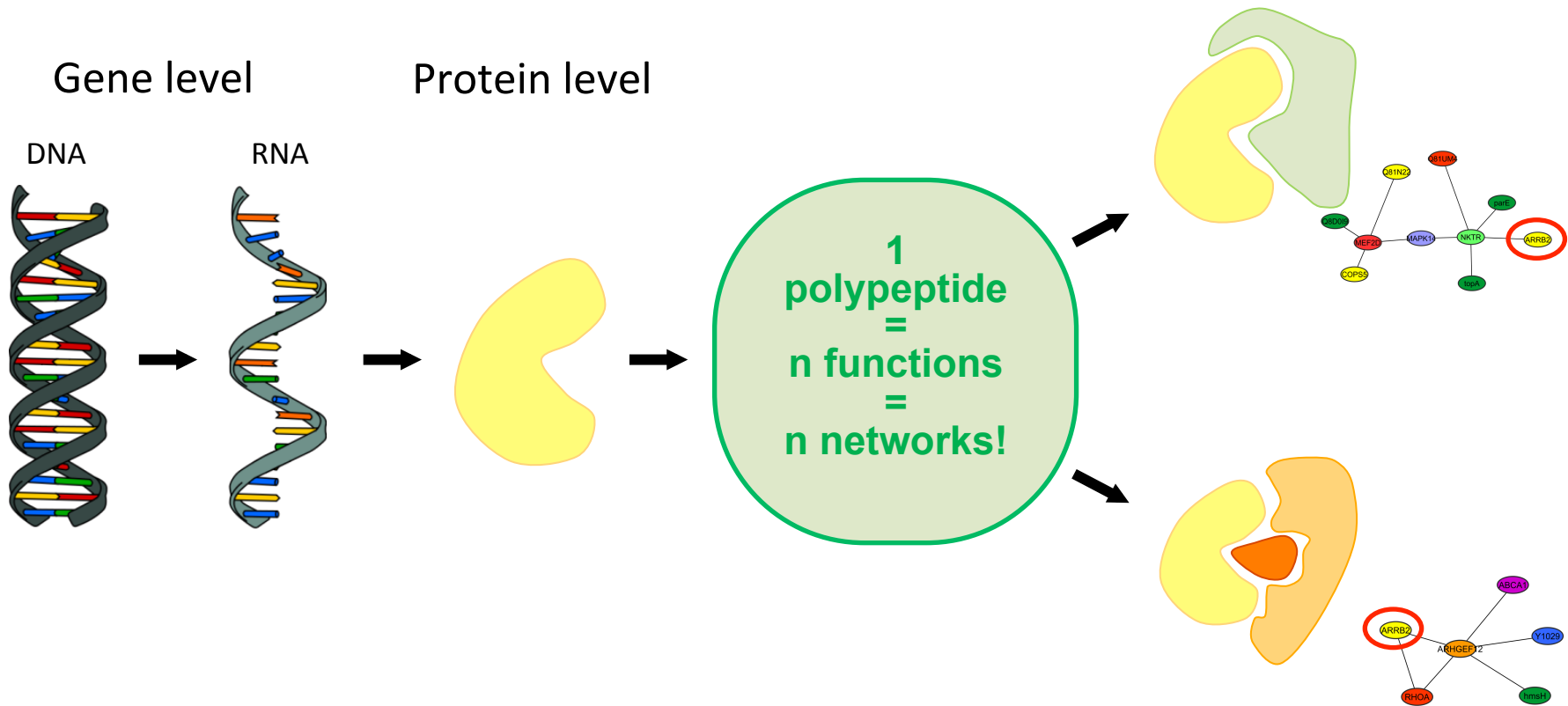
Protein-protein interaction network: **Graphical representation** of a group of PPIs in which proteins are represented as **nodes** and interactions as **edges**.



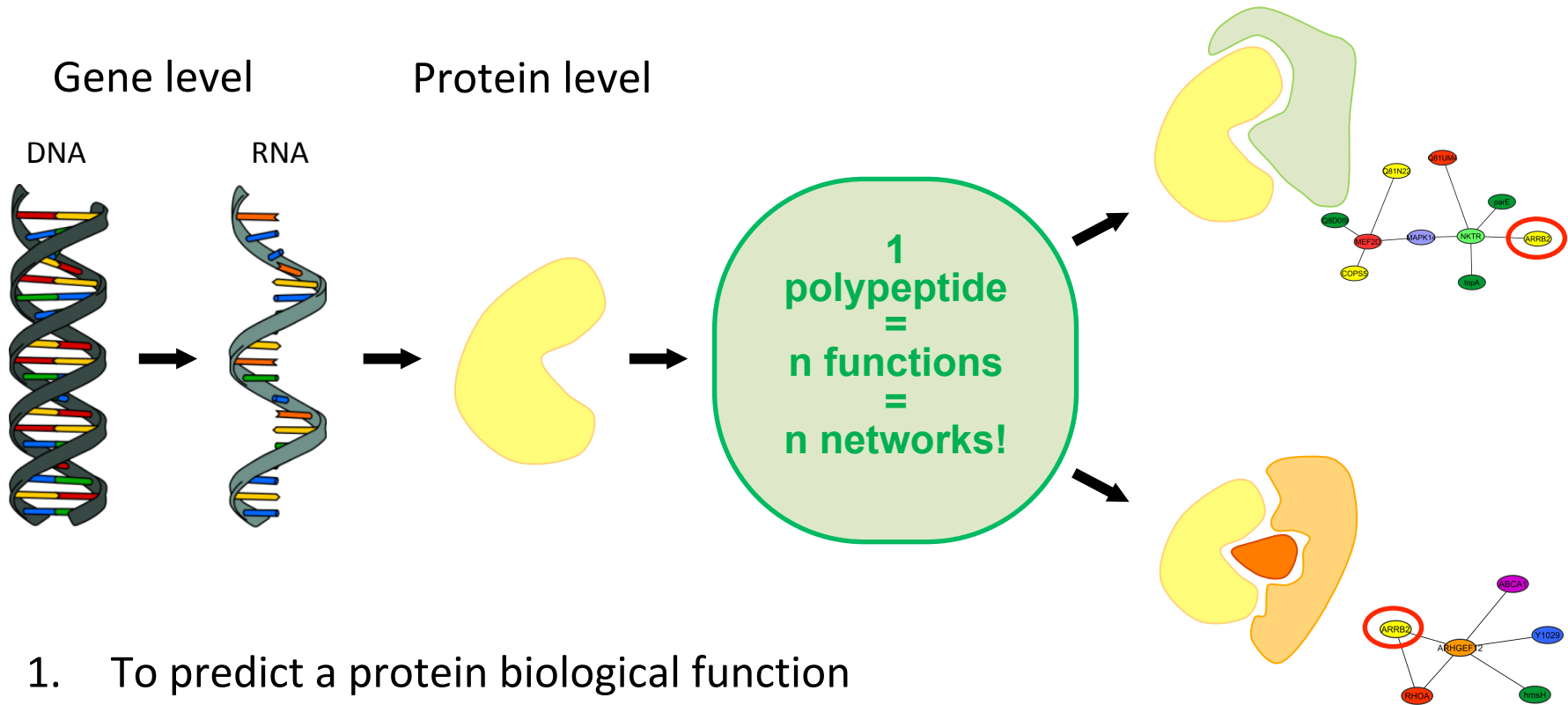
Why protein-protein interactions?



Why protein-protein interactions?

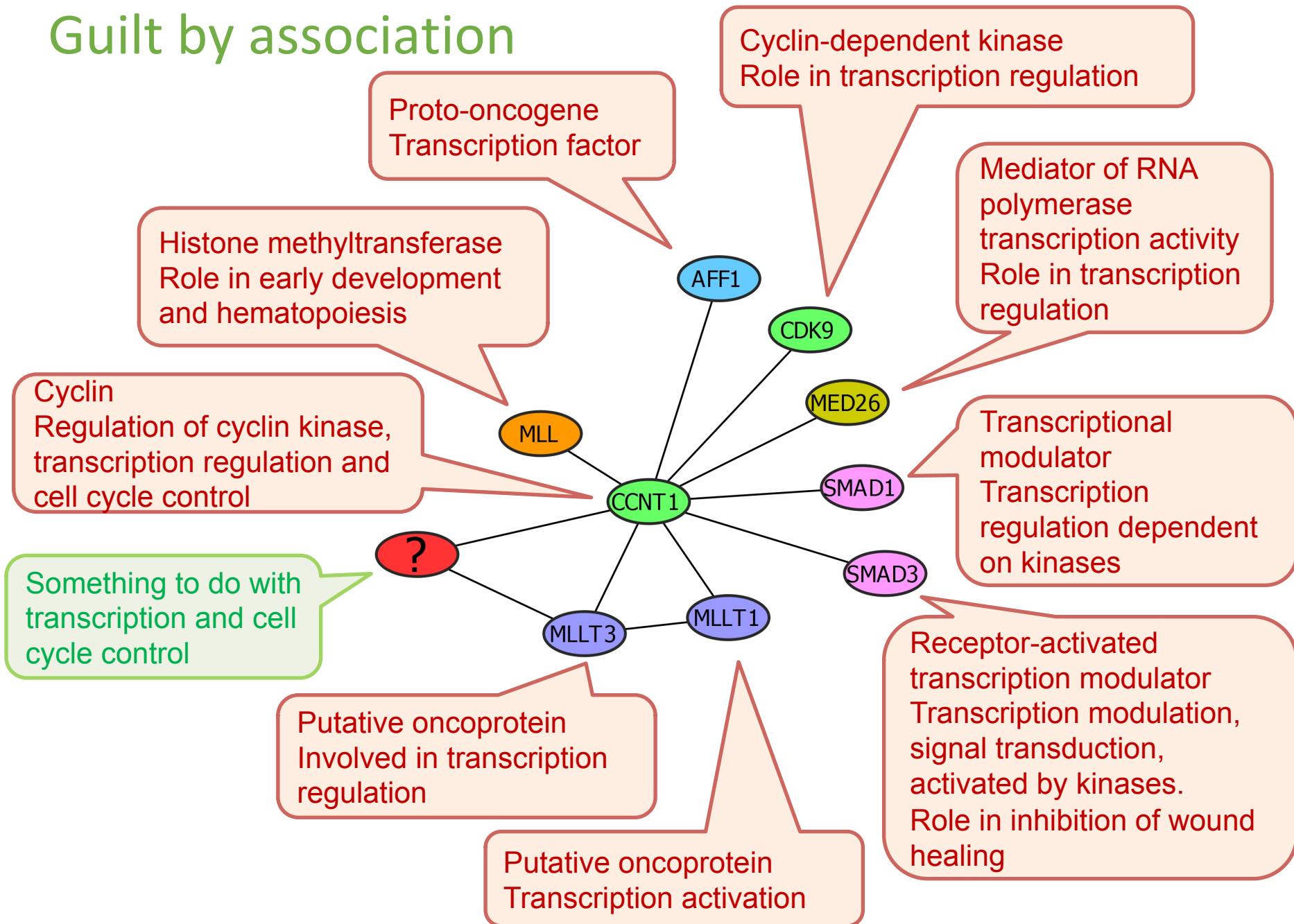


Why protein-protein interactions?

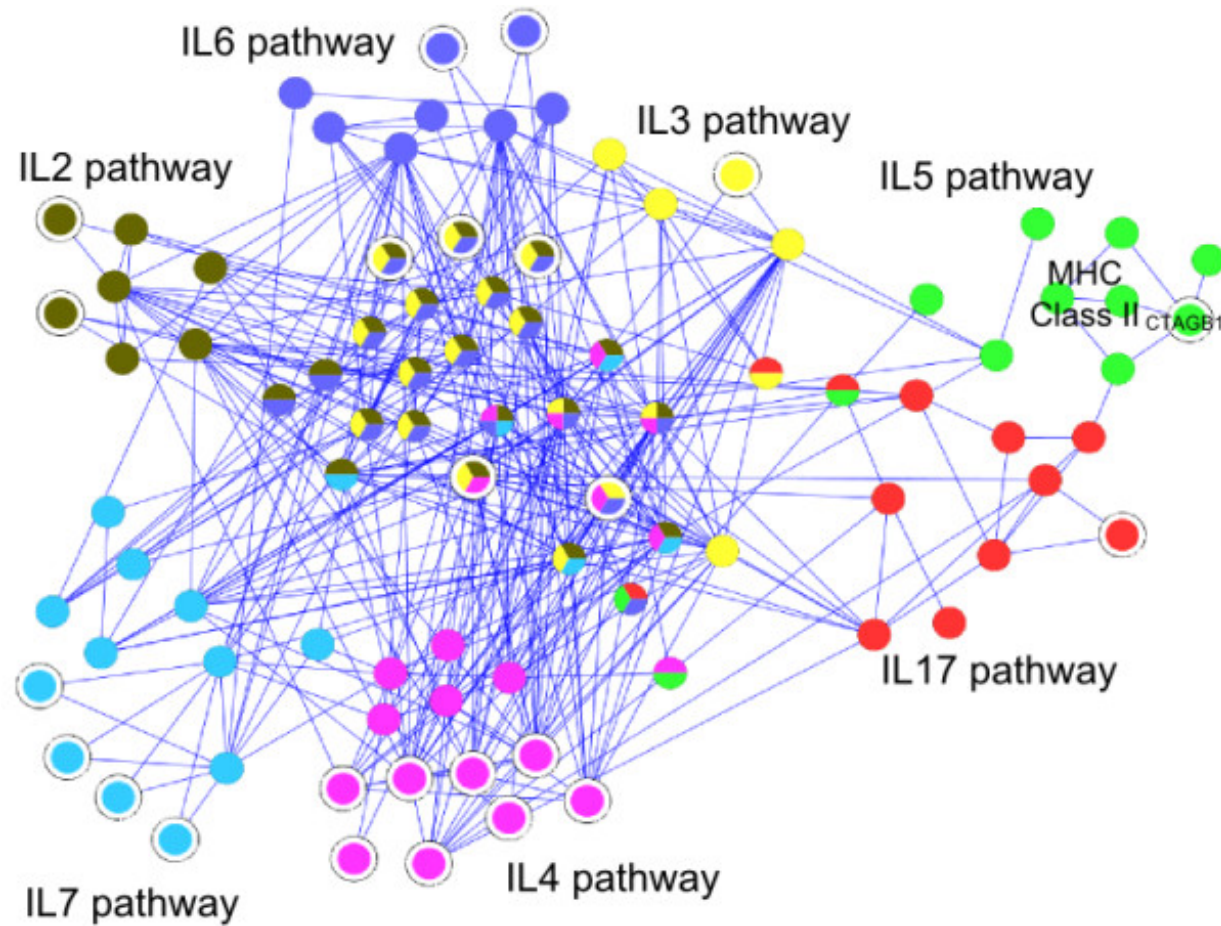


1. To predict a protein biological function
 - “guilt by association”
 - proteins with similar functions should cluster together
2. To improve characterization of protein complexes and pathways
 - interaction networks work as a draft map that brings detail to biological processes and pathways

Guilt by association



Characterization of protein complexes and pathways



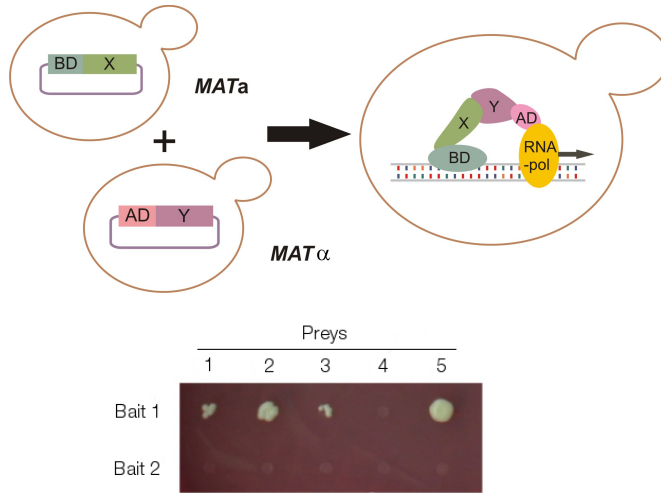
Properties of PPIs

1. PPIs are physical contacts not necessarily functional contacts
2. PPIs are contacts between proteins only (not protein-DNA, protein-RNA etc..)
3. PPIs are specific and occur for a reason. They are not accidental
4. Interaction surfaces should be non-generic (evolved for a purpose)
5. PPIs are not necessarily static but can also be transient (TF and transcription machinery)
6. PPIs occur in specific biological context: not all possible interactions occur in all cells

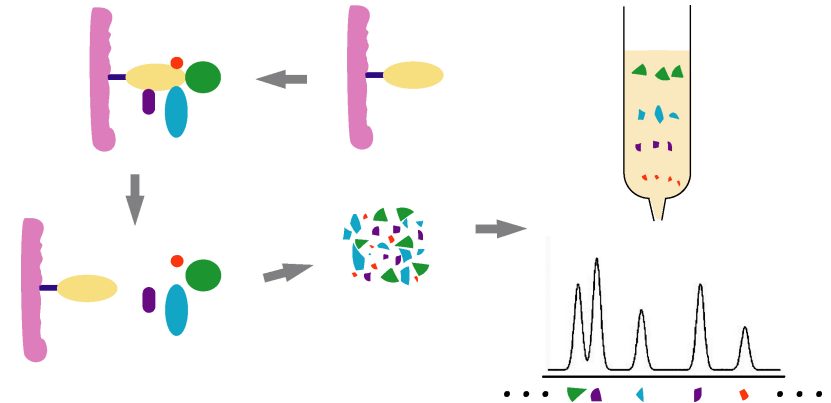
Protein-protein interaction detection methods

High-throughput

Yeast-two hybrid (Y2H)

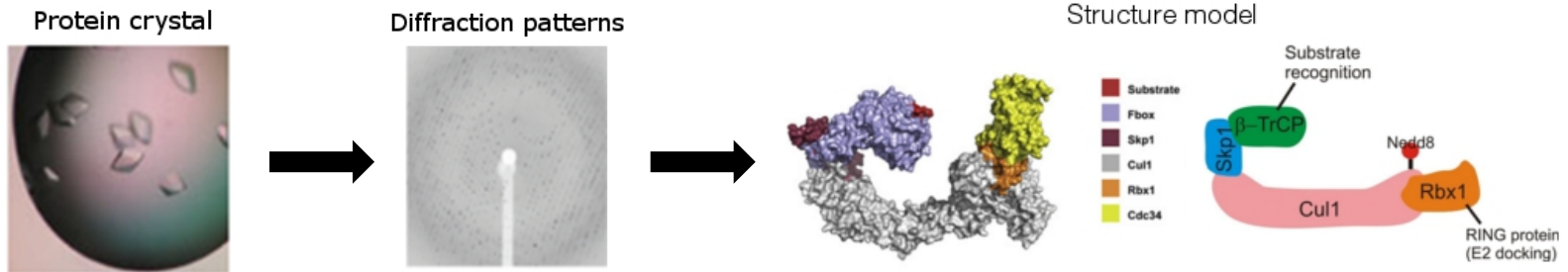


Tandem affinity purification+ mass spectrometry (TAP-MS)

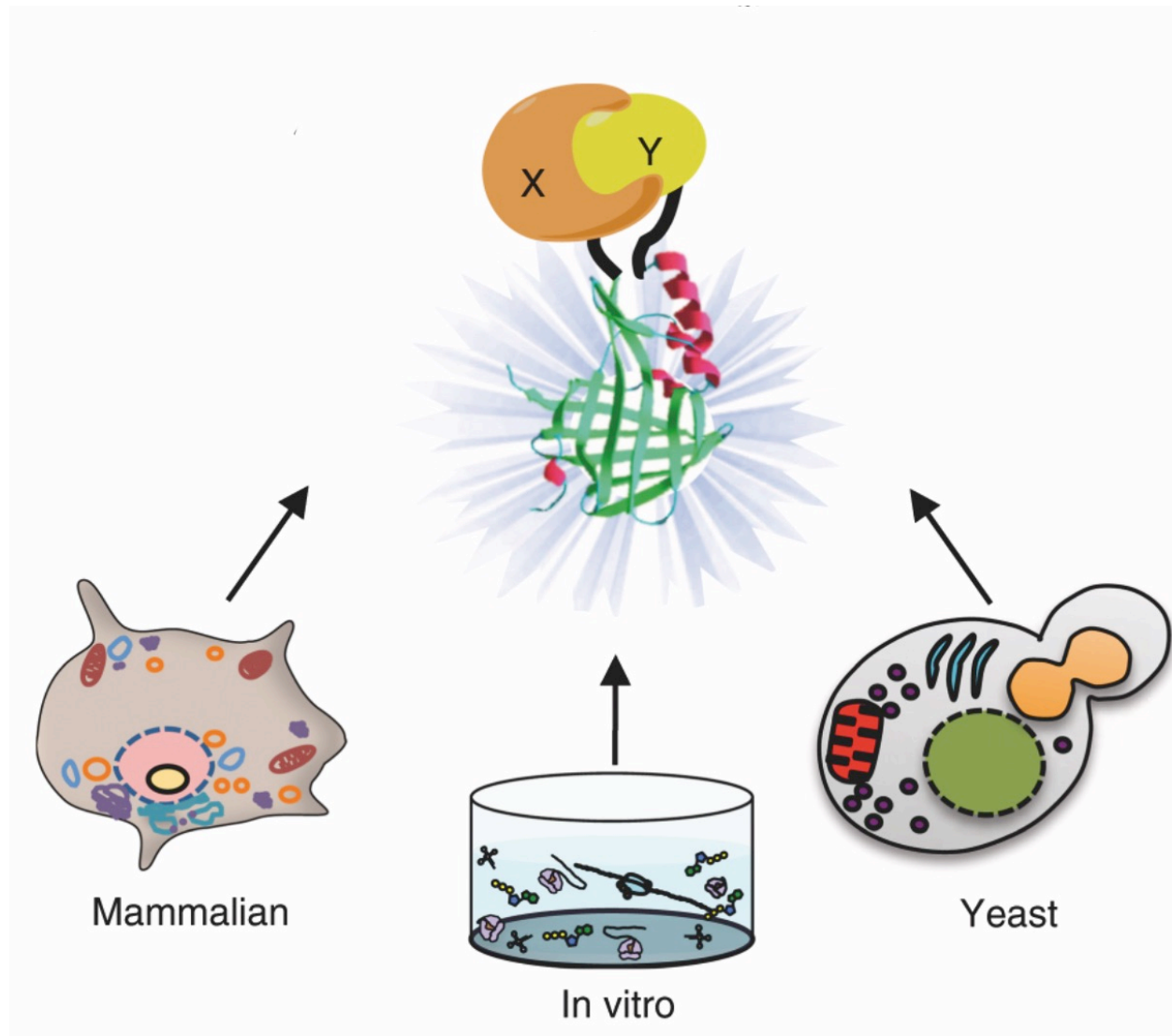


Low-throughput

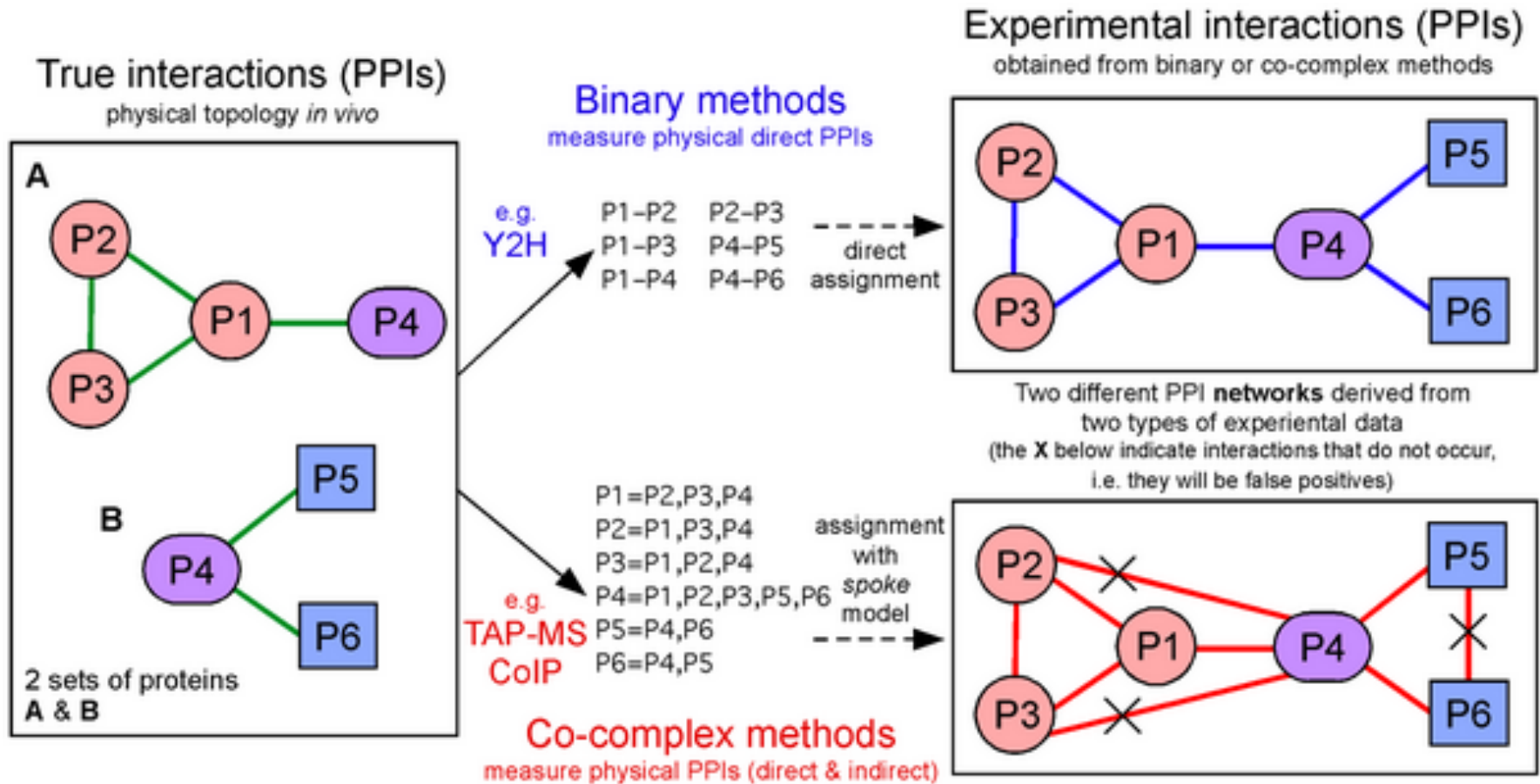
X-ray diffraction studies



Protein-protein interaction detection methods

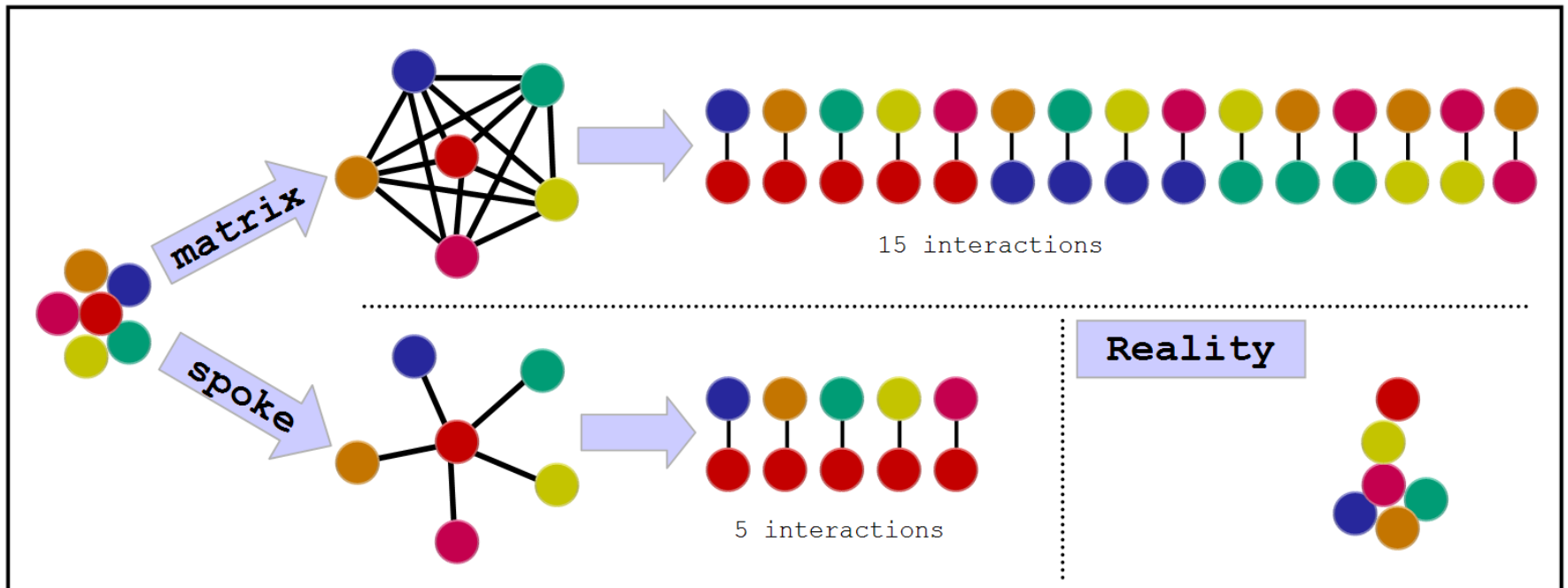


Protein-protein interaction detection methods



The problem with complexes

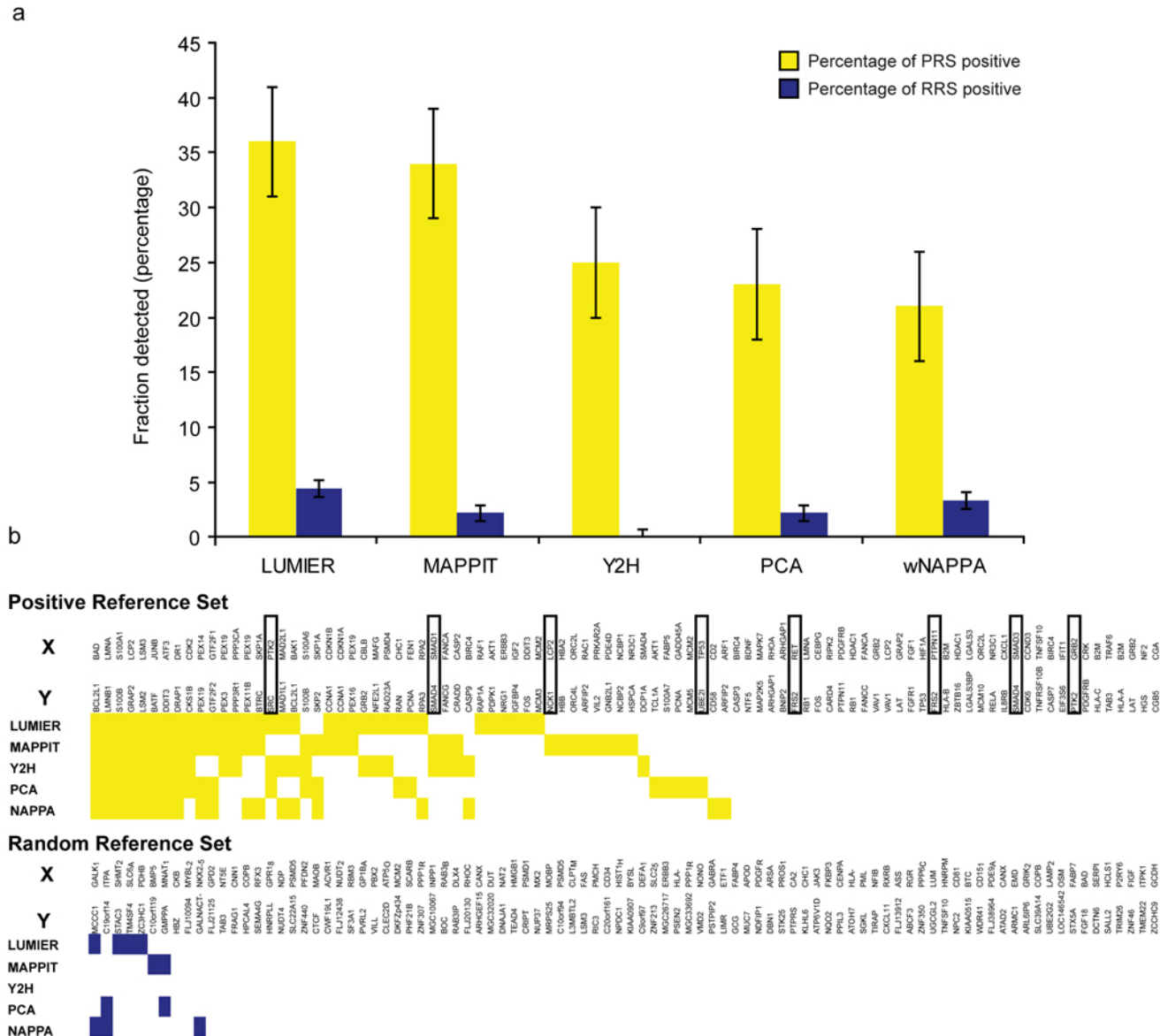
- Some experimental methods generate complex data: **E. g. Tandem affinity purification (TAP)**
- There are two algorithms to transform this information into binary data:



Protein-protein interaction detection methods

No single method can accurately reproduce a true binary interaction observed under physiological conditions – every interaction detected experimentally is fundamentally **artefactual**.

Protein-protein interaction detection methods



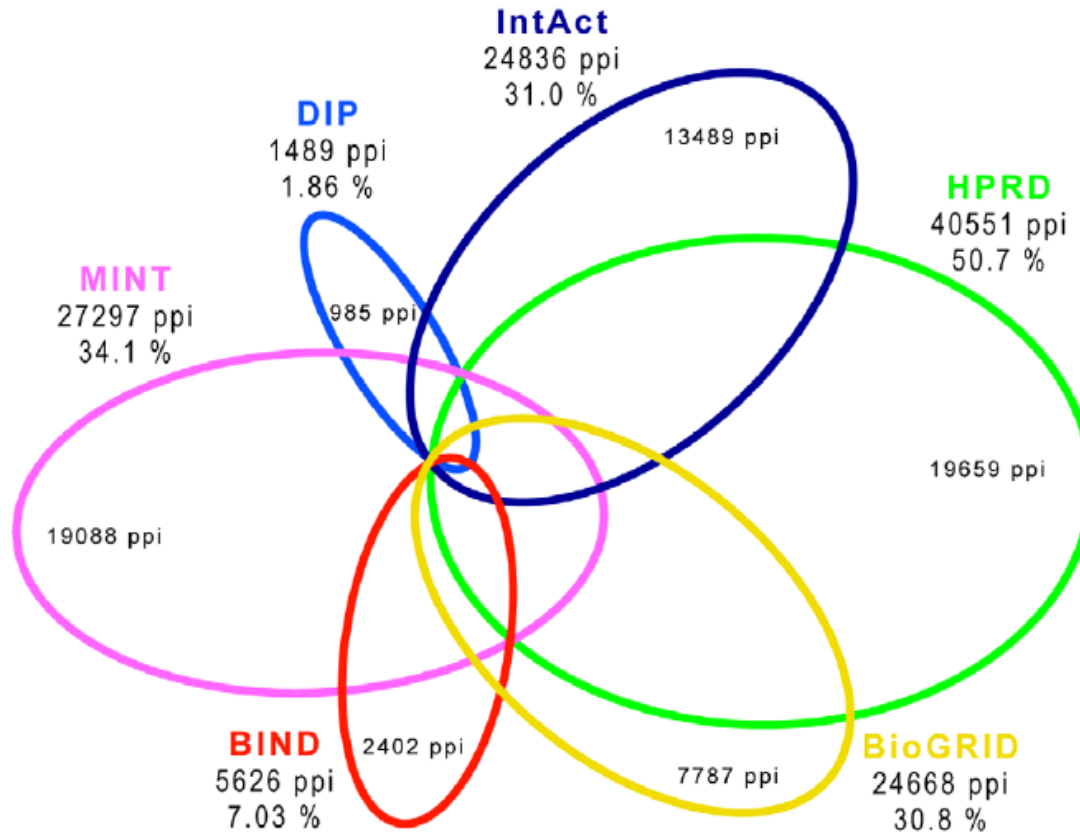
Braun et al., Nat Methods, 2008, PMID: 19060903.

PPI databases and repositories

Acronym	Database Full Name and URL	PPI Sources	Type of MI	Species	n Proteins (Dec. 2009)	n Interactions (Dec. 2009)
Primary Databases: PPI experimental data (curated from specific SSc & LSc published studies)						
BIND	Biomolecular Interaction Network Database, http://bond.unleashedinformatics.com/	SSc & LSc published studies (literature-curated)	PPIs & others	All	[31,972]	[58,266]
BioGRID	Biological General Repository for Interaction Datasets, http://www.thebiogrid.org/	SSc & LSc published studies (literature-curated)	PPIs & others	All	[28,717]	[108,691]
DIP	Database of Interacting Proteins, http://dip.doe-mbi.ucla.edu/dip/	SSc & LSc published studies (literature-curated)	Only PPIs	All	20,728	57,683
HPRD	Human Protein Reference Database, http://www.hprd.org/	SSc & LSc published studies (literature-curated)	Only PPIs	Human	27,081	38,806
IntAct	IntAct Molecular Interaction Database, http://www.ebi.ac.uk/intact/	SSc & LSc published studies (literature-curated)	PPIs & others	All	[60,504]	[202,826]
MINT	Molecular INteraction database, http://mint.bio.uniroma2.it/mint/	SSc & LSc published studies (literature-curated)	Only PPIs	All	30,089	83,744
MIPS-MPact	MIPS protein interaction resource on yeast, http://mips.gsf.de/genre/proj/impact/	Derived from CYGD	Only PPIs	Yeast	1,500	4,300
MIPS-MPPI	MIPS Mammalian Protein-Protein Interaction Database, http://mips.gsf.de/proj/ppi	SSc published studies (literature-curated)	Only PPIs	Mammalian	982	937
Meta-Databases: PPI experimental data (integrated and unified from different public repositories)						
APID	Agile Protein Interaction DataAnalyzer, http://bioinfo.wdep.usal.es/apid/	BIND, BioGRID, DIP, HPRD, IntAct, MINT	Only PPIs	All	56,460	322,579
MPIDB	The Microbial Protein Interaction Database, http://www.jcvi.org/mpidb/	BIND, DIP, IntAct, MINT, other sets (exp & lit-curated)	Only PPIs	Microbial	7,810	24,295
PINA	Protein Interaction Network Analysis platform, http://csb.utdtk.helsinki.fi/pina/	BioGRID, DIP, HPRD, IntAct, MINT, MPact	Only PPIs	All	[?]	188,823
Prediction Databases: PPI experimental and predicted data ("functional interactions", i.e., interactions <i>à la sensu</i> derived from different types of data)						
MIMI	Michigan Molecular Interactions, http://mimi.lncbi.org/MimiWeb/	BIND, BioGRID, DIP, HPRD, IntAct, & nonPPI data	PPIs & others	All	[45,452]	[391,386]
PIPs	Human PPI Prediction database, http://www.compbio.dundee.ac.uk/www-pips/	BIND, DIP, HPRD, OPHID, & nonPPI data	PPIs & others	Human	[?]	[37,606]
OPHID	Online Predicted Human Interaction Database, http://ophid.utoronto.ca/	BIND, BioGRID, HPRD, IntAct, MINT, MPact, & nonPPI data	PPIs & others	Human	[?]	[424,066]
STRING	Known and Predicted Protein-Protein Interactions, http://string.embl.de/	BIND, BioGRID, DIP, HPRD, IntAct, MINT, & nonPPI data	PPIs & others	All	[2,590,259]	[88,633,860]
UniHI	Unified Human Interactome, http://www.mdc-berlin.de/unihi/	BIND, BioGRID, DIP, HPRD, IntAct, MINT, & nonPPI data	PPIs & others	Human	[22,307]	[200,473]

The table is divided in three sections: **primary databases**, which include PPIs from large- and small-scale (LSc & SSc) experimental data that are usually obtained from curation of research articles (8 resources included: BIND, BioGRID, DIP, HPRD, IntAct, MINT, MIPS-MPact, MIPS-MPPI); **meta-databases**, which include PPIs derived from integration and unification of several primary repositories (3 resources: APID, MPIDB, PINA); **prediction databases**, which include PPIs from experimental analyses together with predicted PPIs obtained from the analyses of heterogeneous biological data (5 resources: MIMI, PIPs, OPHID, STRING, UniHI). The table shows the total number of proteins and interactions that were reported by each repository in December 2009 (as far as we could see in the respective Web site). The numbers are in brackets [] when the repository includes PPIs and other types of interactions (e.g., protein-ligand interactions or for the case of prediction databases nonPPI data). The question mark (?) indicates that the number of distinct proteins included in such repository could not be found in the Web. doi:10.1371/journal.pcbi.1000807.t001

PPI databases: coverage



**Human PPIs
coverage in the
main public
primary databases
(Dec 2009)**

some of the experimentally determined PPIs included in the databases are most probably false positives? → increase PPI reliability with 3D data?

An attempt for increased PPIs reliability: the IMEx consortium

www.imexconsortium.org

The screenshot shows the homepage of the IMEx Consortium. At the top, the URL www.imexconsortium.org/home is visible in the browser's address bar. The main header features the IMEx logo and the text "The International Molecular Exchange Consortium". Below the header is a navigation bar with links: Home, Admin, About IMEx, Curation Rules, Submit your data, Training, Licence, Disclaimer, and Contact us. The main content area is divided into several sections. On the left, under the "Home" heading, there is a large, colorful, circular network diagram with the IMEx logo in the center. To the right of this diagram is a search box with the text "Search the IMEx data resource" and a "Search" button. Below the search box, it says "Use as input:" followed by a bulleted list: "Uniprot KB Accs", "Gene names", and "Publication Ids". Further down, the "IMEx data" section lists four bullet points: "A non-redundant set of protein-protein interaction data from a broad taxonomic range of organisms", "Expertly curated from direct submissions or peer-reviewed journals to a consistent high standard.", "Available in standard formats MITAB or PSI-MI XML 2.5", and "Provided by a network of participating major public domain databases." Below this is the "Funding" section, which states: "IMEx is funded by the European Commission under PSIMEx, contract number FP7-HEALTH-2007-223411". On the right side of the page, there is a section titled "IMEx Partners" which displays a grid of logos for various partner databases: DIP, IntAct, MINT, MPact, MatrixDB, J. Craig Venter Institute (MPIDB), BioGRID, and InnateDB. At the bottom of this grid is the logo for Molecular Connections.

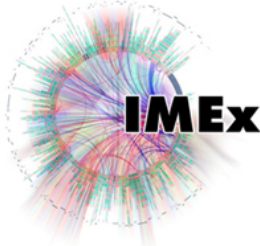
www.imexconsortium.org/home

IMEx The International Molecular Exchange Consortium

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Home



Search the IMEx data resource

Search

Use as input:

- Uniprot KB Accs
- Gene names
- Publication Ids

IMEx data

- A non-redundant set of protein-protein interaction data from a broad taxonomic range of organisms
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Funding

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IMEx Partners

- DIP
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- J. Craig Venter Institute (MPIDB)
- BioGRID
- InnateDB
- Molecular Connections

https://www.ebi.ac.uk/intact/

COVID19-related interactions at IntAct's Coronavirus dataset.

More info: [Dataset description](#)

Browse: [Coronavirus dataset](#)

Download: FTP Coronavirus dataset in [PSI-MI 2.5](#) [PSI-MI 3.0](#)

IntAct Molecular Interaction Database

IntAct provides a freely available, open source database system and analysis tools for molecular interaction data. All interactions are derived from literature curation or direct user submissions and are freely available. The IntAct Team also produce the [Complex Portal](#).

Search in IntAct

Enter search term(s)...

Search

 Search Tips


Examples

- Gene, Protein, RNA or Chemical name: [BRCA2](#), [Staurosporine](#)
- UniProtKB or ChEBI AC: [Q06609](#), [CHEBI:15996](#)
- UniProtKB ID: [LCK_HUMAN](#)
- RNAcentral ID: [URS00004A7003_9606](#)
- PMID: [25416956](#)
- IMEx ID: [IM-23318](#)

Featured Dataset

Interactome Mapping Provides a Network of Neurodegenerative Disease Proteins and Uncovers Widespread Protein Aggregation in Affected Brains..

- Haenig C. et al.  [PSI-MI 2.5](#) [PSI-MI TAB](#)
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