

Computational & Systems Biology *Biological Networks*

Yazdan Asgari
2019

Previous Session

- Systems
 - Thermodynamics (open, closed, isolated, adiabatic)
 - Mathematics (linear, non-linear)
 - Mechanics (static, dynamic)
 - Physics (stable, unstable)
 - Statistics (discrete, continuous)
 - Interdisciplinary (deterministic, probabilistic)
 - Complex theory (simple, complex)
- Systems Biology
 - Molecular Biology vs. Systems Biology
- Working with Cytoscape

How to Describe a System As a Whole?

Networks

The Language of Complex Systems

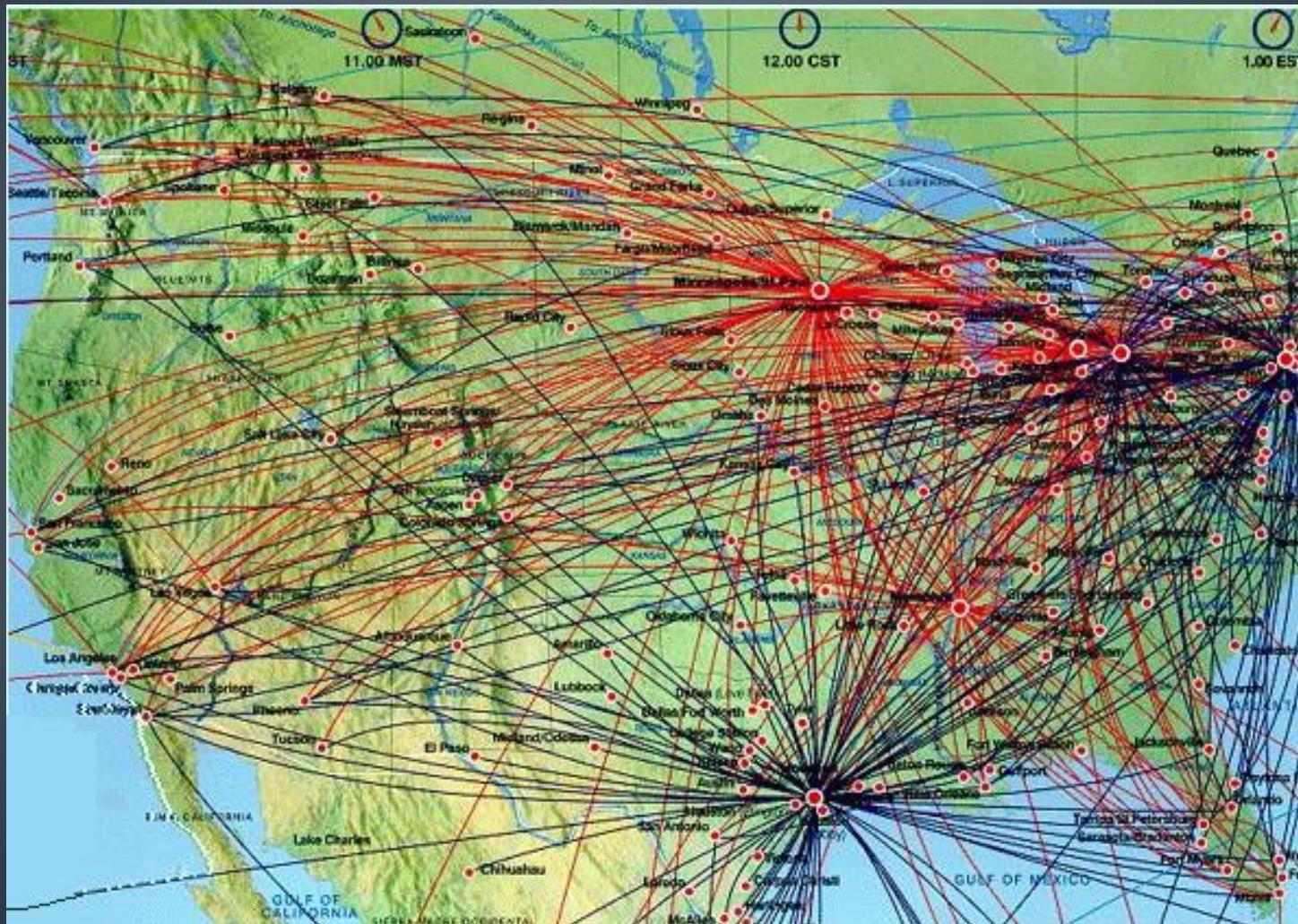
What is a Network?

□ Network is a mathematical structure composed of Points connected by Lines

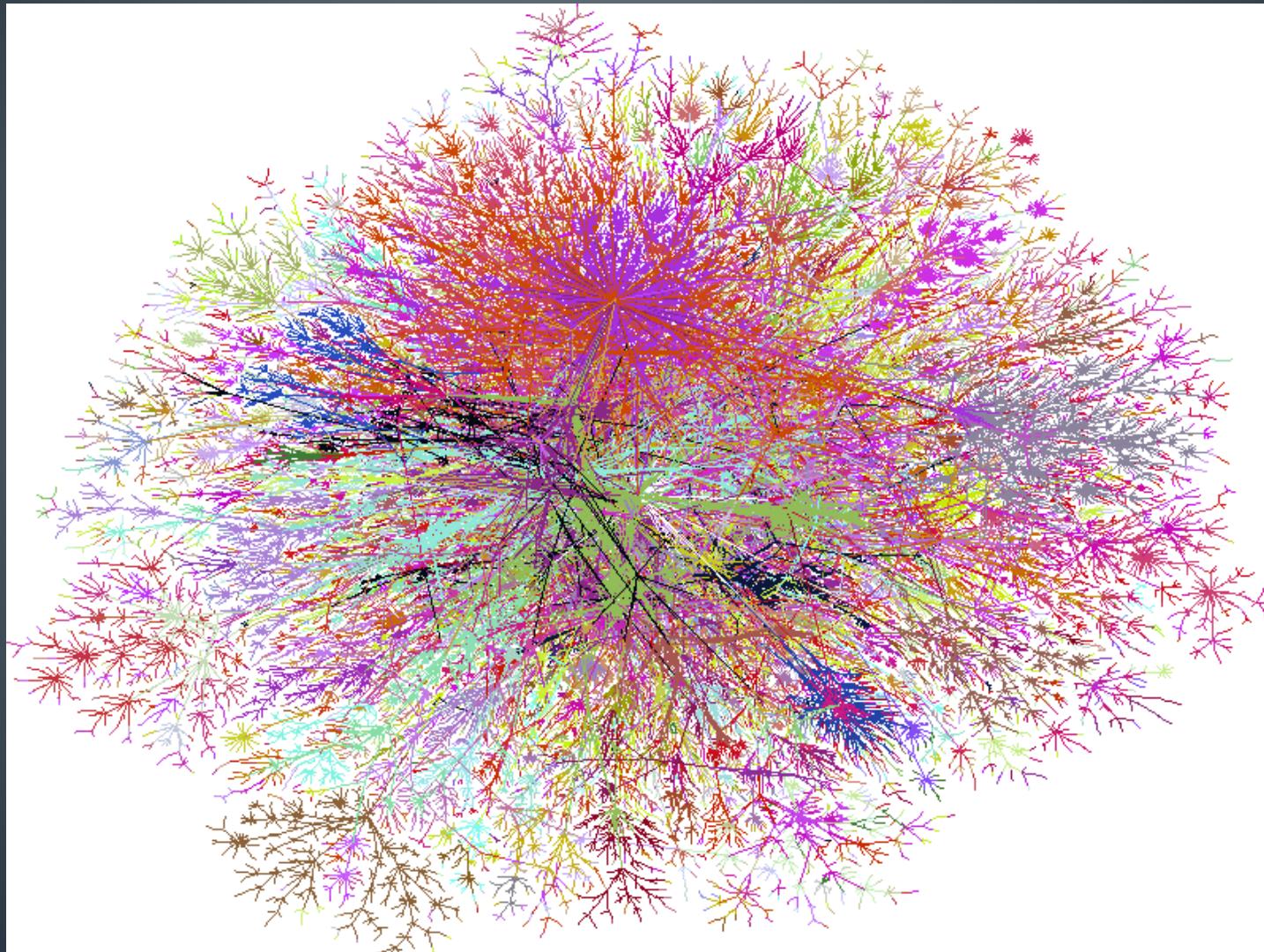
- Network \leftrightarrow Graph
- Points \leftrightarrow Nodes (Vertices)
- Lines \leftrightarrow Links (Edges)

- System vs. Parts = Networks vs. Nodes

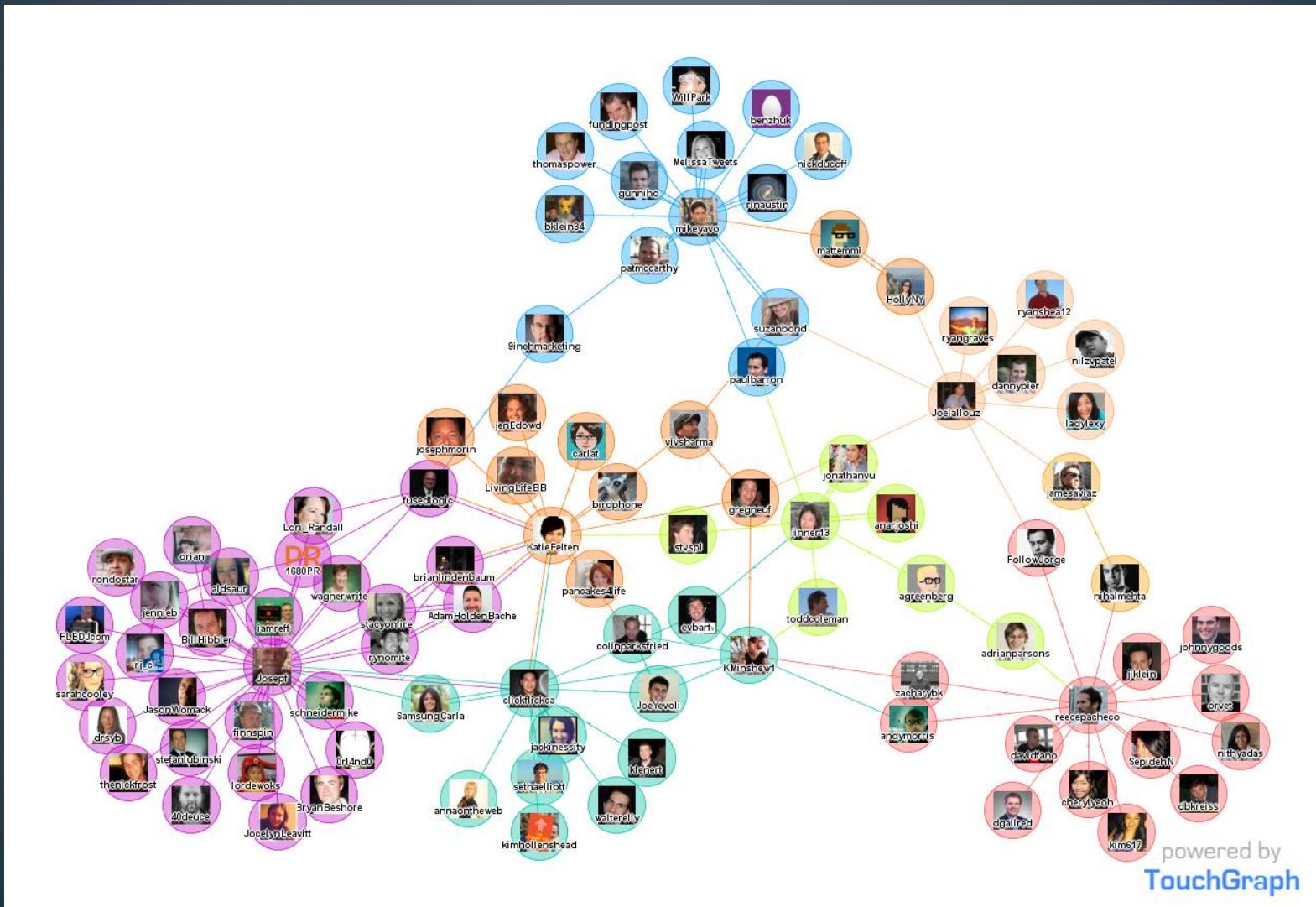
Air Transportation Network



The World Wide Web



Social Network

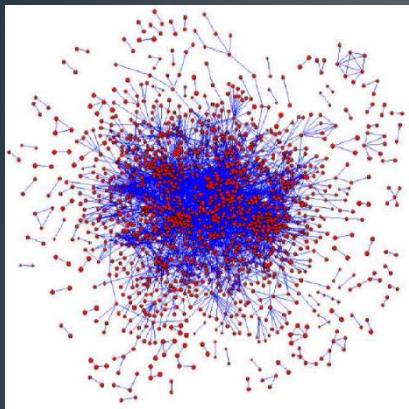


Biological Networks

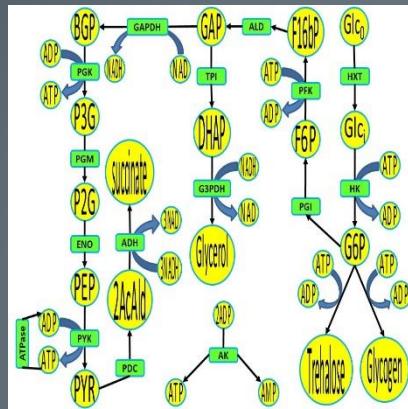
- Protein-Protein Interactions (PPIs) Networks
- Metabolic Networks
- Gene Regulatory Networks (GRNs)
- Signaling Networks
- And every other interaction networks
 - mRNA-miRNA network
 - Co-expression networks
 - Disease networks
 - Neural networks
 - Ecological networks
 - Evolutional network
 - ...

Biological Networks

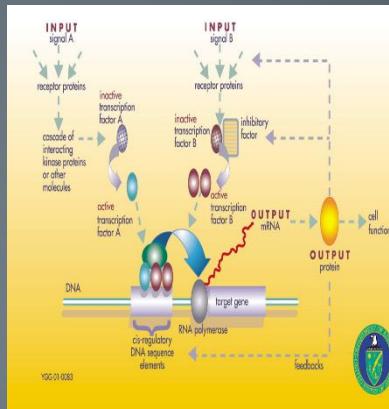
PPI Network



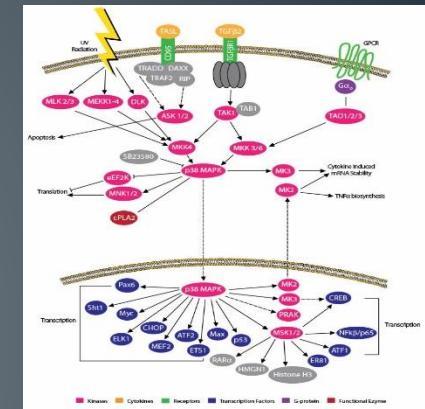
Metabolic Network



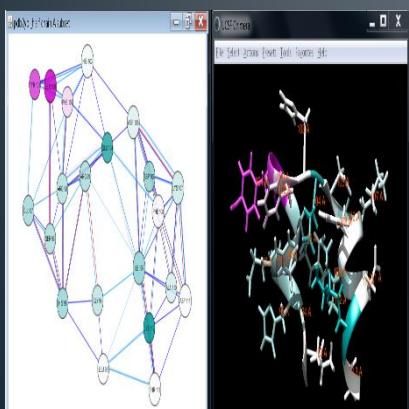
GRN Network



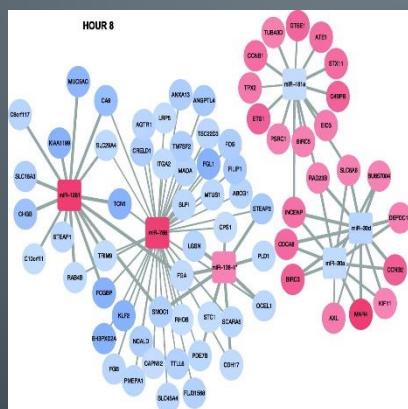
Signaling Network



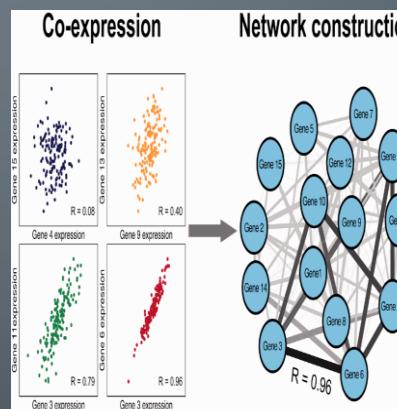
Residue Interactions



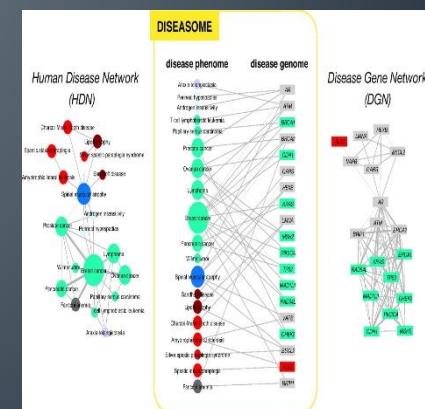
mRNA-miRNA



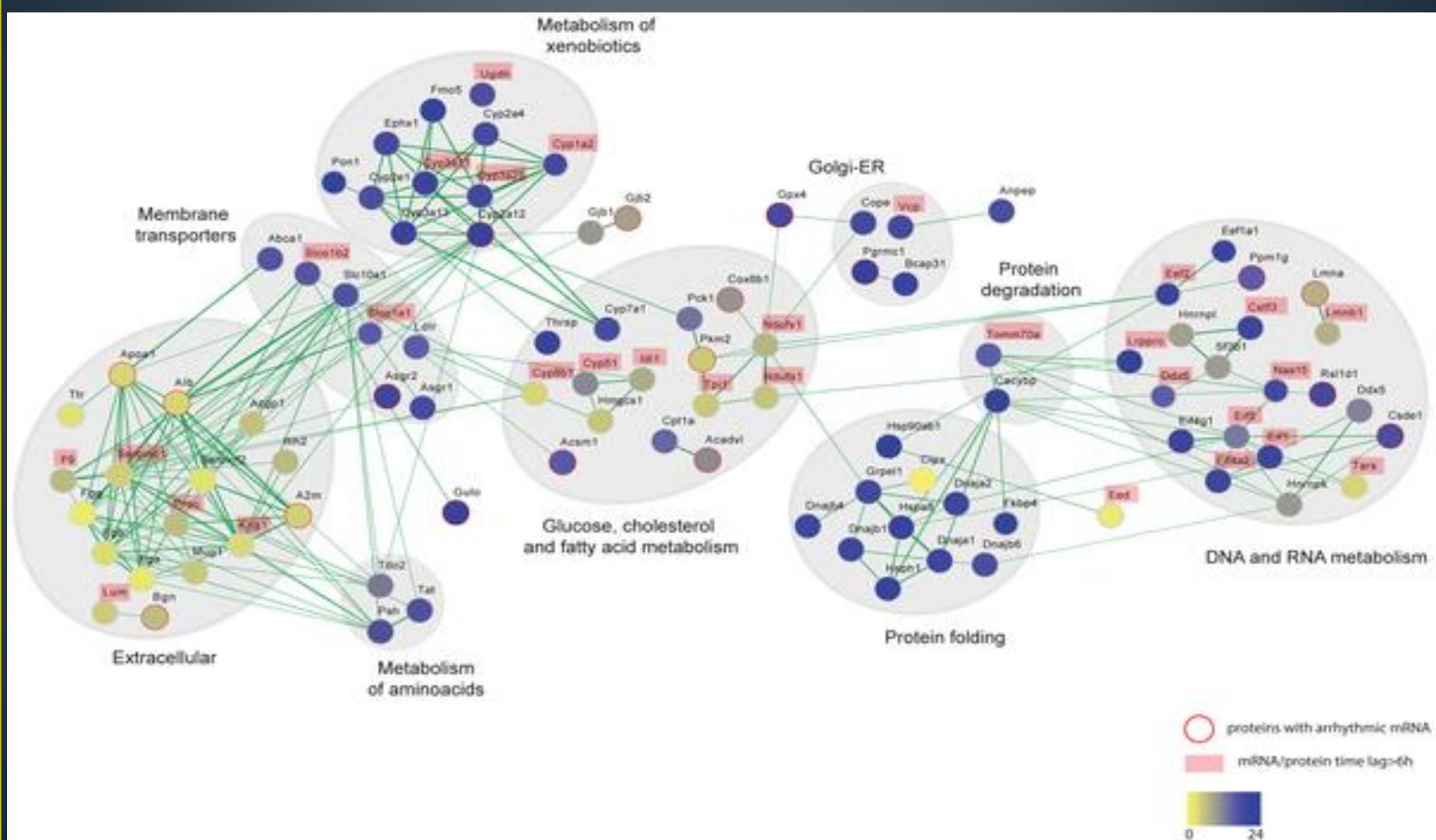
Co-expression



Disease networks



Protein-Protein Interactions Networks



Protein-Protein Interactions Networks

- There are thousands of different active proteins in a cell acting as:
 - Enzymes, catalysts to chemical reactions of the metabolism
 - Components of cellular machinery (e.g. ribosomes)
 - Regulators of gene expression
 - Certain proteins play specific roles in special cellular compartments
 - Others move from one compartment to another as “signals”
- Some proteins perform a function as a complex rather as a single protein
- Knowing whether two proteins interact could help us discover unknown proteins’ functions:
 - If the function of one protein is known, the function of its binding partners are likely to be related- “guilt by association”.

Protein-Protein Interactions Networks

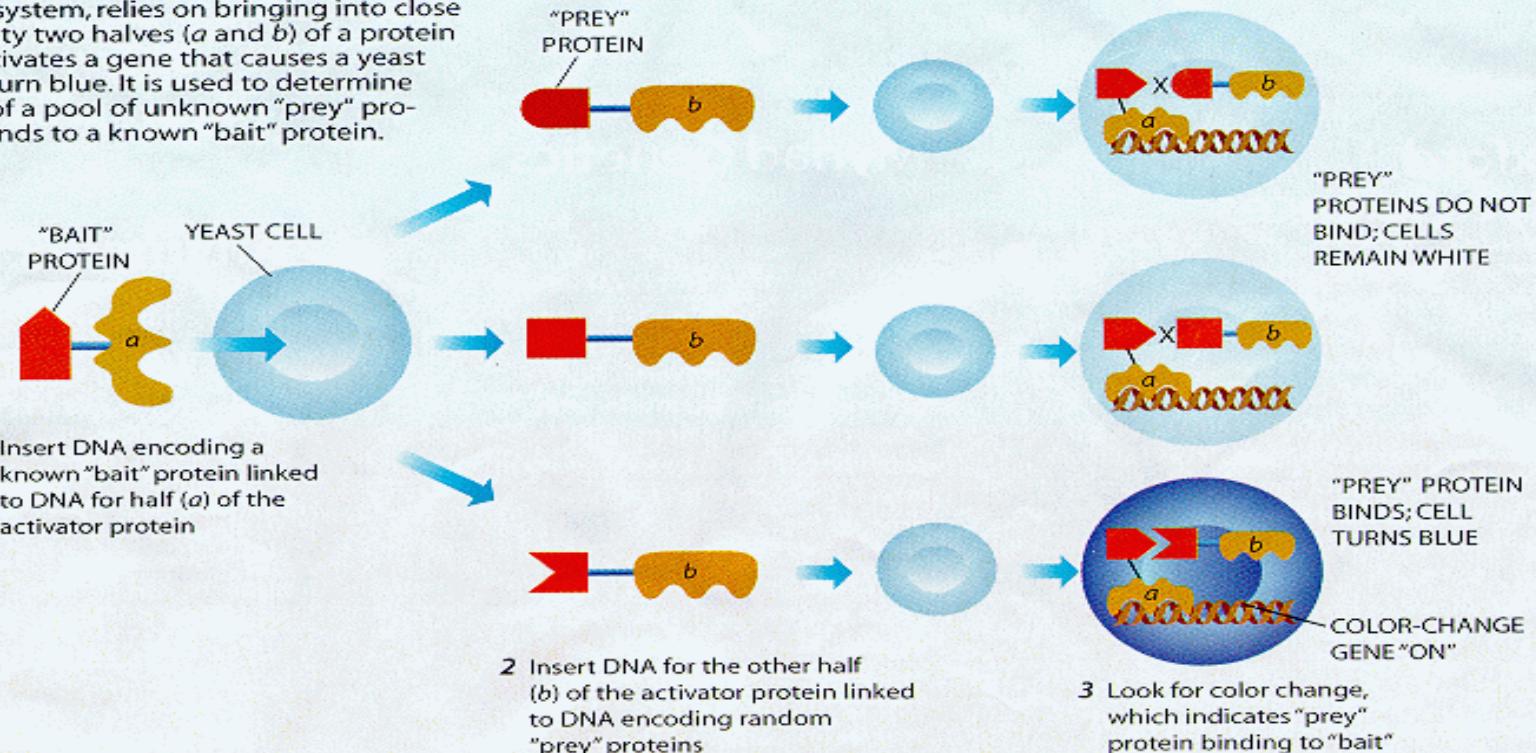
- Thus, having a good method for detecting interactions could allow us to:
 - use some proteins with **known function** to characterize other **unknown proteins** (relate network structure to **biological function**).
 - find protein's relative **position** in a network.
 - develop new, effective **protein-targeting drugs**.
- So we are looking for Proteins that are connected in physical interactions or metabolic and signaling pathways of the cell.

How do we can generate a PPIs network?

Experimental methods such as Yeast-2-Hybrid

Finding Proteins That Interact

One technique, called the yeast two-hybrid system, relies on bringing into close proximity two halves (*a* and *b*) of a protein that activates a gene that causes a yeast cell to turn blue. It is used to determine which of a pool of unknown "prey" proteins binds to a known "bait" protein.

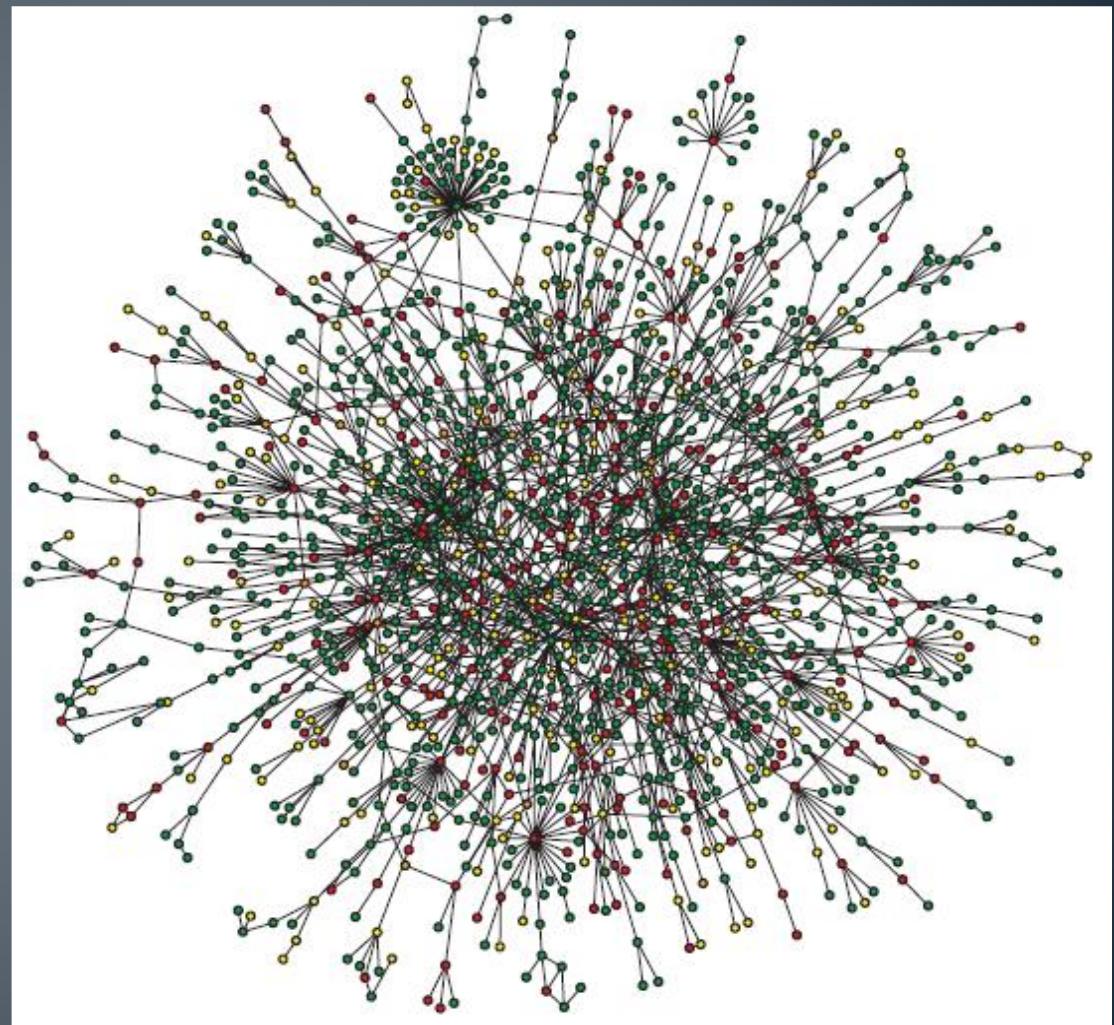


How do we can generate a PPIs network?

- High-throughput data
 - Two-hybrid systems
 - Mass Spectrometry
 - Microarrays
- **Genomic data**
 - Phylogenetic profile
 - Rosetta Stone method
 - Gene neighboring
 - Gene clustering
- ...

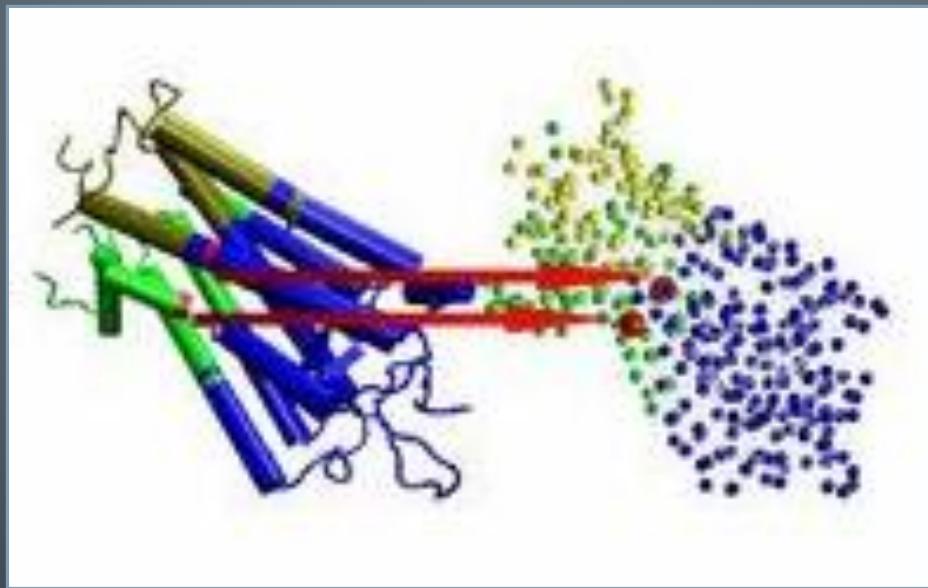
Example: Yeast PPIs Network

- node = protein
- edge = physical interaction
- red = lethal
- green = non-lethal
- yellow = unknown



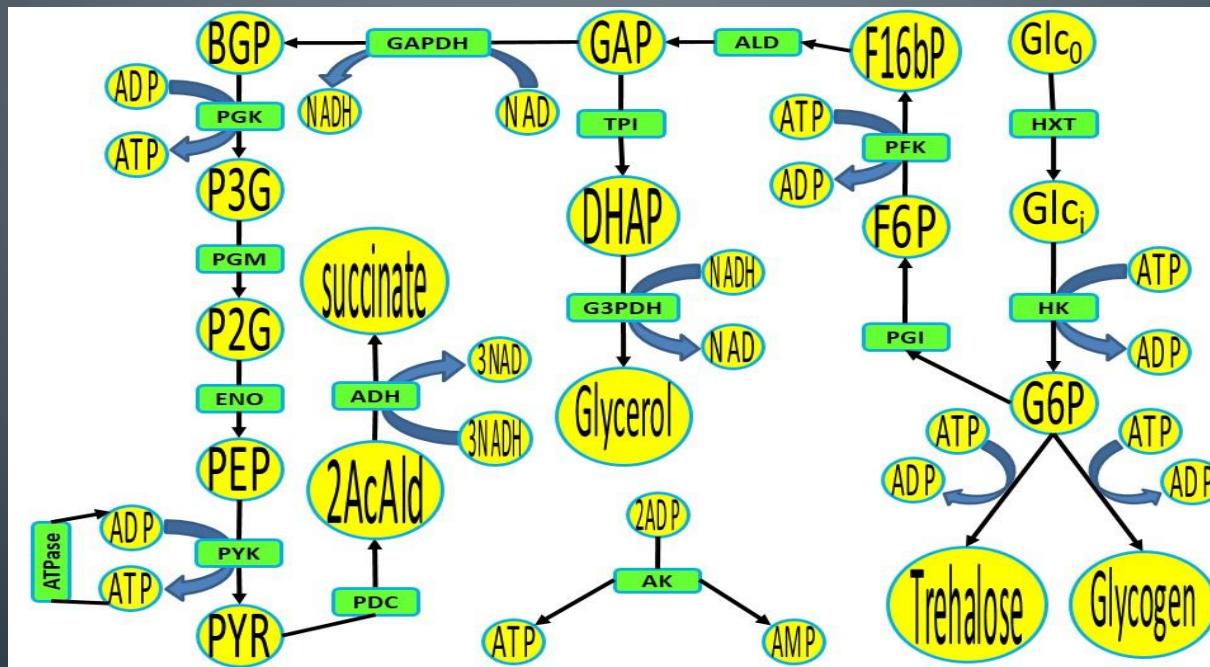
Residue Interactions networks

- To analyze protein stability and folding, allosteric communication, enzyme catalysis, or mutation effect prediction..

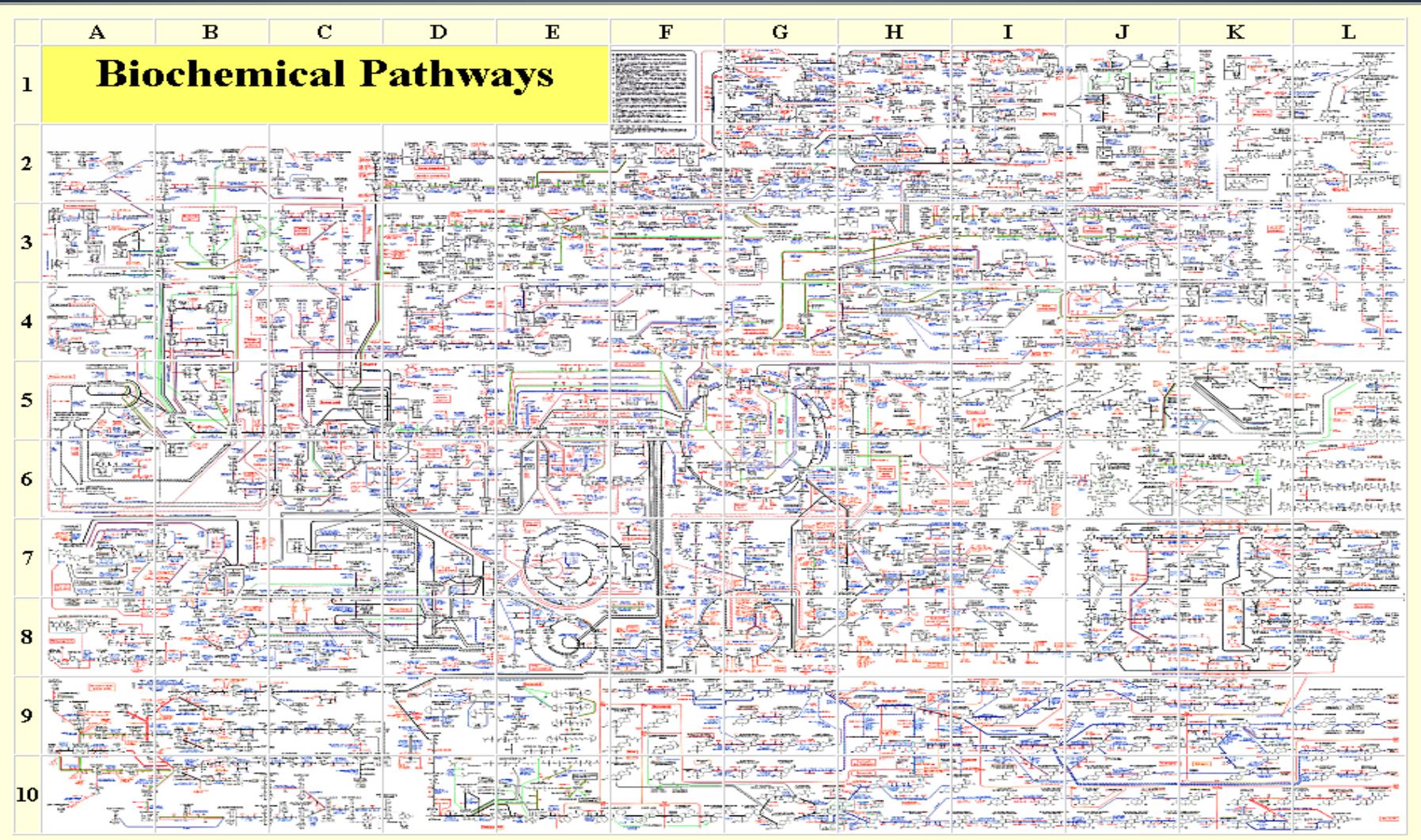


Metabolic Networks

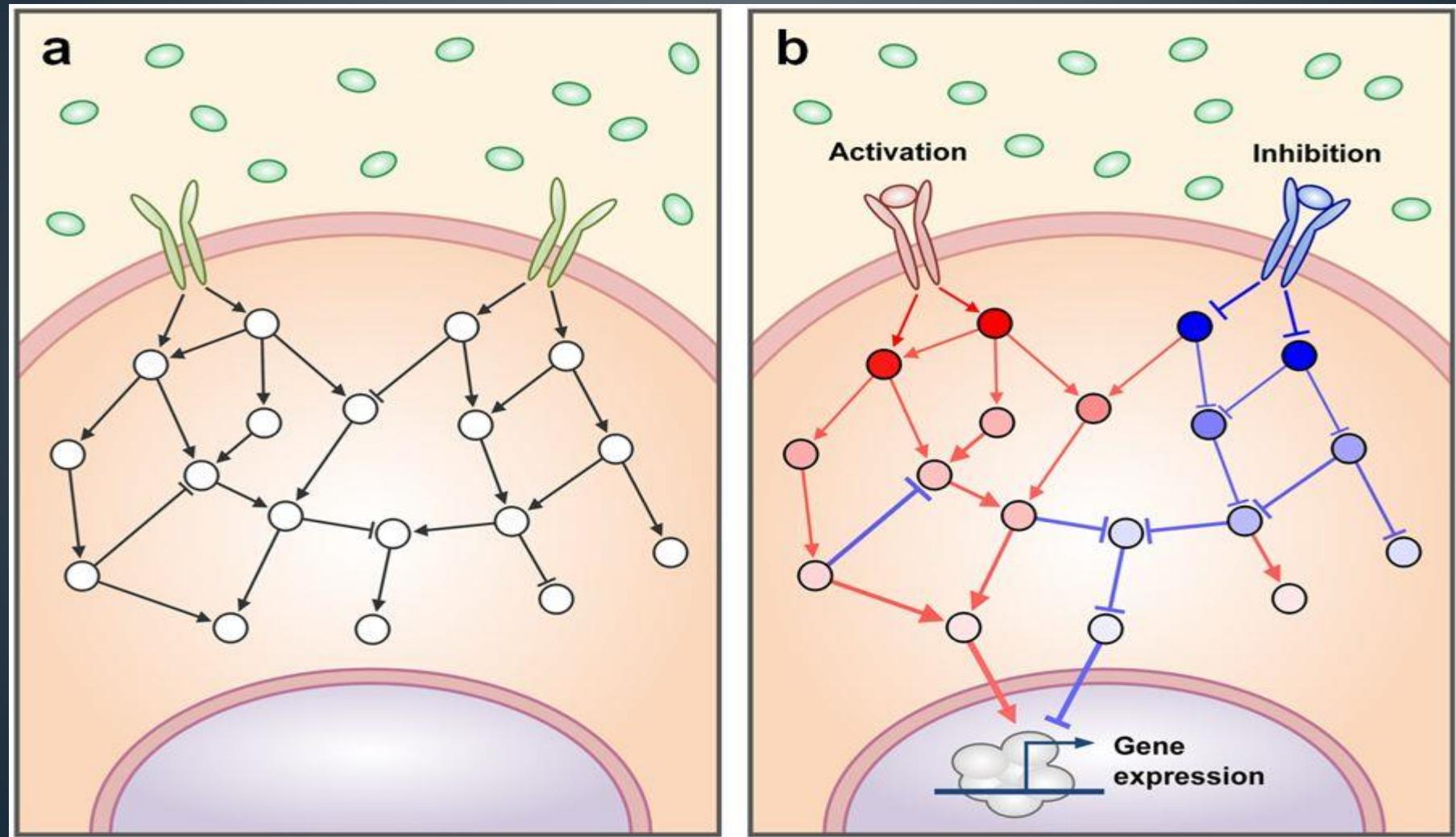
- A series of chemical reactions occurring within a cell, catalyzed by enzymes, resulting in either the formation of a metabolic product to be used or stored by the cell, or the initiation of another metabolic pathway



Metabolic Networks



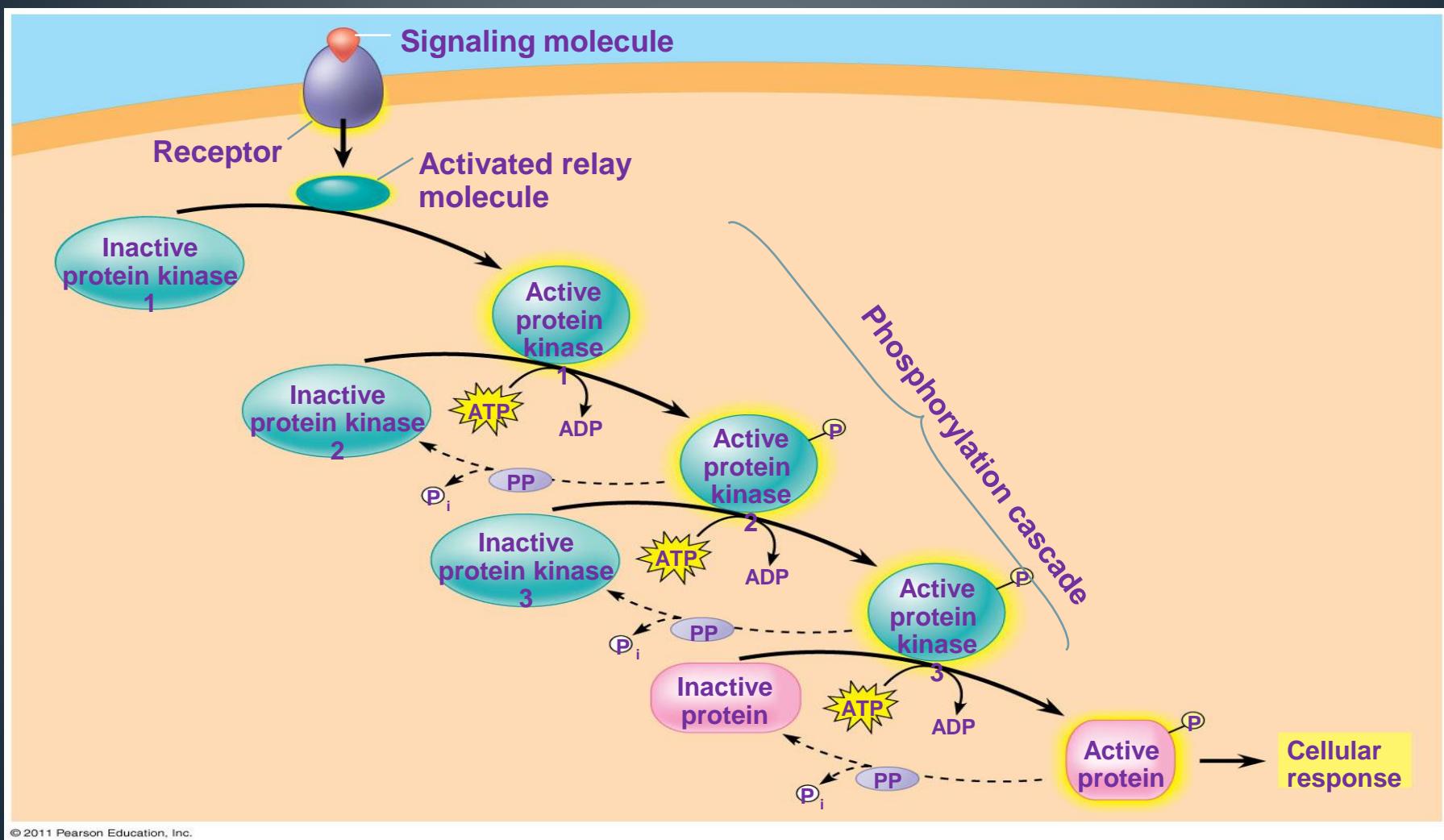
Signaling Networks



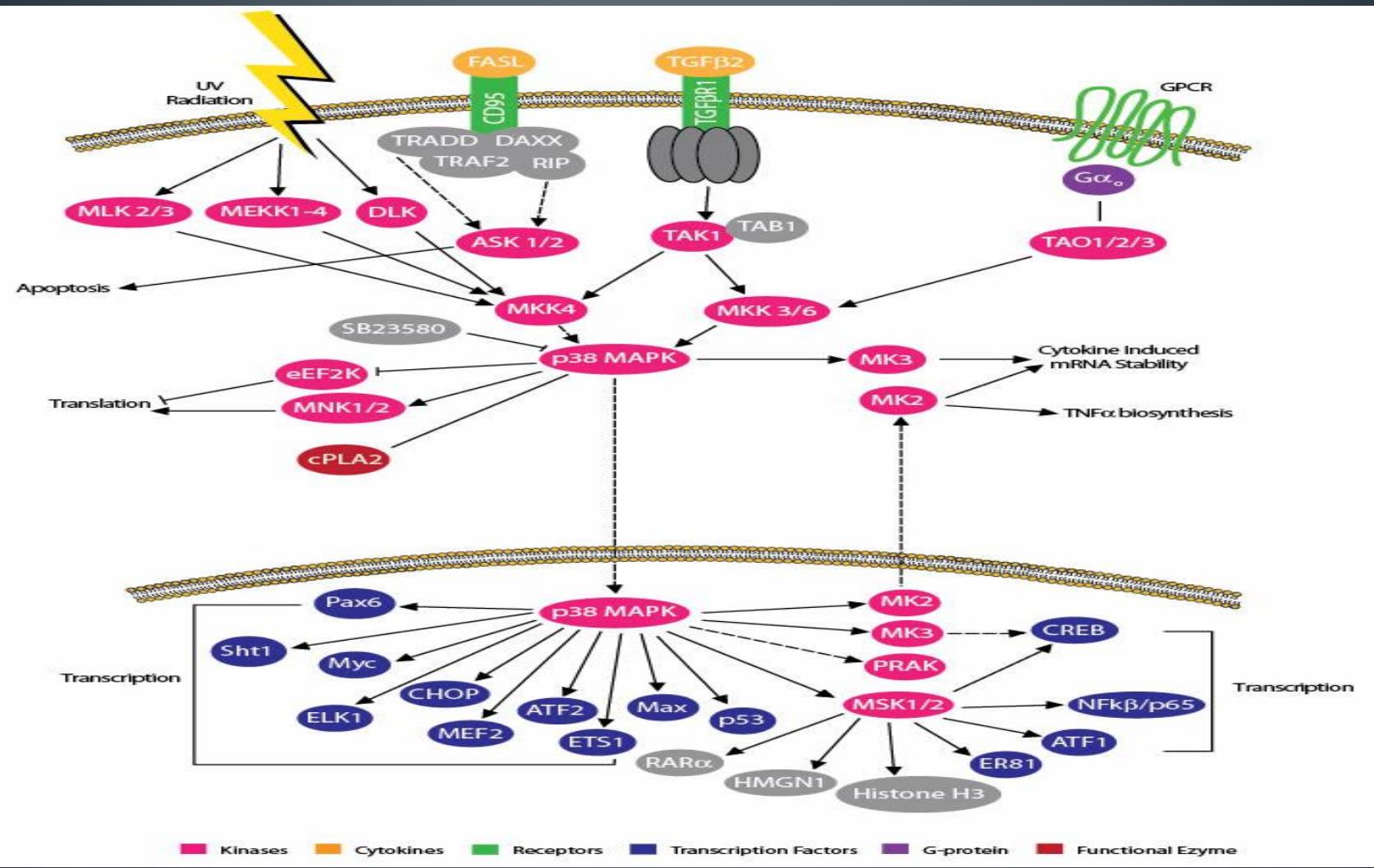
Signaling Networks

- In biology, a signal or biopotential is an electric quantity (voltage, current, or field strength), caused by chemical reactions of charged ions.
- Refers to any process by which a cell converts one kind of signal or stimulus into another.
- Another use of the term lies in describing the transfer of information between and within cells, as in signal transduction.

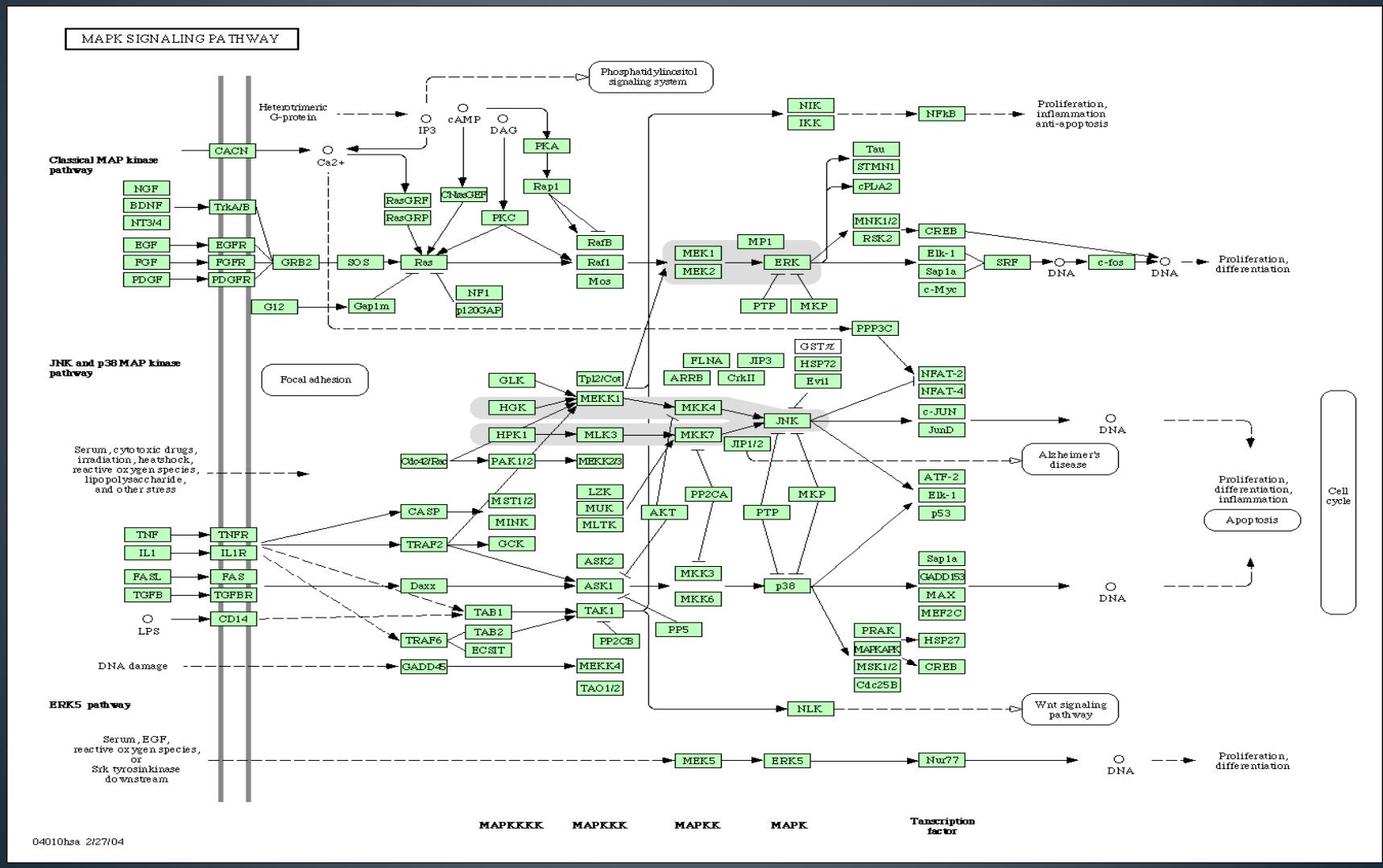
Signaling Networks



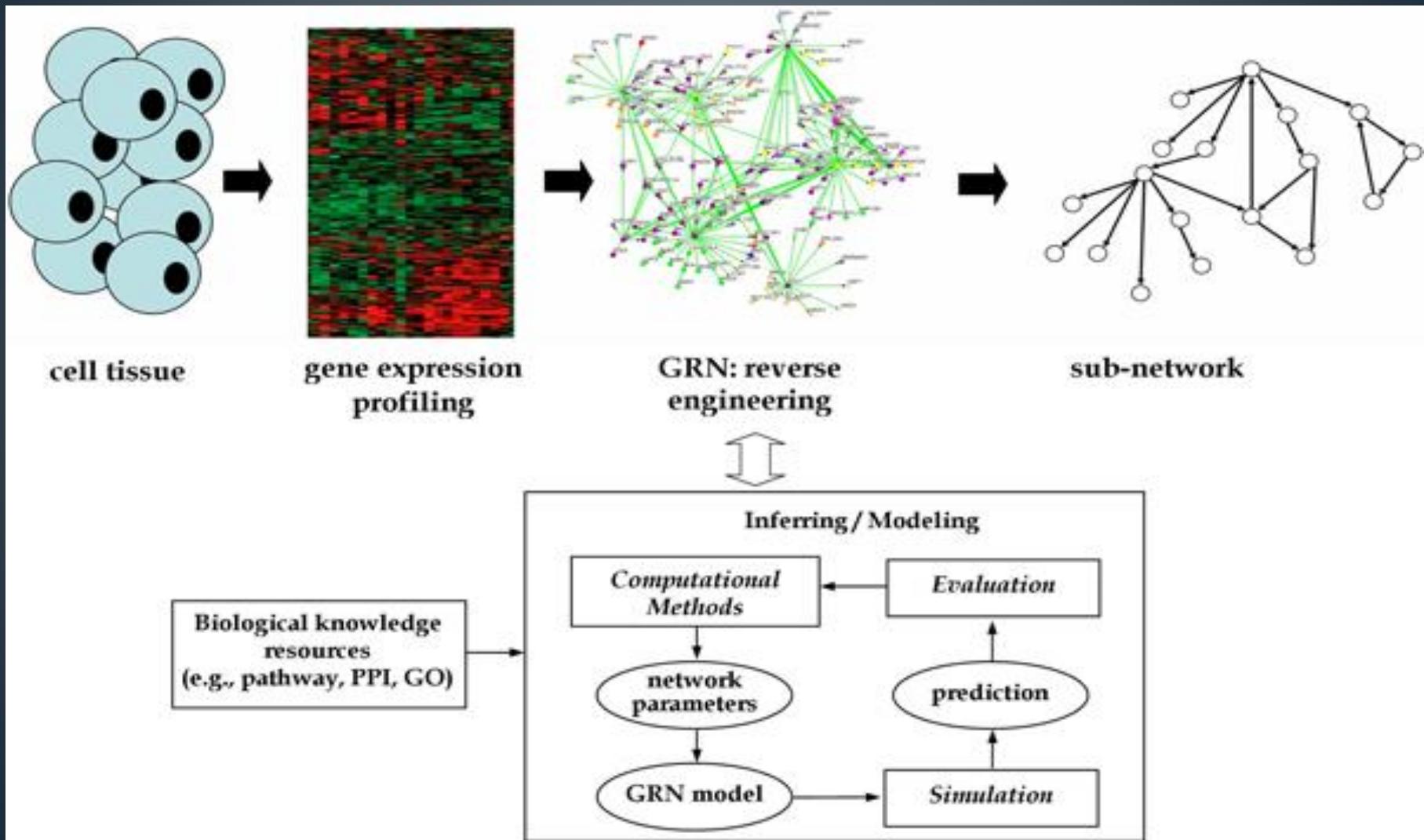
Signaling Networks



Signaling Networks



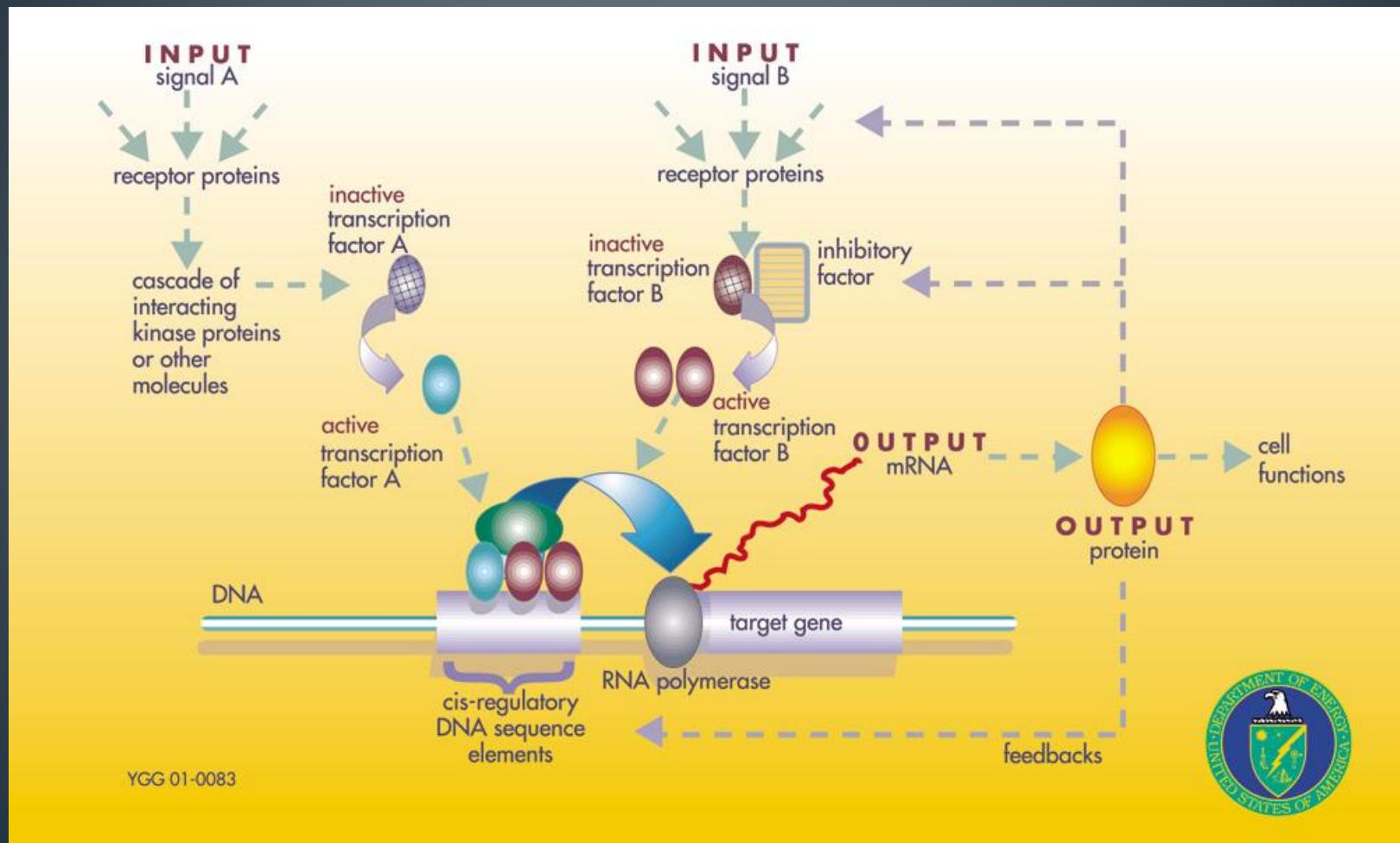
Gene Regulatory Networks



Gene Regulatory Networks

- Two genes are connected if the expression of one gene modulates expression of another one by either activation or inhibition.
- Gene regulatory networks (GRNs) are the on-off switches of a cell operating at the gene level.

Gene Regulatory Networks



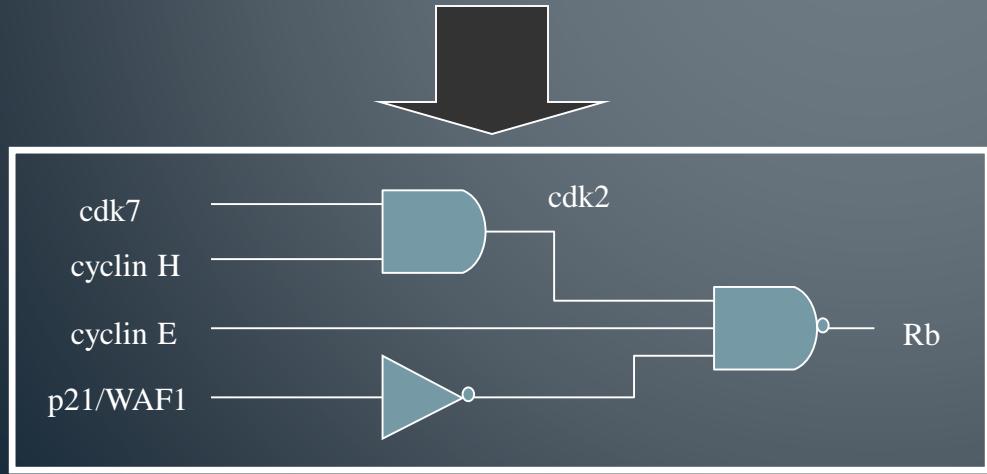
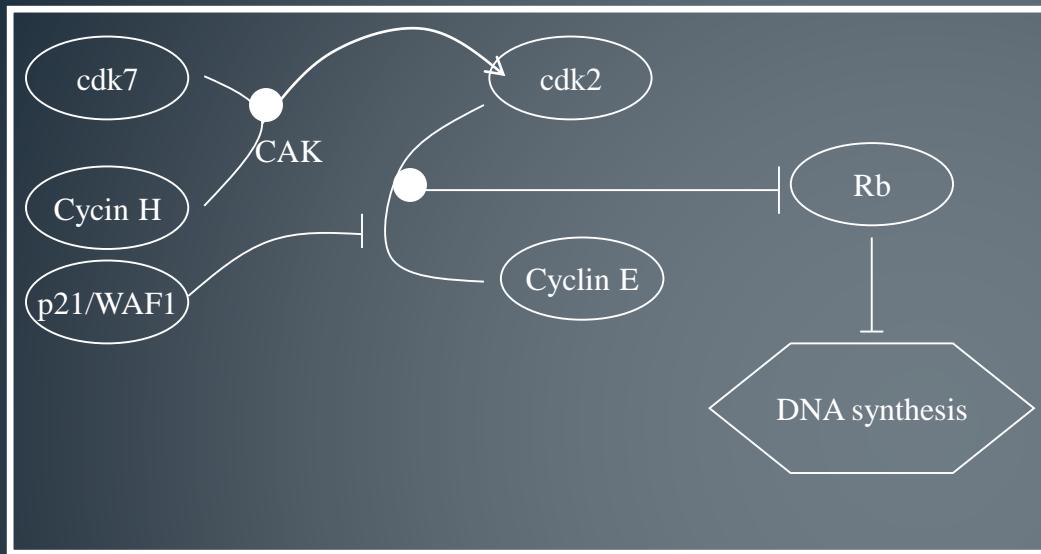
Gene Regulatory Networks

- A gene regulatory network can be represented by a directed graph
- Node represents a gene
- Directed edge stands for the modulation (regulation) of one node by another
- e.g. arrow from gene X to gene Y means gene X affects expression of gene Y

Modeling of Gene Regulatory Networks

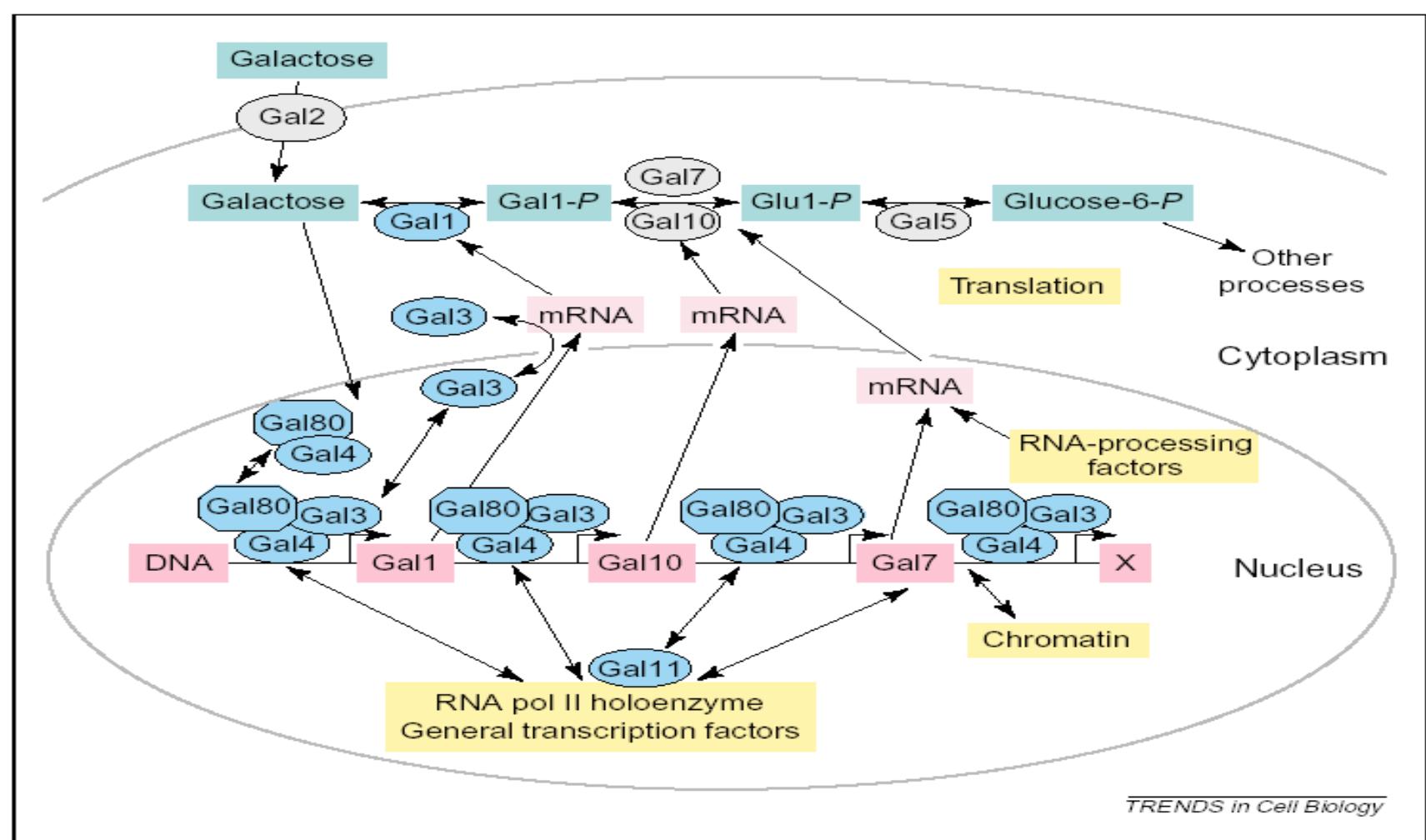
- Linear Model
- Bayesian Networks
- Differential Equations
- Boolean Network
 - Originally introduced by Kauffman (1969)
 - Gene expression is quantized to only two level
 - (1 / On and 0 / OFF)

Boolean Network



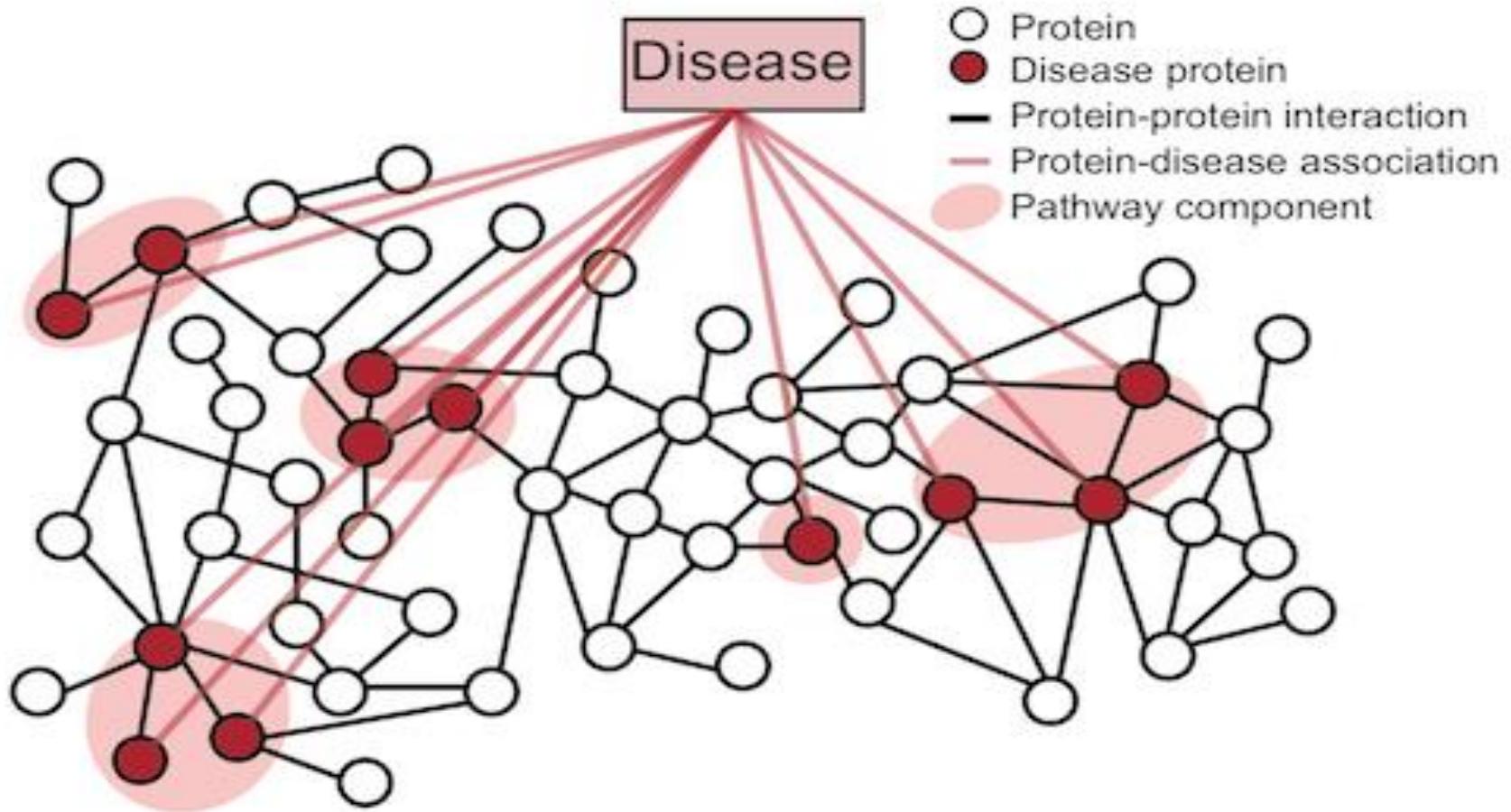
- Cyclin E and cdk2 work together to phosphorylate the Rb protein and inactivate it
- Cdk2/Cyclin E is regulated by two switches:
 - Positive switch complex (CAK)
 - Negative switch P21/WAF1
- CAK complex can be composed of two gene products:
 - Cyclin H
 - Cdk7
- When cyclin H and cdk7 are present, the complex can activate cdk2/cyclin E.

Gene Regulatory Networks

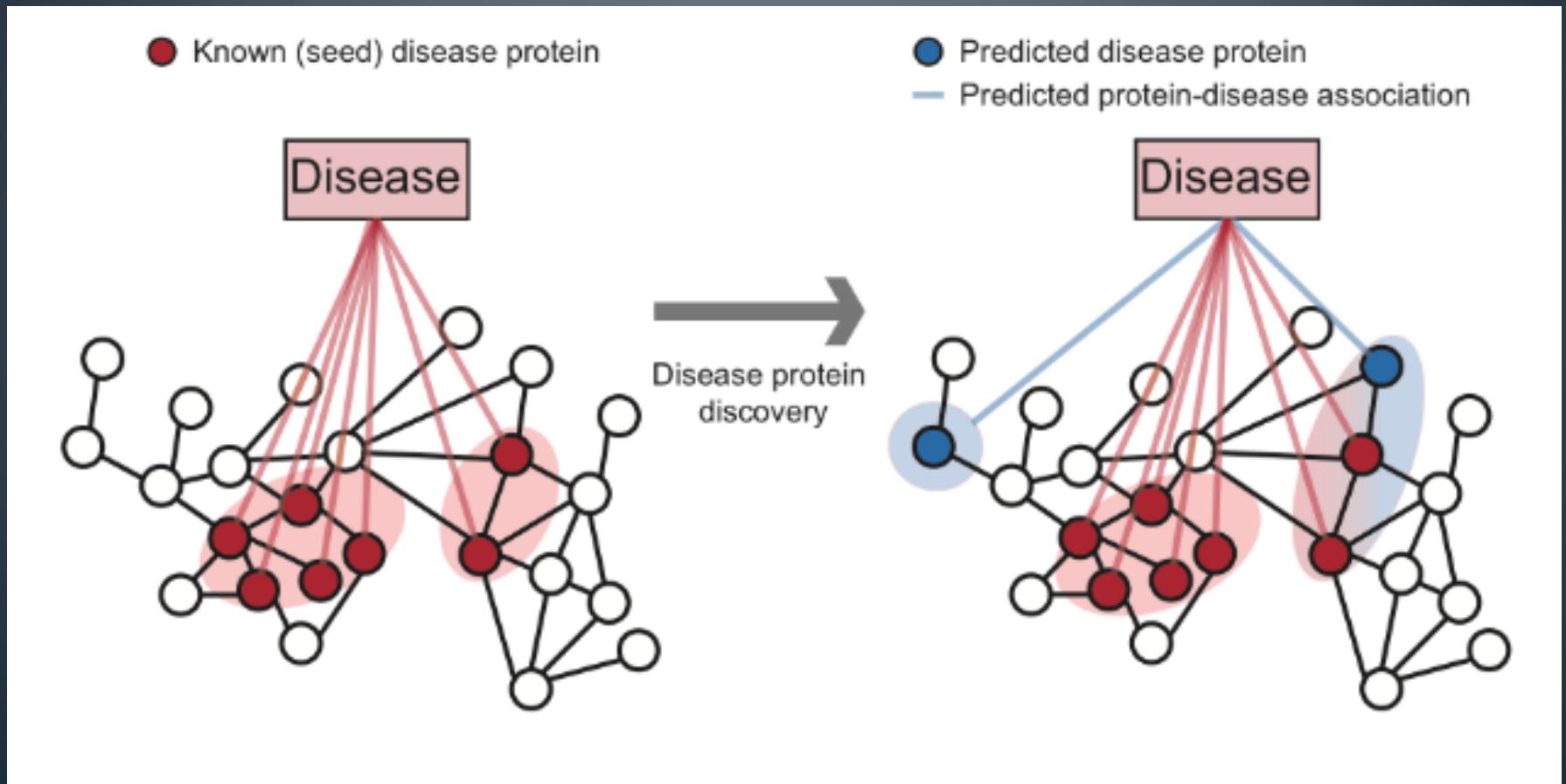


Why Interactions are important?

Why Interactions are important?

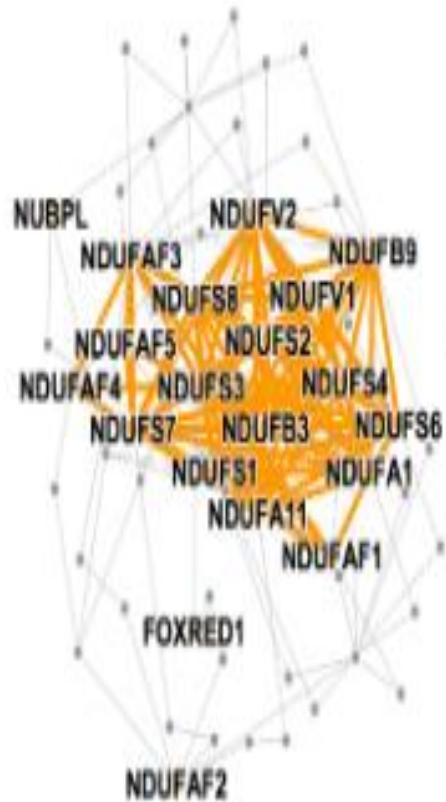


Why Interactions are important?

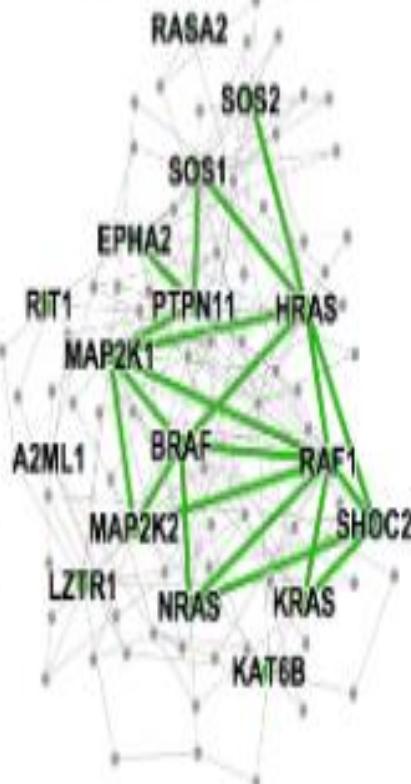


Why Interactions are important?

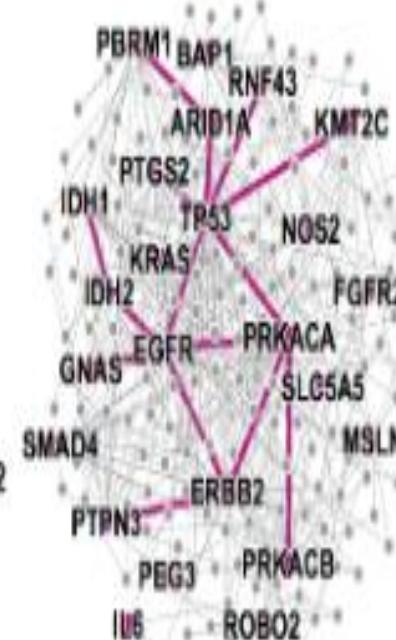
Mitochondrial complex deficiency



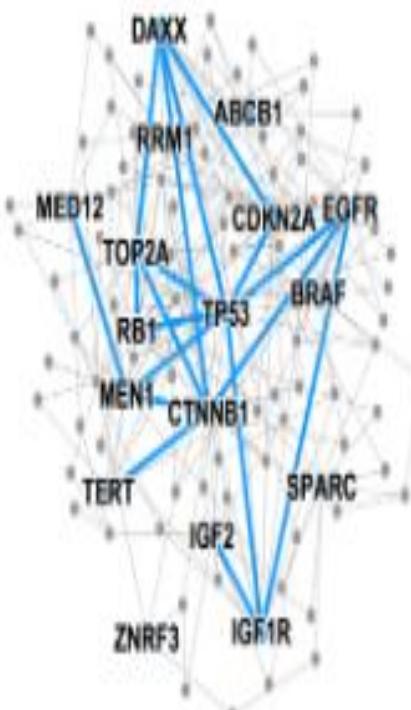
Noonan syndrome



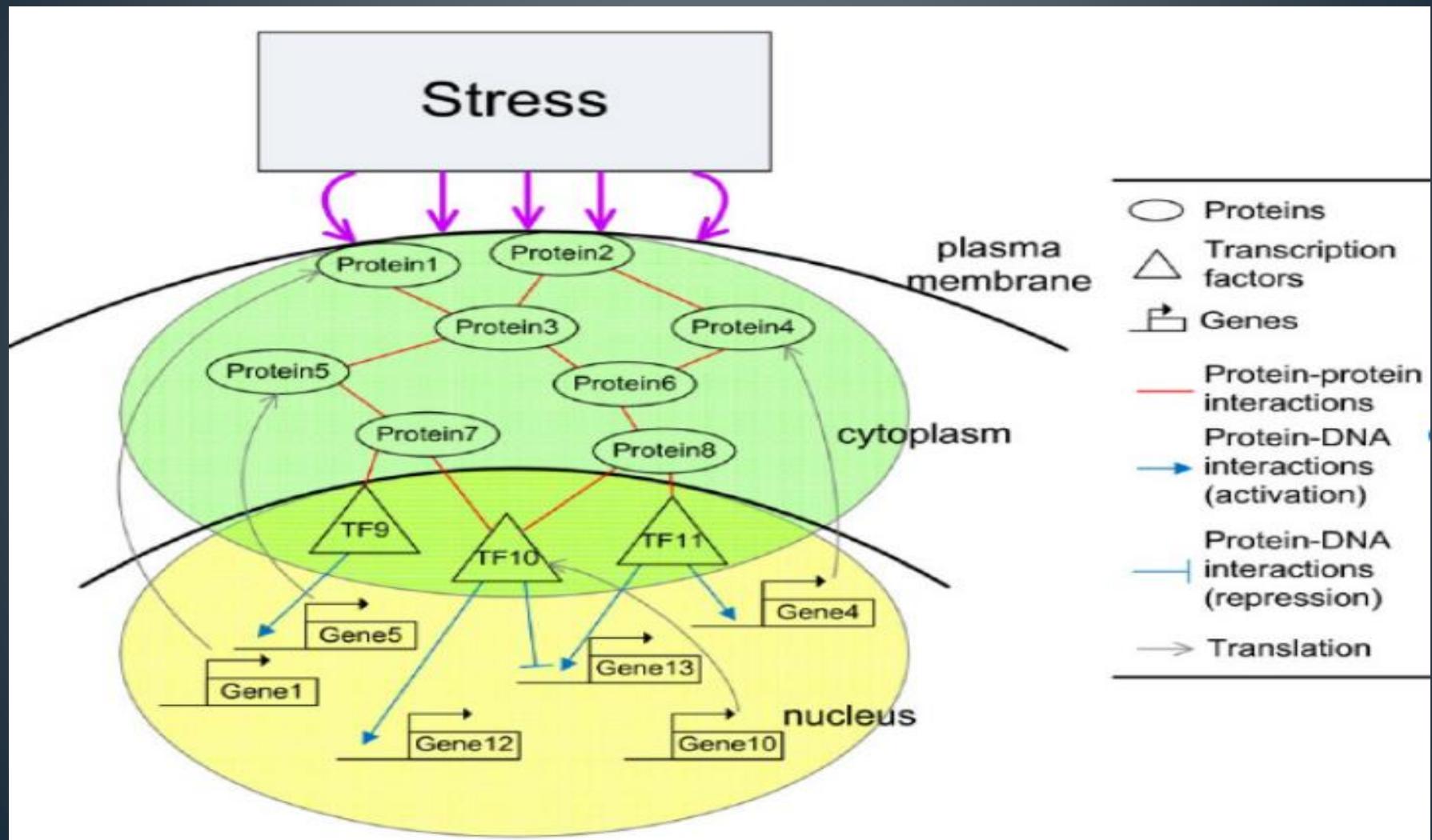
Cholangiocarcinoma



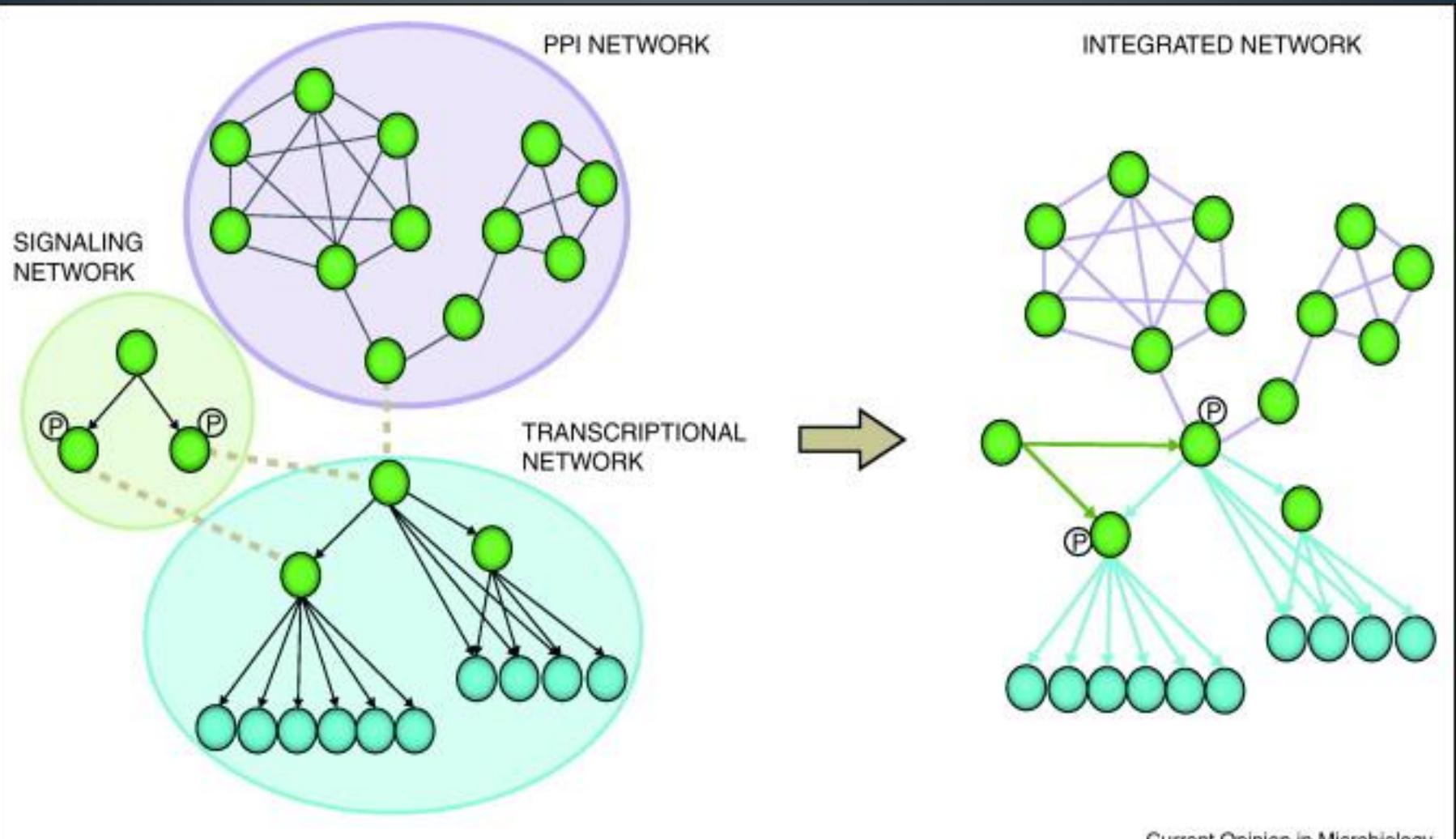
Adrenal cortex carcinoma



Integrated Network

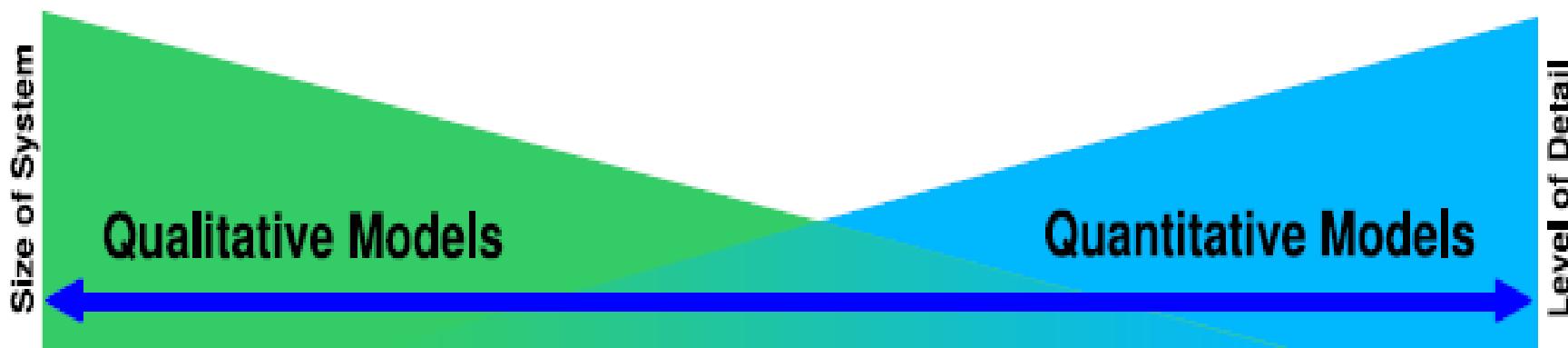


Integrated Network



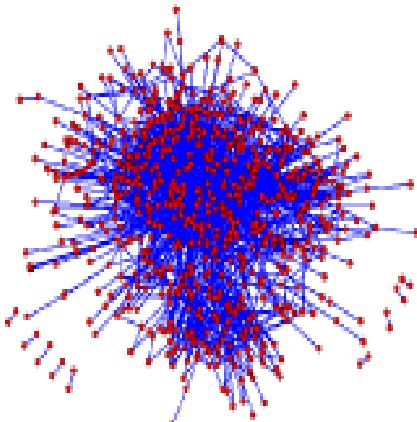
Current Opinion in Microbiology

Modeling Scale



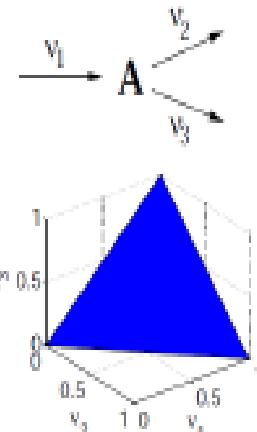
Topological Analysis

- Static description
- No kinetic parameters
- Topological properties



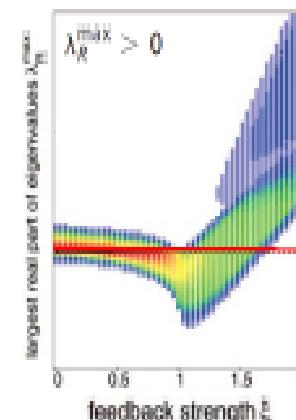
Flux Balance Analysis

- Static description
- No kinetic parameters
- Quantitative predictions



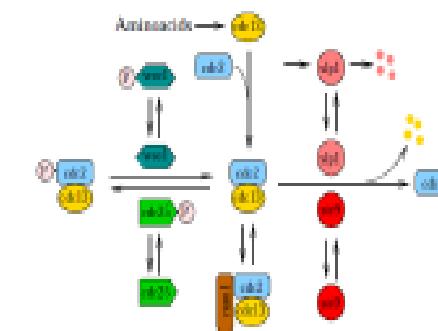
Structural Kinetic Models

- Dynamic description
- No kinetic parameters
- Bifurcation structure



Kinetic Models

- Dynamic description
- Kinetic parameters
- Differential equations



Databases for Network Creation

BioGRID

❖ The Biological General Repository for Interaction Datasets is a curated biological database of protein-protein interactions, genetic interactions, chemical interactions, and post-translational modifications.

The screenshot shows the BioGRID 3.5 homepage with a dark red header and footer. The header includes a navigation bar with links: home, help wiki, tools, contribute, stats, downloads, partners, about us, and a Twitter icon. The main content area features a search bar with placeholder text "Search by identifiers, keywords, and gene names...". Below the search bar is a dropdown menu set to "All Organisms" and a "SUBMIT GENE SEARCH" button. To the right are two vertical buttons: "By Gene" and "By Publication". At the bottom left are two buttons: "INTERACTION STATISTICS" and "LATEST DOWNLOADS". The footer contains the URL <https://thebiogrid.org/>.

Welcome to the Biological General Repository for Interaction Datasets

BioGRID is an interaction repository with data compiled through comprehensive curation efforts. Our current index is version **3.5.169** and searches **68,514** publications for **1,664,026** protein and genetic interactions, **28,093** chemical associations and **726,378** post translational modifications from major model organism species. All data are **freely** provided via our search index and available for download in standardized formats.

INTERACTION STATISTICS LATEST DOWNLOADS

IntAct

- ❖ 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 screenshot shows the IntAct homepage with a dark blue header and a teal navigation bar. The header features the EMBL-EBI logo and the IntAct logo. The navigation bar includes links for Services, Research, Training, About us, Home, Advanced Search, About, Resources, Download, and Feedback. The main content area has a white background. It features a search bar with placeholder text "Enter search term(s)...", a "Search" button, and a "Search Tips" link. To the right, there's a "Examples" section with a list of IDs and names, and a "Featured Dataset" section about protein interaction perturbation profiling. At the bottom, there are links for newsletter sign-up and social media (Twitter) feeds.

EMBL-EBI

IntAct

Services | Research | Training | About us

Home | Advanced Search | About | Resources | Download | Feedback

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: [URS00004C95F4_559292](#)
- PMID: [25416956](#)
- IMEx ID: [IM-23318](#)

Featured Dataset

Protein interaction perturbation profiling at amino-acid resolution.

- Woodsmith et al. [IntAct](#) [PSI-MI 2.5](#)
PSI-MI TAB | Go to Archive

Sign up for our newsletter
[Sign up here](#)

News
Follow [@intact_project](#)
Tweets by [@intact_project](#)

STRING

- ❖ The STRING database contains information from numerous sources, including experimental data, computational prediction methods and public text collections. The resource also serves to highlight functional enrichments in user-provided lists of proteins, using a number of functional classification systems such as GO, Pfam and KEGG.

Version: 11.0 (preview -- version 10.5 still available [here](#))

LOGIN | REGISTER

Search Download Help My Data

Welcome to STRING

Protein-Protein Interaction Networks

ORGANISMS 5090 | PROTEINS 24.6 mio | INTERACTIONS >2000 mio

SEARCH

iRefIndex

- ❖ iRefIndex provides an index of protein interactions available in a number of primary interaction databases including BIND, BioGRID, CORUM, DIP, HPRD, InnateDB, IntAct, MatrixDB, MINT, MPact, MPIDB and MPPI.

The screenshot shows the homepage of iRefIndex. At the top left is a blue and white pixelated logo. Below it is a horizontal menu bar with four buttons: "Page", "Discussion", "View source", and "History". The main title "iRefIndex" is centered above a brief description of the service. A "Download" section is located at the bottom left, featuring a small icon of a computer with a download arrow and the word "Download" next to it. Below this, a link reads "Download version 15.0 of the iRefIndex in PSI-MITAB tab-delimited format."

iRefIndex provides an index of protein interactions available in a number of primary interaction databases including BIND, BioGRID, CORUM, DIP, HPRD, InnateDB, IntAct, MatrixDB, MINT, MPact, MPIDB and MPPI.

Download
Download version 15.0 of the iRefIndex in PSI-MITAB tab-delimited format.

IMEx

- ❖ A non-redundant set of physical molecular interaction data from a broad taxonomic range of organisms.

List of IMEx members

- [DIP \(Active\)](#)
- [HPIDB \(Active\)](#)
- [IntAct \(Active\)](#)
- [MBInfo \(Active\)](#)
- [MINT \(Active\)](#)
- [BioGRID \(Observer\)](#)
- [PrimesDB \(Observer\)](#)
- [MPact \(Inactive\)](#)
- [BIND \(Inactive\)](#)
- [MPIDB \(Inactive\)](#)



IMEx The International Molecular Exchange Consortium

Search the IMEx data resource

Use as input: UniProtKB Accs, Gene names, Publication Ids

[Home](#) [About](#) [Curation](#) [Submit Your Data](#) [Contact us](#)

IMEx data

- A non-redundant set of physical molecular 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](#).
- Provided by a network of participating major public domain databases.

InnateDB

- ❖ InnateDB is a publicly available database of the genes, proteins, experimentally-verified interactions and signaling pathways involved in the innate immune response of humans, mice and bovines to microbial infection.



The screenshot shows the InnateDB homepage. At the top, there's a navigation bar with links for About, Search, Data Analysis, InnateDB Annotation, Download, Other Resources, Statistics, Help, Version 5.4, and Participant login. Below the navigation bar is a large network graph titled "TLR signalling network". To the right of the graph, there's a section titled "Interactions" with a sub-section "Search and visualize experimentally-verified molecular interactions by gene/protein name, interaction type, cell type, etc.". A "Search" button is located below this text. Further down, there are tabs for Home, Genes and proteins, Interactions (which is highlighted), Pathway Analysis, Gene Ontology Analysis, Network analysis, Innate immune genes, and Statistics. A message at the bottom left says "A mirror of InnateDB.com hosted by the David Lynn Group in Australia is available at <http://innatedb.sahmri.com>". On the right side, there's a "News" section with a tweet from "Follow @innatedb" and a link to "Join our mailing list". It also mentions a "2019: Website outage December 17th to 21st. Data uploads restored. (more)" and a note about a scheduled outage on "Oct 22, 2018: Due to a scheduled outage at SFU, innatedb.com".

Reactome

- ❖ Reactome is an open access, manually curated and peer-reviewed pathway database. The core unit of the Reactome data model is the reaction. Entities (nucleic acids, proteins, complexes and small molecules) participating in reactions form a network of biological interactions and are grouped into pathways.

The screenshot shows the Reactome website homepage. At the top is a navigation bar with links for About, Content, Docs, Tools, Community, and Download. Below the navigation is a search bar with the placeholder "e.g. O95631, NTN1, signaling by EGFR, glucose" and a "Go!" button. The main content area features four large blue icons with white symbols: a stack of three cylinders for the Pathway Browser, a bar chart for Analyze Data, a share icon for ReactomeFIViz, and a document icon for Documentation. Each tool has a title and a brief description below it.

reactome

About Content Docs Tools Community Download

Find Reactions, Proteins and Pathways

e.g. O95631, NTN1, signaling by EGFR, glucose Go!

Pathway Browser
Visualize and interact with Reactome biological pathways

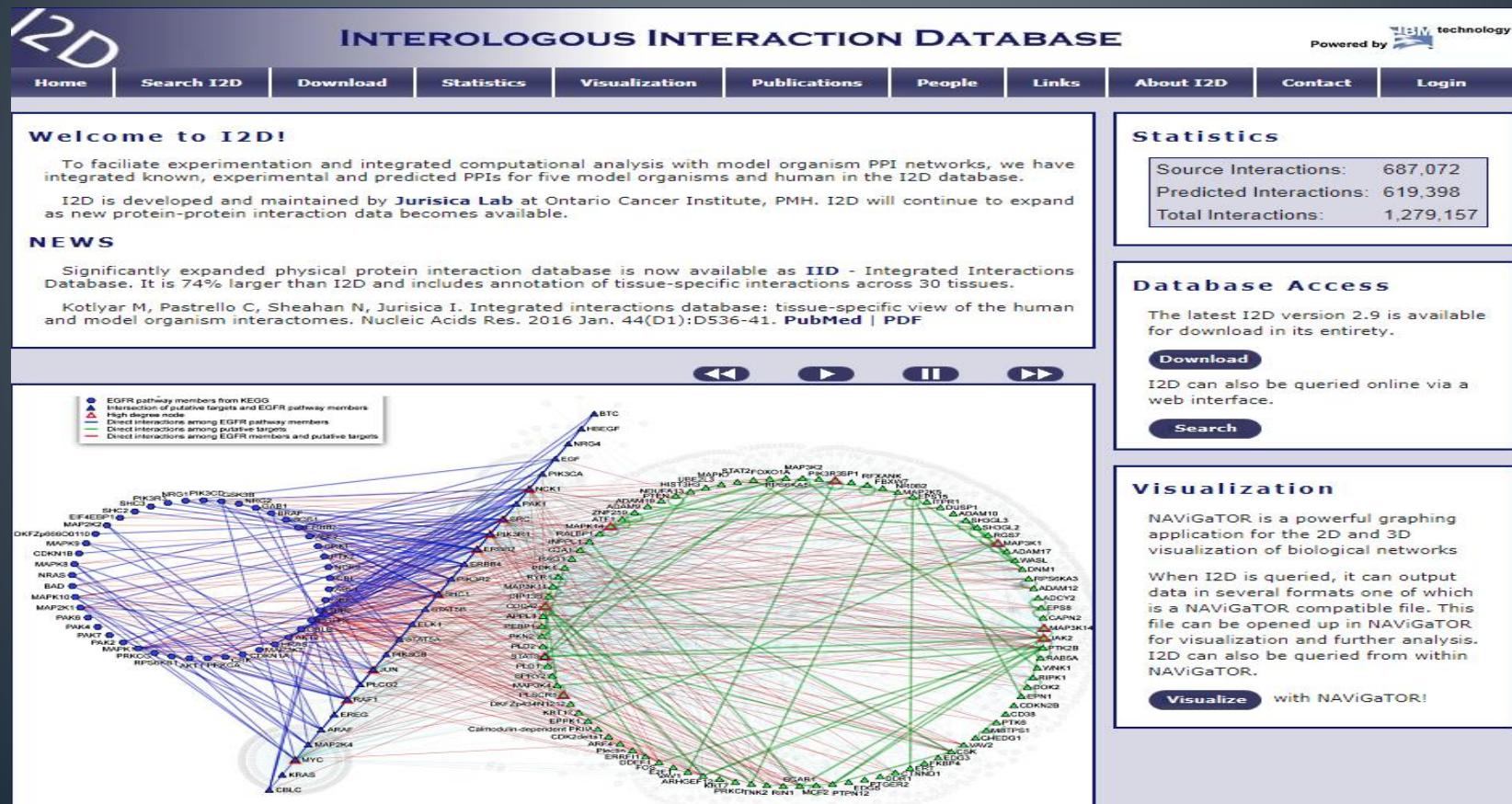
Analyze Data
Merges pathway identifier mapping, over-representation, and expression analysis

ReactomeFIViz
Designed to find pathways and network patterns related to cancer and other types of diseases

Documentation
Information to browse the database and use its principal tools for data analysis

I2D

- ❖ It has been integrated known, experimental and predicted PPIs for five model organisms and human



MINT

❖ MINT focuses on experimentally verified protein-protein interactions mined from the scientific literature by expert curators.



The Molecular INTeraction Database
An ELIXIR Core Resource

Welcome Statistics Download Developers Contacts About

Proteins, genes, public: **Search**

Welcome to MINT, the Molecular INTeraction database
MINT focuses on experimentally verified protein-protein interactions mined from the scientific literature by expert curators.

Protein interaction databases represent unique tools to store, in a computer readable form, the protein interaction information disseminated in the scientific literature. Well organized and easily accessible databases permit the easy retrieval and analysis of large interaction data sets. Here we present MINT, a database designed to store data on functional interactions between proteins. Beyond cataloguing binary complexes, MINT was conceived to store other types of functional interactions, including enzymatic modifications of one of the partners.

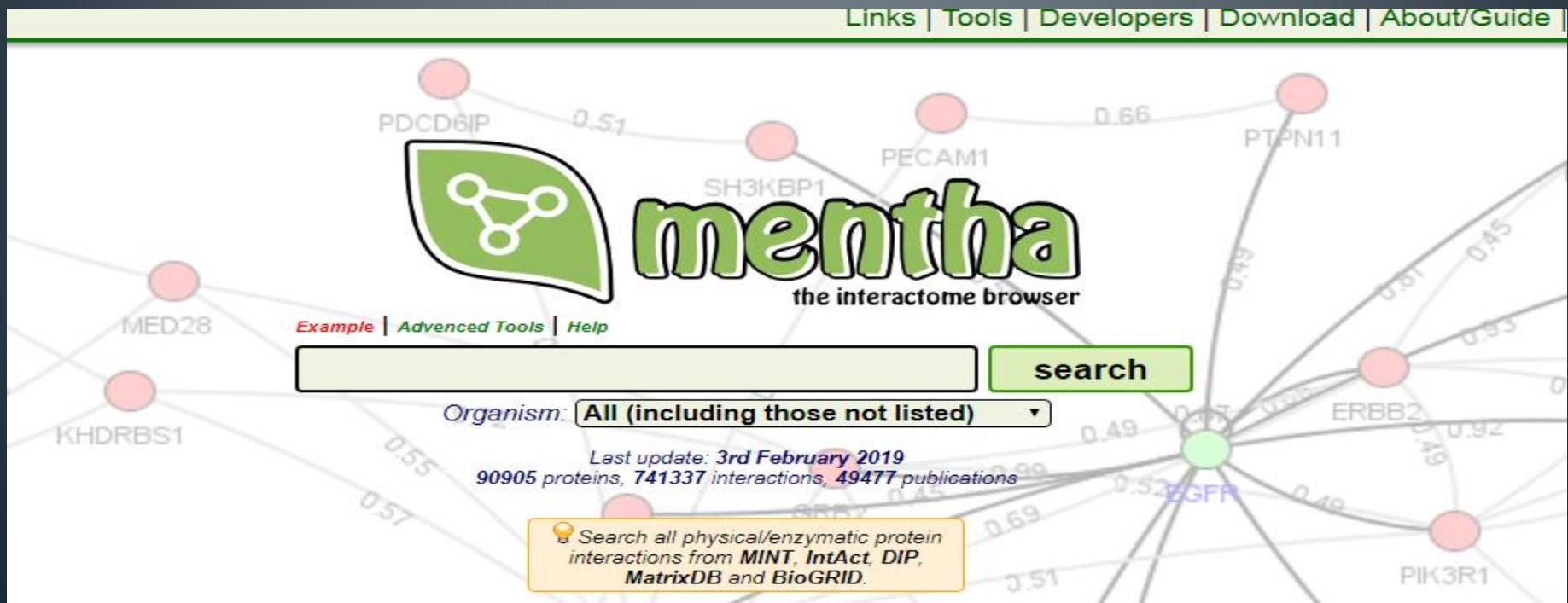
DATA CONTENT

Publications:	6014
Interactions:	126712
Interactors:	25893
Organisms:	645

 **MINT database**
[Follow](#)

Mentha

- ❖ mentha archives evidence about protein-protein interactions collected from different databases.



BAR

❖ Data Analysis Tools for Plant Biology

 The Bio-Analytic Resource for Plant Biology | About | Lists | Publications | Feedback | Legacy BAR | Help | Search

Welcome to the BAR!

Web-based tools for visualizing functional genomics and other data.



 Gene Expression and Protein Tools

 Molecular Markers and Mapping Tools

 Other Genomic Tools and Widgets

View expression patterns as electronic fluorescent pictographs or heatmaps, explore promoters, identify protein-protein interactions and more.

View Next Generation Mapping, or generate your own markers using our molecular marker tools.

Remove duplicates, perform multi-dimensional Venn analyses, or generate random lists of identifiers.

Gene Expression and Protein Tools

View expression patterns as electronic fluorescent pictographs or heatmaps, explore promoters, identify protein-protein interactions and more.

ePlant

ePlant (new version) | Legacy ePlant (PLOS ONE version)

Arabidopsis eFP Browsers

Arabidopsis eFP Browser | Cell eFP Browser | Arabidopsis Seed Coat eFP Browser | Arabidopsis Translome eFP Browser | Arabidopsis Spatio-Temporal Root Stress eFP Browser

Expression Anglers and other Expression Browsers

Expression Angler 2016 | Legacy Expression Angler | Poplar Expression Angler | Sample Angler | e-Northerns w. Expression Browser

Poplar Expression Browser

Other Dicot eFP Browsers

Poplar eFP Browser | Medicago eFP Browser | Soybean eFP Browser | Potato eFP Browser | Tomato eFP Browser

E. salignum eFP Browser | C. sativa eFP Browser | Arachis eFP Browser | Grape eFP Browser | Cannabis eFP Browser

Molecular Markers and Mapping Tools

Perform Next Generation Mapping, or generate your own markers using our molecular marker tools.

Next Generation Mapping

Marker Tracker

Blast Digester

Cap3D

Other Genomic Tools and Widgets

Remove duplicates, perform multi-dimensional Venn analyses, or generate random lists of identifiers.

Arabidopsis Citation Network Viewer

ClustalW with MView Output

DataMetaFormatter

Heatmapper

Heatmapper Plus

Duplicate Remover

Venn selector

Venn Super Selector

Random ID list generator

AGURR

Classification Super Viewer

Medicago Classification Super Viewer

_at to AGI converter

MASTA

GeneMANIA

Topo-phylogeny

MatrixDB

- ❖ MatrixDB is a freely available database focused on interactions established by extracellular matrix proteins, proteoglycans and polysaccharides



The Extracellular Matrix Interaction Database

Search for a biomolecule, keyword, author, publication or IMEx identifier

Current release of MatrixDB: 3.5 - 2019/01/24

MatrixDB is a freely available database focused on interactions established by extracellular matrix proteins, proteoglycans and polysaccharides

MatrixDB stores experimental data established by full-length proteins, matricryptins, glycosaminoglycans, lipids and cations.

MatrixDB reports interactions with individual polypeptide chains or with multimers (e.g. collagens, laminins, thrombospondins) when appropriate. Multimers are treated as permanent complexes, referencing EBI identifiers when possible. Human interactions were inferred from non-human homologous interactions when available.

 MatrixDB is an active member of the International Molecular Exchange (IMEx) consortium. Experiments are reported according to the Minimum Information required for reporting a Molecular Interaction experiment (MIMIx, Orchard *et al.* 2007 Nat Biotechnol. [PubMed](#)) or to the International Molecular Exchange curation rules (IMEx, Orchard *et al.* 2012 Nat Methods. [PubMed](#)). As an IMEx member, MatrixDB uses the PSI-MI controlled vocabulary.

 The MatrixDB web-interface provides an interactive access to a core of data curated in-house, enriched with ECM-associated interactions provided by IMEx partners. Additionally, all the data curated by MatrixDB are provided for programmatic access through a PSICQUIC webservice.

MatrixDB is in charge of the curation of papers published in [Matrix Biology](#) since January 2009.

MatrixDB is currently funded by:

Build Interaction Network

UniProt

- ❖ The mission of UniProt is to provide the scientific community with a comprehensive, high-quality and freely accessible resource of protein sequence and functional information.

The mission of UniProt is to provide the scientific community with a comprehensive, high-quality and freely accessible resource of protein sequence and functional information.

UniProtKB
UniProt Knowledgebase
Swiss-Prot (559,228)
Manually annotated and reviewed.
Records with information extracted from literature and curator-evaluated computational analysis.

TrEMBL (146,106,279)
Automatically annotated and not reviewed.
Records that await full manual annotation.

UniRef
The UniProt Reference Clusters (UniRef) provide clustered sets of sequences from the UniProt Knowledgebase (including isoforms) and selected UniParc records.

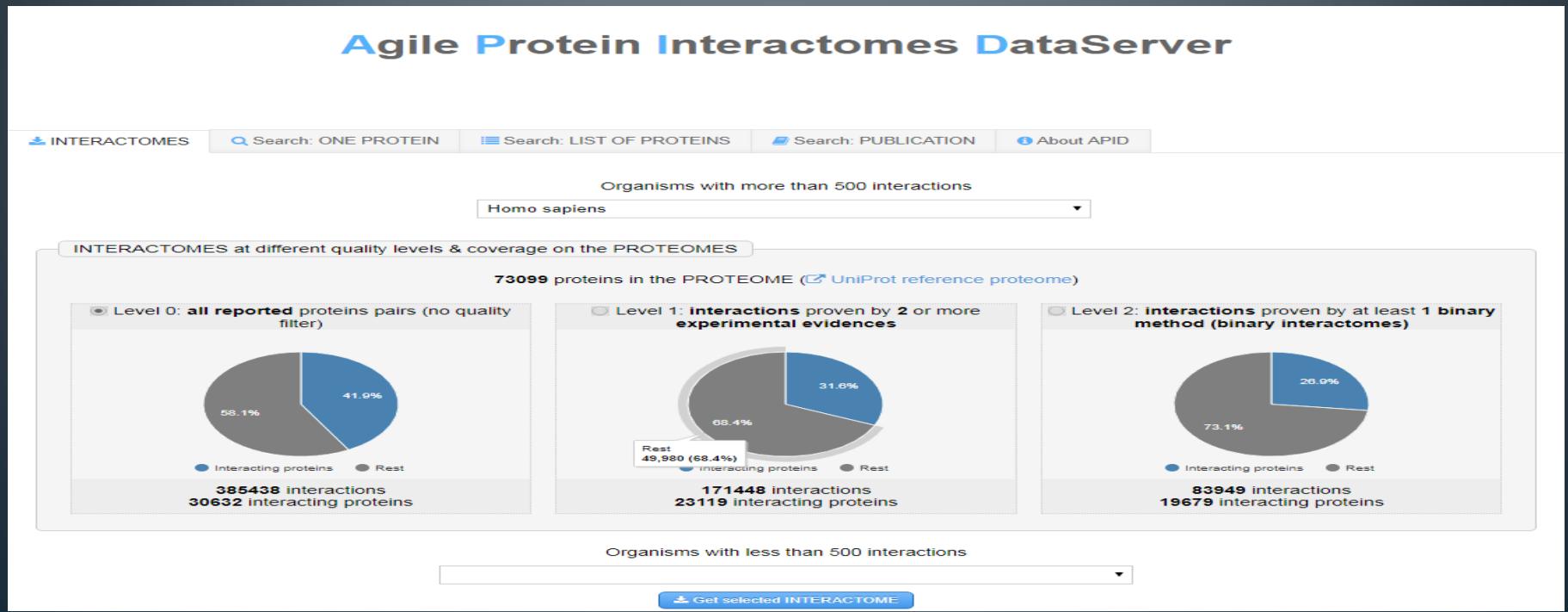
UniParc
UniParc is a comprehensive and non-redundant database that contains most of the publicly available protein sequences in the world.

Proteomes
A proteome is the set of proteins thought to be expressed by an organism. UniProt provides proteomes for species with completely sequenced genomes.

Supporting data
Literature citations
Cross-ref. databases
Taxonomy
Diseases
Subcellular locations
Keywords

APID

- ❖ APID is an interactive bioinformatics web tool developed to integrate and analyze in a unified and comparative platform main currently known information about protein–protein interactions demonstrated by specific small-scale or large-scale experimental methods.



DIP

- ❖ The DIP database catalogs experimentally determined interactions between proteins. The data stored within the DIP database were curated, both, manually by expert curators and also automatically using computational approaches that utilize the knowledge about the protein-protein interaction networks extracted from the most reliable, core subset of the DIP data.

 Database of Interacting Proteins 

Search by: [protein] [sequence] [motif] [article] [IMEx] [pathBLAST] [Help] [LOGIN]

THE DIP DATABASE

The DIP™ database catalogs experimentally determined interactions between proteins. It combines information from a variety of sources to create a single, consistent set of protein-protein interactions. The data stored within the DIP database were curated, both, manually by expert curators and also automatically using computational approaches that utilize the knowledge about the protein-protein interaction networks extracted from the most reliable, core subset of the DIP data. Please, check the [reference](#) page to find articles describing the DIP database in greater detail.

This page serves also as an access point to other projects related to DIP, such as The Database of Ligand-Receptor Partners ([DLRP](#)) and JDIP.

DIP PAGES

NEWS	Announcements about the most recent additions and changes to the database.
REGISTRATION/ACCOUNT	Registration and account maintenance. Registration is required to gain access to most of the DIP features. Registration is free to the members of the academic community. Trial accounts for the commercial users are also available. Please, consult Terms of Use for further details.
STATISTICS	Detailed information about the current state of the database as well as some statistics on server usage.
SATELLITES	DIP-related projects, such as DLRP and JDIP .
SERVICES	DIP-derived services.
ARTICLES	DIP in press. Both, papers published on DIP as well as a list of publications referring to DIP.
SEARCH	Database search. This is the starting point of the database exploration. Once the initial protein is found through keyword or sequence searches the interaction network can be explored by interactively following the interaction links.
LINKS	Links to other protein interaction databases and related sites.
FILES	Download the complete DIP dataset as well as specialized DIP subsets and additional data (<i>registration required</i>).
HELP	A short description of the DIP database.

Interoporc

- ❖ Interoporc is an automatic prediction tool to infer protein-protein interaction networks. It is applicable for lots of species using orthology and known interactions. The interoPORC method is based on the interolog concept and combines source interaction datasets from public databases as well as clusters of orthologous proteins (PORC) available on Integr8.

Interoporc
Automatic molecular interaction predictions

Welcome to Interoporc

Interoporc is an automatic prediction tool to infer protein-protein interaction networks. It is applicable for lots of species using orthology and known interactions. The interoPORC method is based on the interolog concept and combines source interaction datasets from public databases as well as clusters of orthologous proteins (PORC) available on Integr8.

You can use this page to ask Interoporc for all species present in Integr8. Some results are already computed and you can run Interoporc to investigate any other species. If you publish work in which you have used Interoporc, please cite the associated publication.

Currently, the following databases are processed and merged (with datetime of the last available public release for each database used):

Database	Type	Last available public release
IntAct	Molecular interactions	2008-08-22
MIINT	Molecular interactions	2008-05-16
OIP	Molecular interactions	2008-07-08
Integr8	Orthologous clusters	2008-09-23

Direct links to most studied species

Species	Taxid	Interactions	Results	Date
Synechocystis	1148	2037	PSI25-XML MITAB25 [Details]	2008-09-29
E. coli	562	88864	PSI25-XML MITAB25 [Details]	2008-09-29
H. pylori	210	11375	PSI25-XML MITAB25 [Details]	2008-09-29
S. cerevisiae	4932	1791	PSI25-XML MITAB25 [Details]	2008-09-29
C. elegans	6239	11205	PSI25-XML MITAB25 [Details]	2008-09-29
D. melanogaster	7227	13255	PSI25-XML MITAB25 [Details]	2008-09-29
A. thaliana	3702	14722	PSI25-XML MITAB25 [Details]	2008-09-29
M. musculus	10090	32161	PSI25-XML MITAB25 [Details]	2008-09-29
R. norvegicus	10116	15864	PSI25-XML MITAB25 [Details]	2008-09-29
H. sapiens	9606	17284	PSI25-XML MITAB25 [Details]	2008-09-29

 EMBL-EBI 

[Home](#) [Source code](#) [Download binaries](#) [References](#)

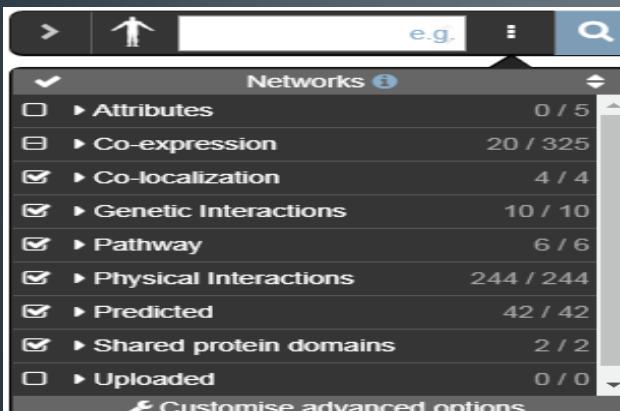
[Comment and request:](#) [Coordinator](#)
Contributors:
IntAct team (EBI)
LBI team (CEA)

<http://biodev.extra.cea.fr/interoporc/Default.aspx>

54

GeneMANIA

- ❖ GeneMANIA finds other genes that are related to a set of input genes, using a very large set of functional association data. Association data include protein and genetic interactions, pathways, co-expression, co-localization and protein domain similarity.



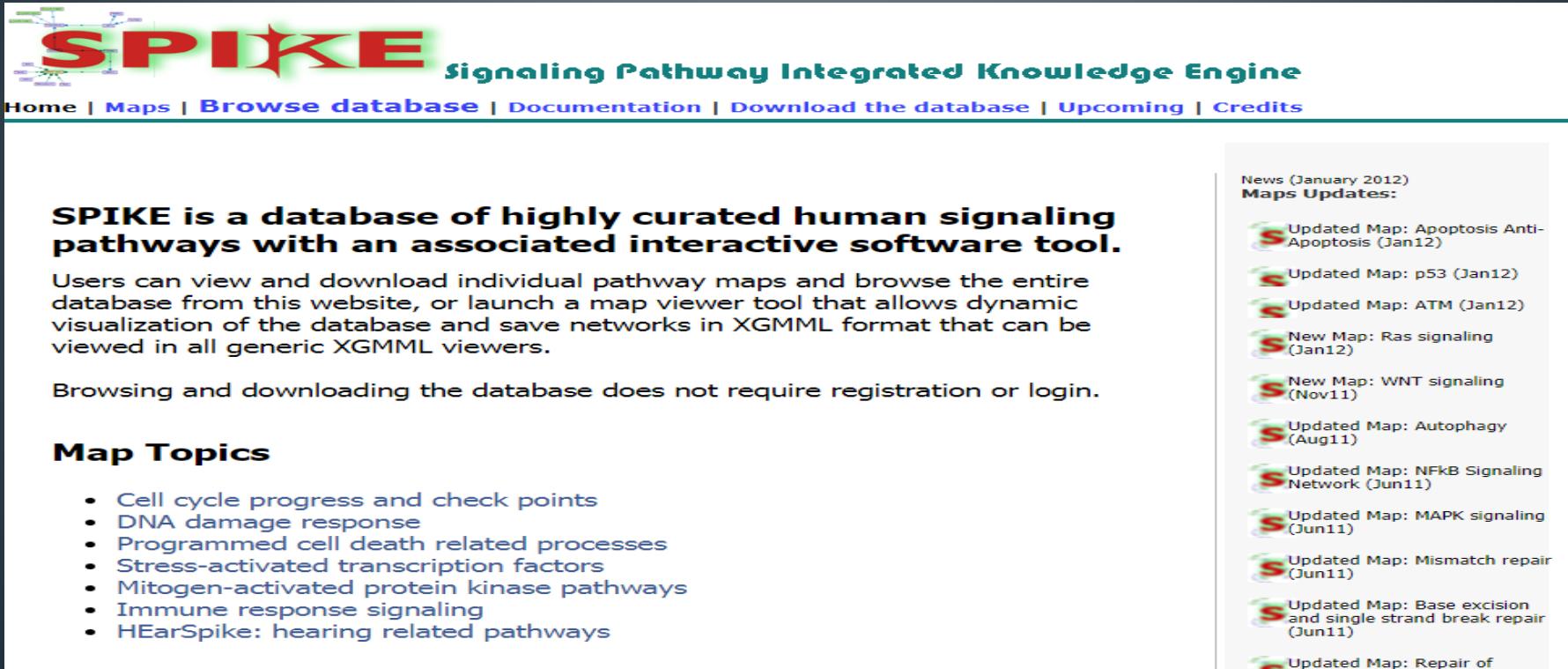
The screenshot shows the GeneMANIA web interface. At the top, there is a search bar with placeholder text "e.g.:" and a magnifying glass icon. Below the search bar is a navigation menu with icons for back, forward, user profile, and help. The main content area is titled "Networks" and displays a list of association types with their counts:

Network Type	Count
Attributes	0 / 5
Co-expression	20 / 325
Co-localization	4 / 4
Genetic Interactions	10 / 10
Pathway	6 / 6
Physical Interactions	244 / 244
Predicted	42 / 42
Shared protein domains	2 / 2
Uploaded	0 / 0

At the bottom of this panel is a link "Customise advanced options". To the right of the networks panel, the main page features the "GENEMANIA" logo in large, bold, sans-serif letters. Below the logo, there is a horizontal line of links: "Cytoscape app" | "Help" | "Contact" | "Cite" | "@ UToronto". A descriptive text block below the links states: "GeneMANIA helps you predict the function of your favourite genes and gene sets. Indexing 2,277 association networks containing 597,392,998 interactions mapped to 163,599 genes from 9 organisms." At the very bottom of the page is a URL: <https://genemania.org/>.

SPIKE

- ❖ SPIKE is a database of highly curated human signaling pathways with an associated interactive software tool.



The screenshot shows the SPIKE website homepage. At the top, there is a logo with the word "SPIKE" in large red letters and "Signaling Pathway Integrated Knowledge Engine" in smaller blue text. Below the logo is a navigation bar with links: Home, Maps, Browse database, Documentation, Download the database, Upcoming, and Credits. The main content area features a bold statement: "SPIKE is a database of highly curated human signaling pathways with an associated interactive software tool." Below this statement, there is a paragraph explaining that users can view and download individual pathway maps and browse the entire database from the website, or launch a map viewer tool that allows dynamic visualization of the database and save networks in XGMML format that can be viewed in all generic XGMML viewers. It also states that browsing and downloading the database does not require registration or login. A section titled "Map Topics" lists various cellular processes: Cell cycle progress and check points, DNA damage response, Programmed cell death related processes, Stress-activated transcription factors, Mitogen-activated protein kinase pathways, Immune response signaling, and HEarSpike: hearing related pathways. At the bottom left, there are two references: [1] R. Elkon, R. Vesterman, N. Amit, J. Assa, I. Ulitsky, G. Steinfeld, R. Blechman, Y. Shiloh, R. Shamir. "SPIKE – a database, visualization and analysis tool of cellular signaling pathways". BMC Bioinformatics 9:110 (2008) and [2] Arnon Paz, Zippora Brownstein, Yaara Ber, Shani Bialik, Eyal David, Dorit Sagir, Igor Ulitsky, Ran Elkon, Adi Kimchi, Karen B. Avraham, Yosef Shiloh and Ron Shamir "SPIKE: a database of highly curated human signaling pathways". Nucleic Acids Research, 2011, Vol. 39, Database issue. On the right side, there is a sidebar titled "Maps Updates:" which lists several updated maps with their names and update dates: Updated Map: Apoptosis Anti-Apoptosis (Jan12), Updated Map: p53 (Jan12), Updated Map: ATM (Jan12), New Map: Ras signaling (Jan12), New Map: WNT signaling (Nov11), Updated Map: Autophagy (Aug11), Updated Map: NFkB Signaling Network (Jun11), Updated Map: MAPK signaling (Jun11), Updated Map: Mismatch repair (Jun11), Updated Map: Base excision and single strand break repair (Jun11), Updated Map: Repair of Interstrand Crosslinks (May11), and Updated Map: Nucleotide excision repair (Apr11). A link "see the Maps section" is also present.

VirHostNet

- ❖ VirHostNet is a knowledgebase dedicated to the network-based exploration of **virus-host** protein-protein interactions.

The screenshot shows the homepage of VirHostNet 2.0. At the top left is a logo featuring a red virus-like particle and a blue circular motif with binary code (010110100010). To the right are navigation links: Home (highlighted in blue), Help, Cite, Contact, and Download. The main title "VirHostNet 2.0" is centered above a subtitle: "Surfing on the web of Virus/Host molecular interactions.". Below this are search and browse buttons: "Search", "Browse", and "Interology". A search bar at the bottom contains a "Protein" dropdown set to "STAT1_HUMAN" and a "Search" button. A red banner at the bottom left announces: "What's new in VirHostnet 2.0 (release January 2019) ?". A bulleted list details the new features.

- 34.760 virus-host and virus-virus manually biocurated protein-protein interactions, including more than 6.000 new interactions since the last January 2018 release
- A VirHostNet SOLR PSICQUIC webservice that provides annotations in PSI MI-TAB 2.5 format ([download](#))
- The use of UniProtkb/Swiss-Prot TrEMBL ([release January 2019](#)) and ReFSeq ([release 92 January 2019](#)) as references

HPIDB

- ❖ HPIDB is a resource that helps annotate, predict and display host-pathogen interactions (HPI)

HPIDB 3.0
Host-Pathogen
Interaction Database

MENU

Search Database By


SEQUENCE
Search using a single protein sequence in FASTA format.


KEYWORD
Search by accession, gene symbol, taxon.


HOMOLOGOUS HPI
Search multiple host and/or pathogen sequences. File upload required.

Our Purpose

HPIDB 3.0 is a resource that helps annotate, predict and display host-pathogen interactions (HPI). HPI that underpin infectious diseases are critical for developing novel intervention strategies. Currently our database contains 62,782 curated entries.

[LEARN MORE](#)

ChEMBL

- ❖ ChEMBL or ChEMBLdb is a manually curated chemical database of bioactive molecules with drug-like properties.

The screenshot shows the ChEMBL website interface. At the top, there's a navigation bar with links for Services, Research, Training, and About us. The main header features the ChEMBL logo and a Wellcome Trust logo. A yellow banner at the top right encourages users to check out the New Interface (Beta) and provides a Learn More link. Below the banner, the URL EBI > Databases > Small Molecules > ChEMBL Database > Home is displayed. The main content area includes a search bar with dropdowns for Compounds, Targets, Assays, Documents, Cells, Tissues, and an Exact Match checkbox. There are also buttons for Ligand Search, Target Search, Browse Targets, Browse Drugs, Browse Drug Targets, Browse Drug Indications, and About. On the left, a sidebar lists various EBI services like ChEMBL, Downloads, UniChem, SureChEMBL, Malaria Data, ChEMBL-NTD, ADMEx SARfari, Web Services, myChEMBL, EBI RDF Platform, FAQ, Web status page, Funding, Internships (New), and ChEMBL Statistics. The statistics section shows DB: ChEMBL_24, Targets: 12,091, Compound records: 2,275,906, and Distinct compounds: 1,000. The central part of the page features the Marvin JS interface, which includes a molecular editor with a toolbar, a periodic table, and a Marvin JS logo. To the right, there are sections for List Search (with radio buttons for SMILES Search, ChEMBL ID Search, and Keyword Search) and Biologicals Blast Search. A large input field for SMILES search is present in the List Search section.

BindingDB

- ❖ BindingDB is a public, web-accessible database of measured binding affinities, focusing chiefly on the interactions of protein considered to be drug-targets with small, drug-like molecules. BindingDB contains 1,558,402 binding data, for 7,223 protein targets and 697,594 small molecules.



The Binding Database

Home Info Download About us Email us Contribute data Web Services

myBDB logout

Search and Browse

Target
Sequence
Name &
Ki IC50 Kd EC50
Rate constants
 ΔG° ΔH° - ΔS°
pH (Enzymatic Assay)
pH (ITC)
Substrate or Competitor
Compound Mol. Wt.
Chemical Structure
Pathways
Source Organism
Number of Compounds
Monomer List in csv
Het List in SDF

Compound
FDA Drugs
Important Compounds
Chemical Structure
Name
etc...

Simple Search
Article Titles, Authors, Assays, Compound Names, Target Names

Advanced Search
Combine multiple search criteria, such as chemical structures, target names, and numerical affinities; restrict searches by data source, such as BindingDB, ChEMBL, PubChem, and Patents.

Messages
From 11/2017 to 10/2018, BindingDB curators extracted over 48,000 data (27,500 compounds and 400 targets) from US Patents! (November 09, 2018)

Patent Curation by BindingDB
Patents: 2,449
Binding measurements: 306,071
Compounds: 184,650
Target proteins: 1,494
Assays: 3,538
Average Number of Targets per Patent: 1.95

BindingDB News

November 2017. If you are interested in preparing a multi-targeted compound collection, you may be interested in our new download. This file lists all purchasable compounds for all Targets in BindingDB, with an affinity better than 10 micromolar, and includes catalog information. See "Purchasable Compounds by Target" on our Download page.

September 2017. The Advanced Search page has been simplified and made more unified with other BindingDB pages.

June 2017. We are pleased to report that the NIH has renewed its support for BindingDB. Thanks to all who filled out our survey and provided supporting messages!

June 2017. Drug Design Data Resource (D3R) datasets have been integrated into BindingDB

ZINC

- ❖ A free database of commercially-available compounds for virtual screening.

ZINC 12

Not Authenticated – sign in

Active cart: Temporary Cart (0 items)

About **Search** **Subsets** **Help** **Social** **G+** **Quick Search Bar...** **Go**

Please consider switching to [ZINC15](#), which is superior to ZINC12 in most ways. If you prefer ZINC12 after trying ZINC15, we would like to know why @chem4biology so that we can get you to make the switch.

Welcome to ZINC, a free database of commercially-available compounds for virtual screening. ZINC contains over 35 million purchasable compounds in ready-to-dock, 3D formats. ZINC is provided by the [Irwin](#) and [Shoichet](#) Laboratories in the Department of Pharmaceutical Chemistry at the University of California, San Francisco (UCSF). To cite ZINC, please reference: Irwin, Sterling, Mysinger, Bolstad and Coleman, *J. Chem. Inf. Model.* 2012 [DOI: 10.1021/ci3001277](#). The original publication is Irwin and Shoichet, *J. Chem. Inf. Model.* 2005;45(1):177-82 [PDF](#), [DOI](#). We thank [NIGMS](#) for financial support (GM71896).

Molecule of the Week [64565919](#)

ZINC ID, Drug Name, SMILES, Catalog, Vendor Code, Target & r **Go**

Structure/Draw Physical Properties Catalogs & Vendors ZINC IDs Targets Rings Combination

DrugBank

- ❖ The DrugBank database is a unique bioinformatics and cheminformatics resource that combines detailed drug data with comprehensive drug target information.

The screenshot shows the DrugBank homepage with a pink header bar. The header includes the DRUGBANK logo, navigation links for Browse, Search, Downloads, About, Help, Blog, and Contact Us, and a search bar with the placeholder "WHAT ARE YOU LOOKING FOR?". Below the search bar, the query "Tylenol" is entered, and the "Drugs" category is selected. The main content area features the DRUGBANK logo and a brief description of the database's purpose. A sidebar contains a paragraph about the latest release statistics and links to "About DrugBank" and "Cite DrugBank".

WHAT ARE YOU LOOKING FOR?

Tylenol

Drugs Targets Pathways Indications

DRUGBANK

The DrugBank database is a unique bioinformatics and cheminformatics resource that combines detailed drug data with comprehensive drug target information.

The latest release of DrugBank (version 5.1.2, released 2018-12-20) contains 11,938 drug entries including 2,541 approved small molecule drugs, 1,195 approved biotech (protein/peptide) drugs, 130 nutraceuticals and over 5,771 experimental drugs. Additionally, 5,134 non-redundant protein (i.e. drug target/enzyme/transporter/carrier) sequences are linked to these drug entries. Each DrugCard entry contains more than 200 data fields with half of the information being devoted to drug/chemical data and the other half devoted to drug target or protein data.

About DrugBank > Cite DrugBank +

PSICQUIC

- ❖ PSICQUIC is a project within the HUPO Proteomics Standard Initiative. It standardises programmatic access to molecular interaction databases.

EMBL-EBI

Services Research Training About us

PSICQUIC View

* Examples: BRCA2_Q06609_dmc1_10831611 Search

Input Form Browse Help Feedback

Input Form > Browse

10,255,473 binary interactions found for search term *

<input type="checkbox"/> API Interactomes	<input type="checkbox"/> BAR	<input checked="" type="checkbox"/> bhf-ucl - 4,019	<input type="checkbox"/> BIND
<input checked="" type="checkbox"/> BindingDB - 1,011,029	<input checked="" type="checkbox"/> BioGrid - 1,513,281	<input checked="" type="checkbox"/> ChEMBL - 628,504	<input type="checkbox"/> DIP
<input type="checkbox"/> DIP-IMEx	<input type="checkbox"/> DrugBank	<input checked="" type="checkbox"/> EBI-GOA-miRNA - 3,339	<input checked="" type="checkbox"/> EBI-GOA-nonIntAct - 70,093
<input type="checkbox"/> GeneMANIA	<input checked="" type="checkbox"/> HPIDb - 5,046	<input checked="" type="checkbox"/> I2D - 817,915	<input checked="" type="checkbox"/> IMEx - 701,246
<input checked="" type="checkbox"/> InnateDB - 33,295	<input checked="" type="checkbox"/> InnateDB-All - 578,350	<input checked="" type="checkbox"/> IntAct - 670,129	<input type="checkbox"/> Interoporc
<input checked="" type="checkbox"/> iRefIndex - 2,338,337	<input checked="" type="checkbox"/> MatrixDB - 65,000	<input checked="" type="checkbox"/> MBInfo - 638	<input checked="" type="checkbox"/> mentha - 1,272,096
<input checked="" type="checkbox"/> MINT - 127,197	<input checked="" type="checkbox"/> MPIDB - 1,751	<input checked="" type="checkbox"/> Reactome - 141,996	<input checked="" type="checkbox"/> Reactome-Fls - 209,988
<input type="checkbox"/> Spike	<input type="checkbox"/> TopFind	<input checked="" type="checkbox"/> UniProt - 18,967	<input checked="" type="checkbox"/> VirHostNet - 34,760
<input checked="" type="checkbox"/> ZINC - 8,497			

Status of the service

- ONLINE
- OFFLINE
- WARNING: Time out
- ERROR: Unexpected Error

10,255,473 selected interactions

To many interactions to cluster. Please reduce the number to less than 5000 interactions.

version: 1.4.11

Modeling Environments



A screenshot of the Microsoft Excel 2010 ribbon interface. The ribbon is divided into several tabs: File, Home, Insert, Page Layout, Formulas, Data, Review, and View. The Home tab is currently selected, as indicated by the green background and bold text. Below the ribbon, there is a toolbar with various icons for font selection (Font, Font Size, Bold, Italic, Underline), alignment (Align Left, Align Center, Align Right, Wrap Text, Merge & Center), number formats (General, Number, Currency, Percentage, Date, Time, etc.), styles (Conditional Formatting, Format as Table, Cell Styles), and cells (Insert, Delete, Format). On the far right of the ribbon, there are additional buttons for AutoSum, Fill, Clear, Sort & Filter, and Find & Select. The main workspace shows a blank worksheet with columns labeled A through S and rows labeled 1 through 12. Cell A1 is currently selected.

JUST RELEASED

Wolfram Mathematica® 9

Seamlessly Flow Ideas to Results:
Compute, Develop, Deploy the *Mathematica* Way



bifurcation.nb *

File Edit Insert Format Cell Graphics Evaluation Palettes Window Help

```
in[6]:= bifurcate[f_, a0_, k0_, k_, while_] := NestWhileList[f, a0, while, 2, k0 + k - 1] // Drop[#, k0] &
logistic = {x, y} \[Mapsto] x y (1 - y);

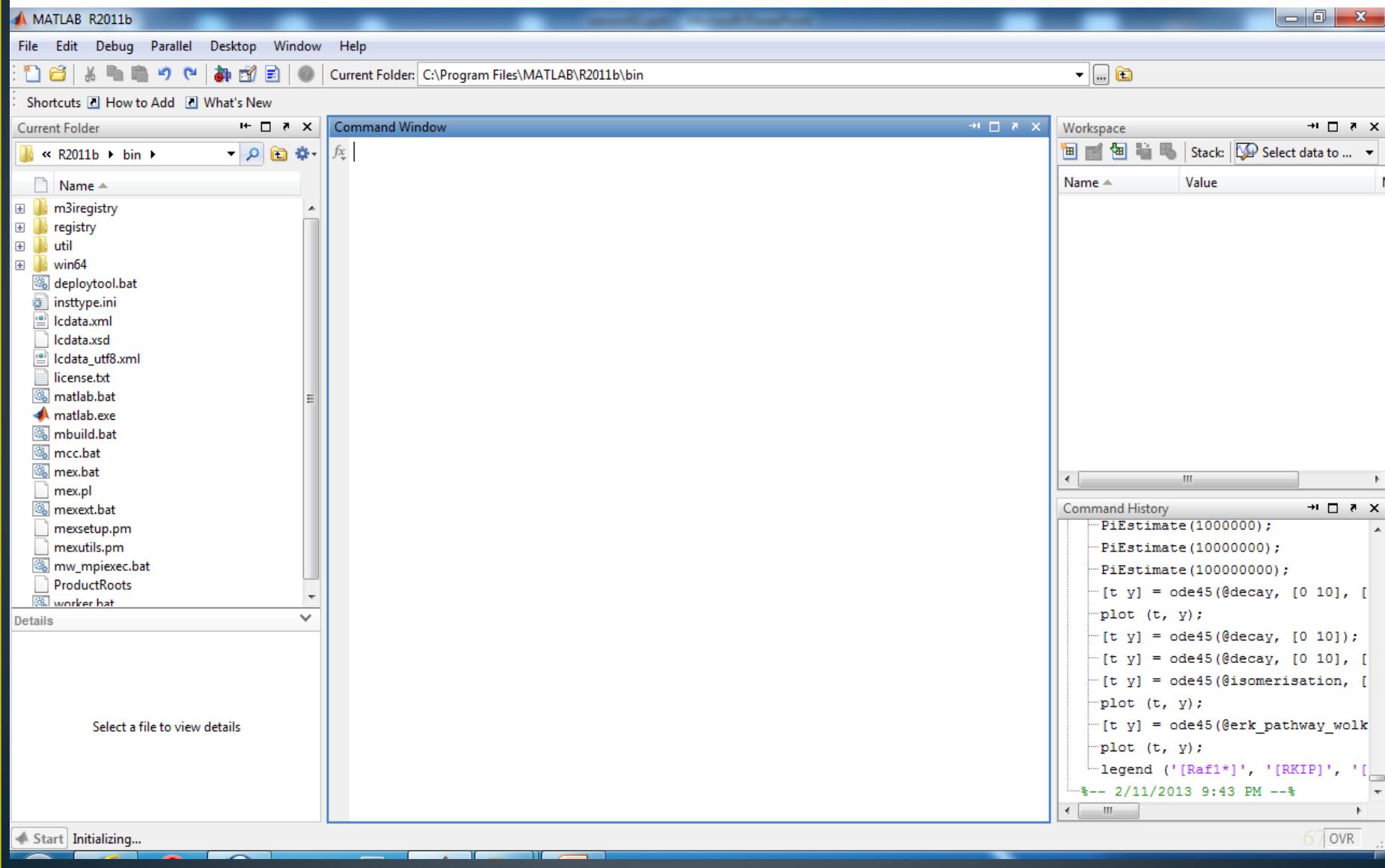
in[8]:= Row@{"Initial value: ", a0 = RandomReal[{0.1, 0.9}]}
Row@{ "Points per r: ", density = 10^2}
Row@{ "Initial k: ", k0 = 10^4}
Row@{ "Time taken: ", Timing[
  plotData = ParallelTable[{ConstantArray[x, density], bifurcate[logistic[x, #] &, a0, k0, density]} &,
    {x, 3.5, 4, 0.0001}] // Flatten[#, 1] &,
  1][[1]], " s"}
Row@{"Data length: ", plotData // Length}

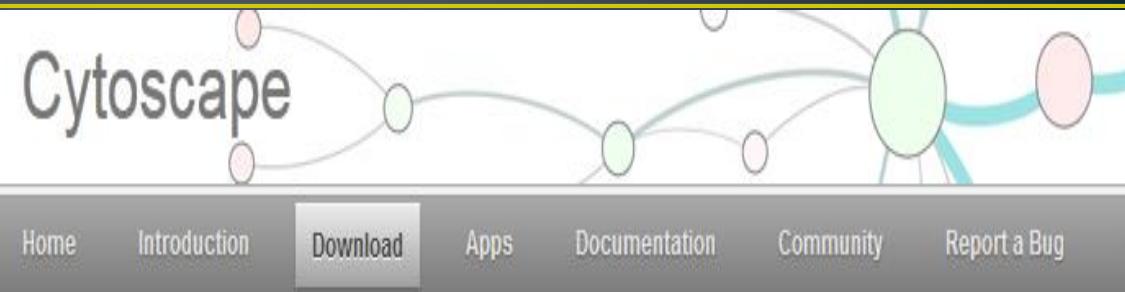
out[8]= Initial value: 0.728935
out[9]= Points per r: 100
out[10]= Initial k: 10000
out[11]= Time taken: 41.1666 s
out[12]= Data length: 500100

in[18]:= ListPlot[plotData, PlotStyle \[Rule] {PointSize[0], Opacity[0.1]}, ImageSize \[Rule] 800, PlotRange \[Rule] {All, {0, 1}},
LabelStyle \[Rule] 16]
```

MATLAB®

The Language of Technical Computing





JBuilder 9 - /opt/JBuilder9/samples/Welcome/src/com/borland/samples/welcome/WelcomeApp.java

File Edit Search View Project Run Team Wizards Tools Window Help

Welcome.jpx Welcome

```
24 package com.borland.samples.welcome;
25
26 import java.awt.*;
27 import javax.swing.UIManager;
28
29 public class WelcomeApp {
30     boolean packFrame = false;
31
32     // Construct the application
33     public WelcomeApp() {
34         WelcomeFrame frame = new WelcomeFrame();
35
36         //Pack frames that have useful preferred size info, e.g. from their layout
37         //Validate frames that have preset sizes
38         if (packFrame)
39             frame.pack();
40         else
41             frame.validate();
42
43         // Center the frame
44         Dimension screenSize = Toolkit.getDefaultToolkit().getScreenSize();
45         Dimension frameSize = frame.getSize();
46         if (frameSize.height > screenSize.height)
47             frameSize.height = screenSize.height;
48         if (frameSize.width > screenSize.width)
49             frameSize.width = screenSize.width;
50         frame.setLocation((screenSize.width - frameSize.width) / 2, (screenSize.height - frameSize.height) / 2);
51
52         frame.setVisible(true);
53     }
54 }
```

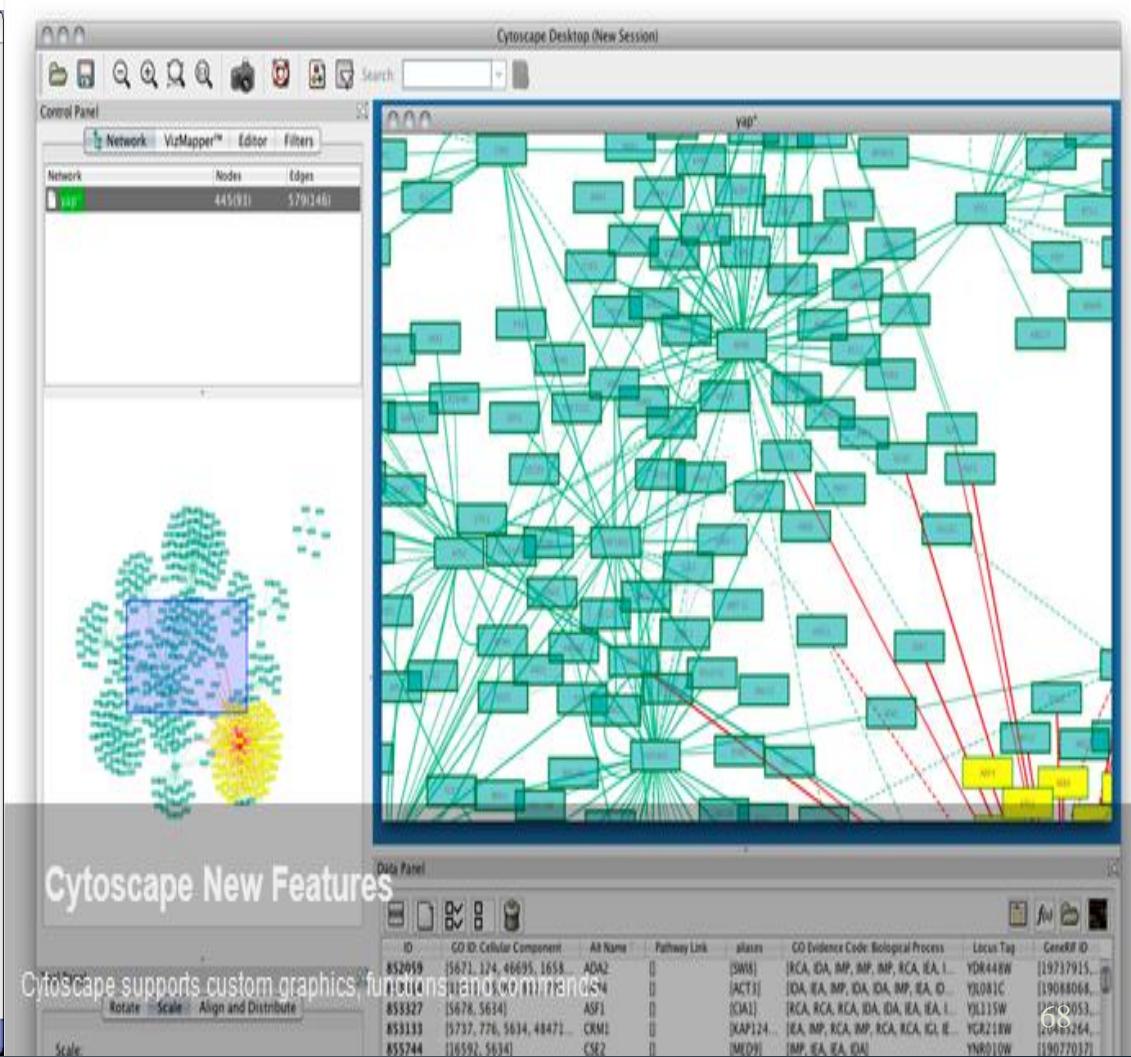
Errors

- cannot resolve symbol: class WelcomeFrame
- cannot resolve symbol: class WelcomeFrame

Imports

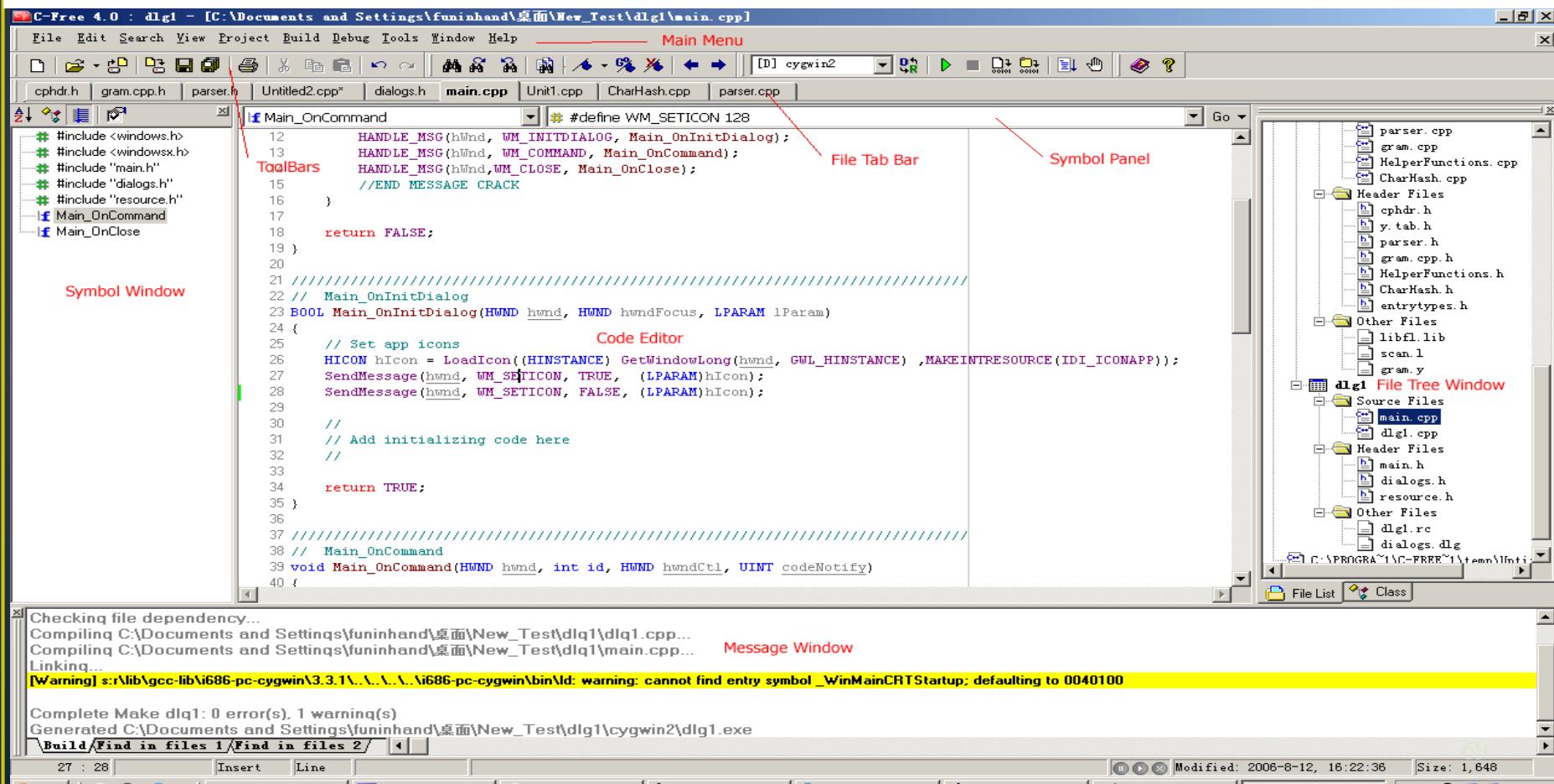
- WelcomeApp
- > WelcomeApp()
- > main(String[] args)
- > packFrame

Source Design Bean UML Doc History



#include <stdio.h>
int main(void)
{
 printf("Hello World!!\n");
 return 0;
}

C++



R R Console

File Edit Misc Packages Help

```
R version 2.4.1 (2006-12-18)
Copyright (C) 2006 The R Foundation for Statistical Computing
ISBN 3-900051-07-0
```

```
R is free software and comes with ABSOLUTELY NO WARRANTY.
You are welcome to redistribute it under certain conditions.
Type 'license()' or 'licence()' for distribution details.
```

```
R is a collaborative project with many contributors.
Type 'contributors()' for more information and
'citation()' on how to cite R or R packages in publications.
```

```
Type 'demo()' for some demos, 'help()' for on-line help, or
'help.start()' for an HTML browser interface to help.
Type 'q()' to quit R.
```

```
> source("http://sensominer.free.fr/install-senso.r")
```

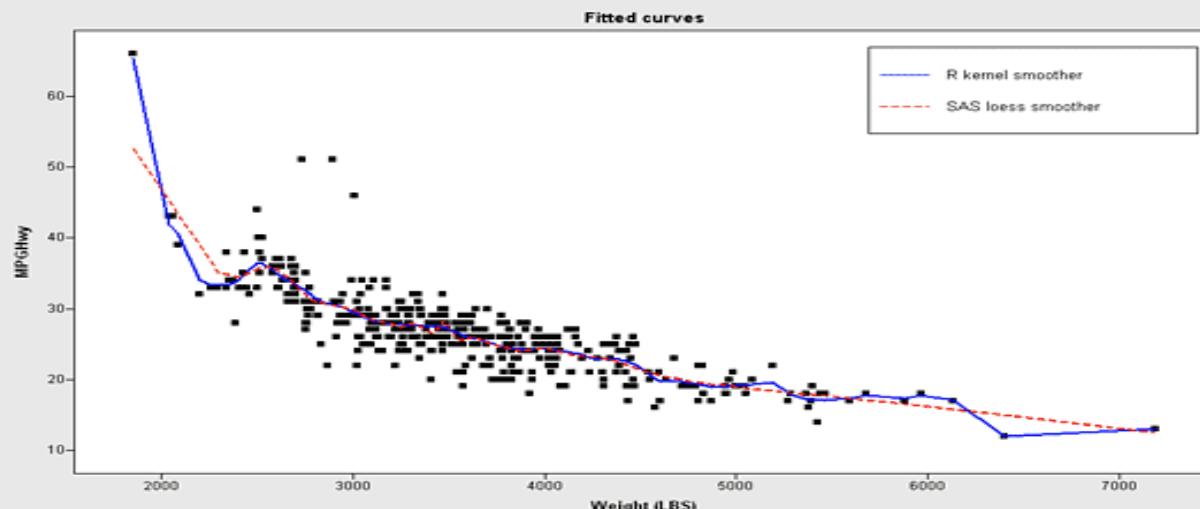
SAS/IML Studio - cars (KernelRegression)

File Edit View Program Graph Analysis Tools Window Help

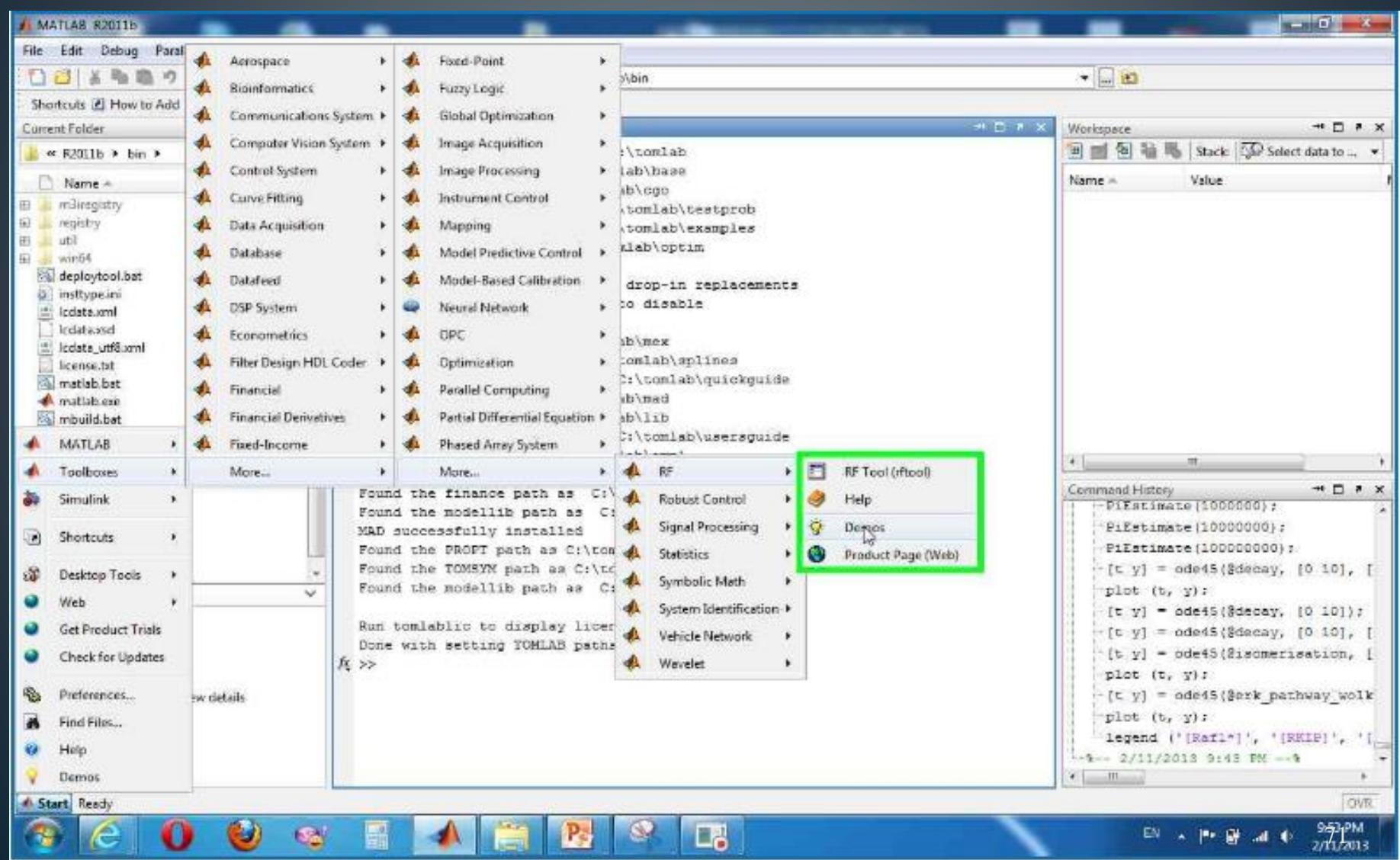
KernelRegression.sx

```
run DefineData();  
  
/* DataName = "gas"; Xvar = "E"; Yvar  
DataName = "cars"; Xvar = "Weight"; Yvar  
declare DataObject dobj = DataObject;  
/* Show the data */  
declare ScatterPlot plot = ScatterPlot;  
pause;  
OutputDocument.GetDefault().SetWindowP  
***** R Computations ***  
/* Export DataObject to R as a data frame  
dobj.ExportToR( DataName );  
  
/* In R, we use nonparametric kernel regression  
t0 = time();  
submit Xvar Yvar DataName / R;  
# load and use np package  
require(np)  
bw <- npregbw(cYvar ~ cXvar, data=dobj)  
model <- npreg(bws=bw)  
summary(model)  
pred <- fitted(model)  
endsubmit;  
t1 = time();  
print "*** Time for R kernel regression  
  
/* KerPred and KerResid are read from  
dobj.AddVarFromR( "KerPred", "pred" )  
dobj.AddVarFromR( "KerResid", "residual"  
***** SAS Computations ***  
  
/* Compare Kernel regression to proc loess  
t0 = time();  
submit Xvar Yvar DataName;  
proc loess data=&DataName;  
model cYvar ~ cXvar / select=A  
score /;  
ods output ScoreResults = Loes  
endsubmit;
```

Scatter Plot of cars (KernelRegression)



Toolboxes (Ex. MATLAB)



Plugins (Ex.Cytoscape)

Win prizes by finding bugs in Cytoscape 3.0!

Categories



- [network generation](#)
- [online data import](#)
- [graph analysis](#)
- [data visualization](#)
- [utility](#)
- [integrated analysis](#)
- [clustering](#)
- [ontology analysis](#)
- [scripting](#)
- [layout](#)

[more »](#)

Featured Apps

[Get Started with the App Store »](#)



PSICQUICUniversalClient

PSICQUIC Web Service Client for importing interactions from public



BiNGO

Calculates overrepresented GO terms in the network and display



ClueGO

Creates and visualizes a functionally grouped network of



DynNetwork

Visualize dynamic networks in Cytoscape 3.0

Top Voted Apps

GENEMANIA

GeneMANIA

3.0



PathExplorer

72 3.0

Operating Systems

MEMORABLE LINUX MILESTONES

CELEBRATING 20 YEARS OF LINUX

LINUS TORVALDS POSTS FAMOUS MESSAGE - "HELLO EVERYBODY OUT THERE...!" - AND RELEASES FIRST LINUX CODE

SLACKWARE BECOMES FIRST WIDELY ADOPTED DISTRIBUTION

TECH GIANTS BEGIN ANNOUNCING PLATFORM SUPPORT FOR LINUX

IBM RUNS FAMOUS LINUX AD DURING THE SUPERBOWL
THE LINUX FOUNDATION IS FORMED TO PROMOTE, PROTECT AND STANDARDIZE LINUX
LINUS IS A FELLOW

LINUX TURNS 20 AND POWERS THE WORLD'S SUPERCOMPUTERS, STOCK EXCHANGES, PHONES, ATMs, HEALTHCARE RECORDS, SMART GRIDS, THE LIST GOES ON



1991

1992

1993

1996

1998

1999

2003

2005

2007

2010

2011

LINUS LICENSES LINUX UNDER THE GPL, AN IMPORTANT DECISION THAT WILL CONTRIBUTE TO ITS SUCCESS IN THE COMING YEARS

LINUS VISITS AQUARIUM, GETS BIT BY A PENGUIN AND CHOOSES IT AS LINUX MASCOT

RED HAT GOES PUBLIC

LINUS APPEARS ON THE COVER OF BUSINESS WEEK WITH A STORY THAT HAILS LINUX AS A BUSINESS SUCCESS

THE LINUX-BASED ANDROID OS OUTSHIPS ALL OTHER SMARTPHONE OSES IN THE U.S. AND CLIMBS TO DOMINANCE



<http://www.linuxfoundation.org/>



Copyright © 2011 Linux Foundation. All rights reserved. Linux is a registered trademark of Linus Torvalds. Slackware® is a registered trademark of Slackware Linux, Inc. Red Hat® is a registered trademark of Red Hat, Inc. Android™ is a trademark of Google Inc. Use of this trademark is subject to Google Permissions. BusinessWeek is a trademark of BLOOMBERG L.P.

Windows 7



74

```

load averages: 0.45, 0.39, 0.37
90 processes: 89 idle, 1 on processor
CPU0 states: 0.0% user, 0.0% nice, 0.0% system, 0.0% interrupt, 100% idle
CPU1 states: 0.0% user, 0.0% nice, 0.0% system, 0.0% interrupt, 100% idle
Memory: Real: 68M/324M act/tot Free: 0K/1660M Swap: 0K/1660M used/tot

```

PID	USERNAME	PRI	NICE	SIZE	RES	STATE	WAIT	TIME	CPU	COMMAND
26309	nicholas	2	0	1776K	4789K	sleep/1	poll	0:06	0.0%	mpd
16366	nicholas	2	0	1520K	4556K	sleep/1	poll	1:34	0.0%	mpd
23280	nicholas	2	0	4172K	2944K	sleep/0	poll	0:00	0.0%	mpd
2790	nicholas	2	0	3360K	1852K	sleep/1	poll	0:00	0.0%	scmpc
12068	root	2	0	456K	796K	sleep/0	kqread	0:00	0.0%	opmd
7401	www	2	0	1548K	2548K	sleep/1	select	0:00	0.0%	httpd
1953	root	2	0	1548K	2548K	sleep/1	select	0:00	0.0%	sendmail
8064	root	2	0	1844K	1188K	sleep/1	poll	0:01	0.0%	crond
15182	nicholas	2	0	3384K	2260K	sleep/0	select	0:02	0.0%	sshd
1688	root	2	0	148K	144K	idle	nfsd	0:02	0.0%	nfsd
26598	root	2	0	148K	144K	idle	nfsd	0:01	0.0%	nfsd
76	nicholas	2	0	1384K	2124K	sleep/0	poll	0:00	0.0%	tmux
20891	root	2	0	612K	952K	idle	select	0:00	0.0%	cron
18549	nicholas	2	0	520K	620K	idle	twayn	0:00	0.0%	ksh
18971	syslogd	2	0	524K	840K	sleep/0	poll	0:00	0.0%	syslogd
19861	nicholas	2	0	972K	2704K	sleep/1	poll	0:00	0.0%	ncmpc
27153	nicholas	2	0	1500K	11M	sleep/0	select	0:00	0.0%	emacs

```

-client_msg_fn_detach(struct hdr *hdr, struct client_ctxt *cctx)
+client_msg_fn_detach(struct imgmsg *imsg, struct client_ctxt *cctx)
{
-    if (Chdr->size != 8)
+    if (Cimg->hdr_len != IMSG_HEADER_SIZE)
        fatalx("bad MSG_DETACH size");

    client_write_server(cctx, MSG_EXITING, NULL, 0);
00 -96.9 +107.9 00

int
client_msg_fn_shutdown(
-    struct hdr *hdr, struct client_ctxt *cctx)
+    struct imgmsg *imsg, struct client_ctxt *cctx)
{
-    if (Chdr->size != 8)
+    if (Cimg->hdr_len != IMSG_HEADER_SIZE)
        fatalx("bad MSG_SHUTDOWN size");
    client_write_server(cctx, MSG_EXITING, NULL, 0);
00 -108.9 +119.9 00
=====--F1 tmux-imsg-12diff.diff 17% (134,0) Hg-0 (Diff)-----

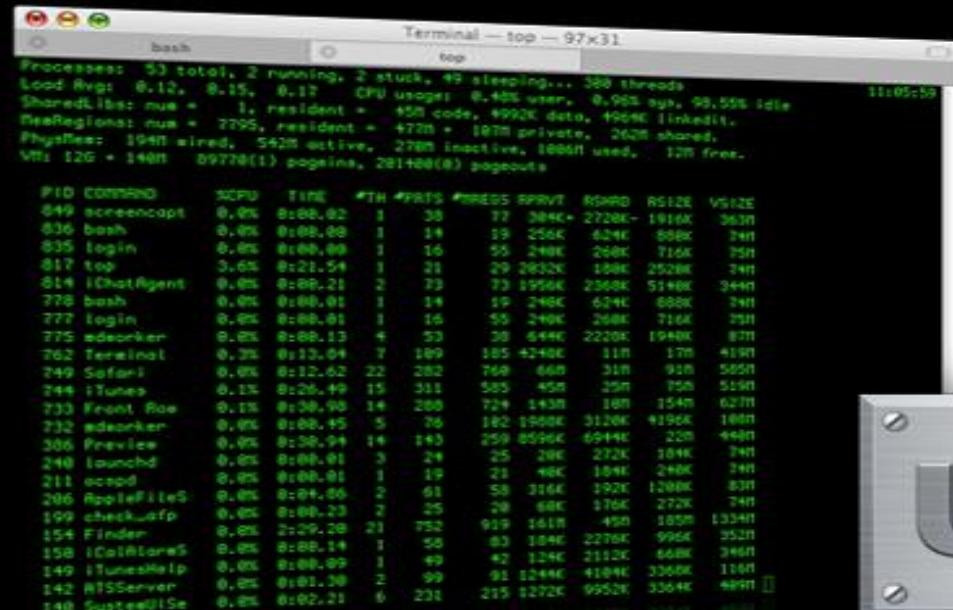
```

```
(0) 0:irssi# 1:todo 2:ncmpc- 3:mutt 4:gnome-terminal: 5:ksh 6:ksh 7:ksh 8:ksh 9:ksh 10:ksh 11:ksh
```

```

20:28:31 nicholas@yelena 0 1 ~$ ls tmux-
tmux-borders.diff
tmux-bsdauth.diff
tmux-cfgcur.diff
tmux-print.diff
tmux-imsg-12diff.diff
tmux-imsq1.diff
tmux-modesearch.diff
tmux-sessenv-new-old.diff
tmux-sessenv-new.diff
tmux-visual.diff
nicholas@yelena 0 1 ~$
```

```
"" 20:28:24 Jul -89
```



So, in overall, we have

- ❖ Operating Systems

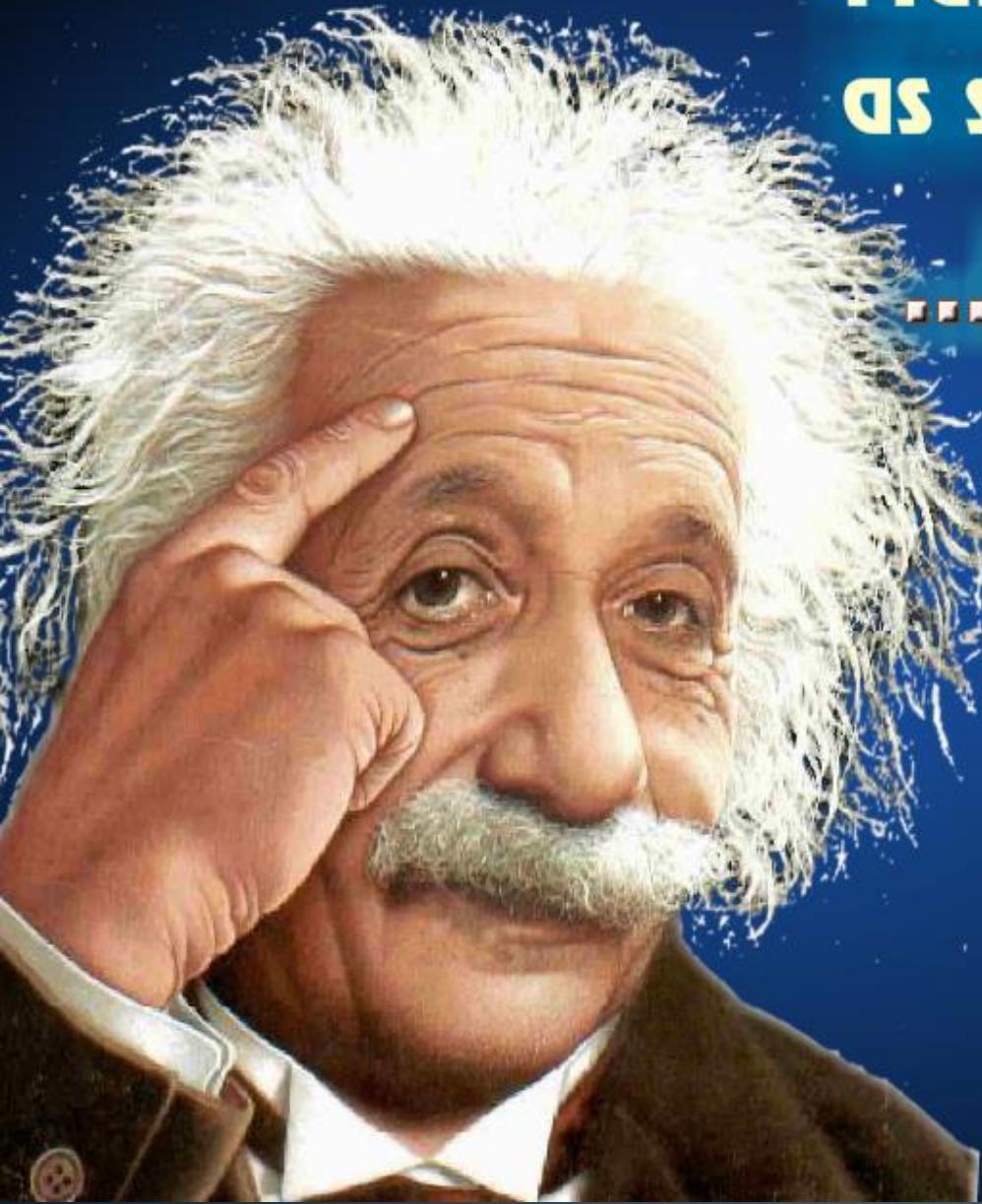
- Windows
- Linux
- Mac OS
- ...

- ❖ Modeling Environments

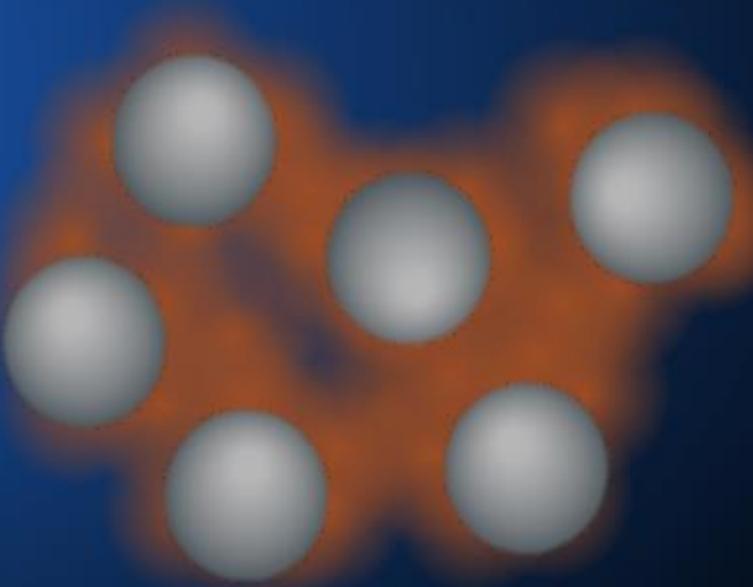
- Excel
- Programming Languages (C/C++/Java)
- Mathematica
- MATLAB
 - ✓ Toolbox
- Cytoscape
 - ✓ Plugings (Apps)
- ...

Summary

- Biological Networks
 - Protein-Protein Interactions Networks
 - Metabolic Networks
 - Gene Regulatory Networks
 - Signaling Networks
 - mRNA-miRNA network
 - Co-expression networks
 - Disease networks
 - ...
- Databases for Network Creation
- Operating Systems
- Modeling Environment

A portrait of Albert Einstein with his hand resting against his forehead, looking thoughtfully at the viewer.

**Make everything
as simple as possible.
...but not simpler.**



Systems biology