

Dénes Türei

Saez-Rodriguez group (EMBL Hinxton)
Overington group (EMBL Hinxton)
Gavin group (EMBL Heidelberg)

EMBL-EBI 

27th November 2015

Sources of signaling data

Signaling
pathway
resources

Dénes Türei

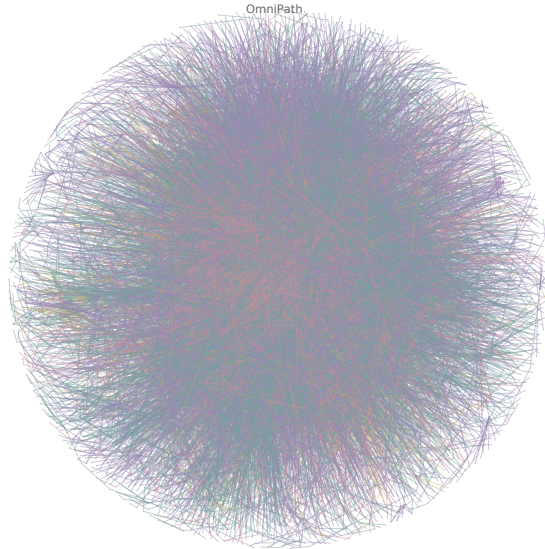
Resources

Coverage

Literature

Annotations

Applications



Sources of signaling data

Signaling
pathway
resources

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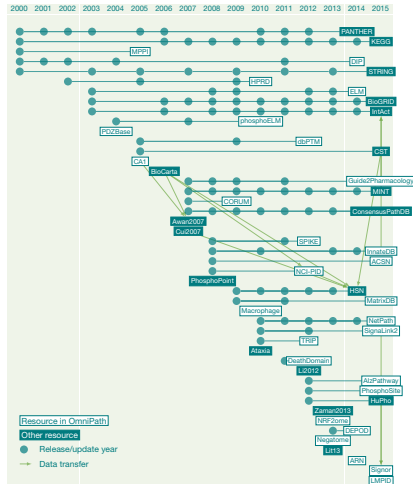
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Sources of signaling data

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Protein interaction
databases

In silico or
experimental evidences?

Predicted

Large screenings or
small scale experiments?

High-throughput

Computational text mining or
expert controlled?

Literature mined

Literature curated

Interacting pairs, w/o direction or effect

Interaction

Directed interactions with effect sign

Pathway

PTM enzyme-substrate relationships

PTM

Equations of reactants and products

Reaction

Directions and effects

Signaling
pathway
resources

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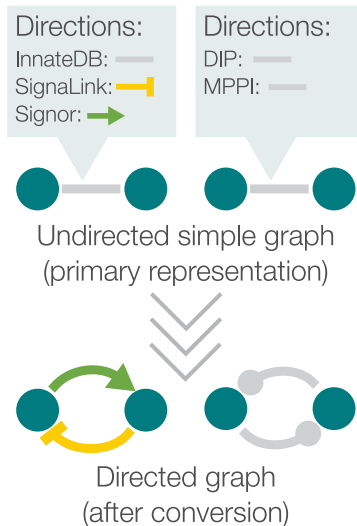
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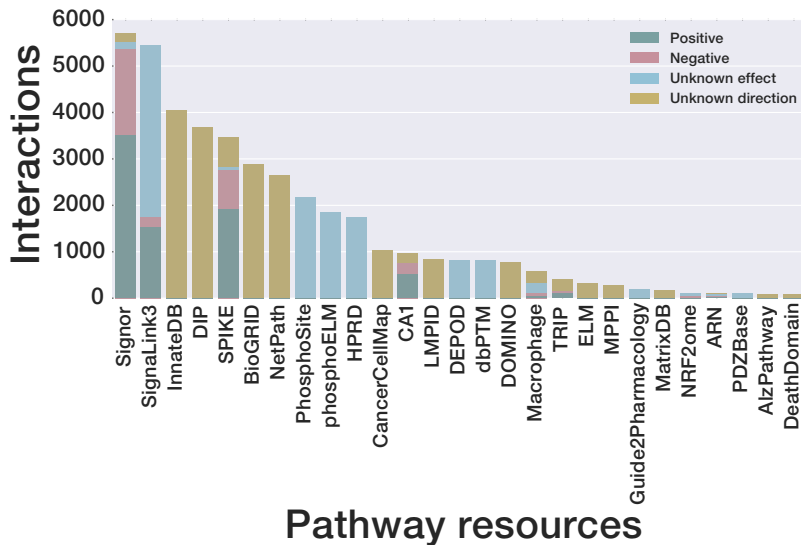
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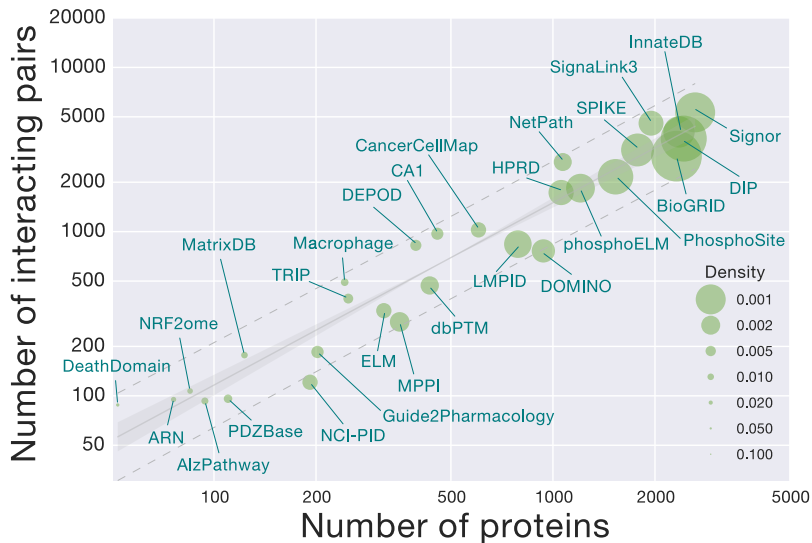
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Directions and effects



Boundaries of our knowledge



Boundaries of our knowledge

Signaling
pathway
resources

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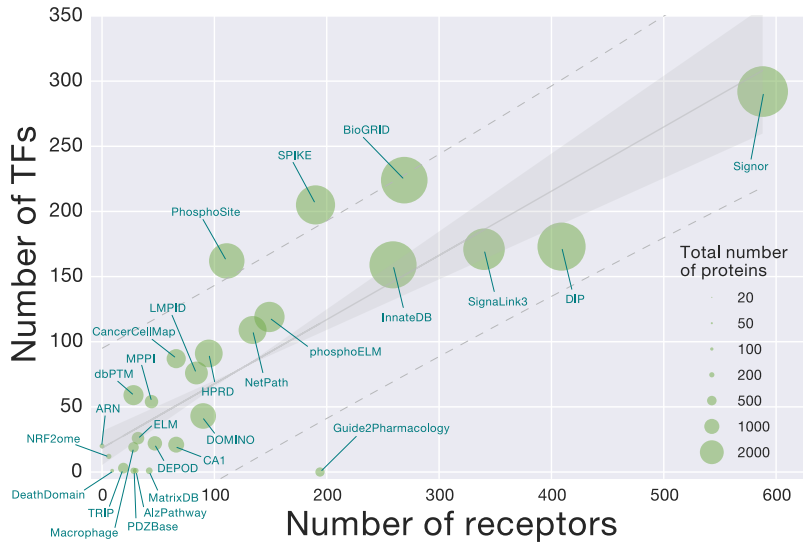
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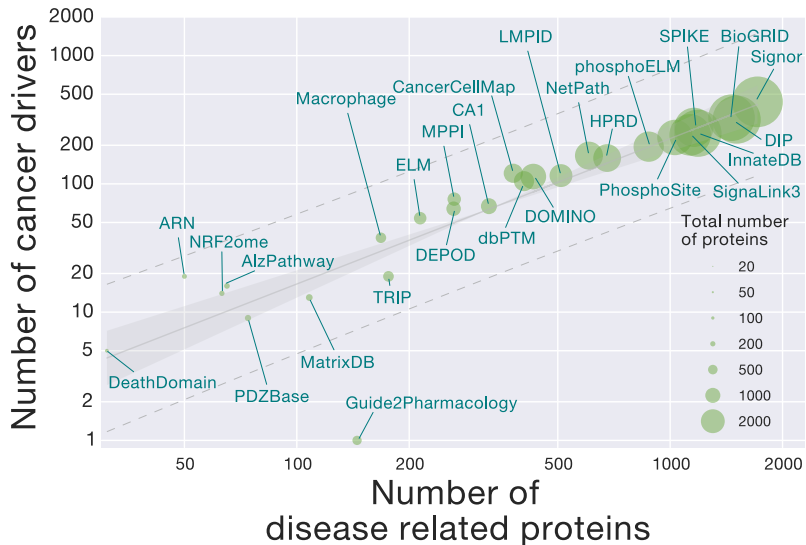
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Boundaries of our knowledge



Boundaries of our knowledge

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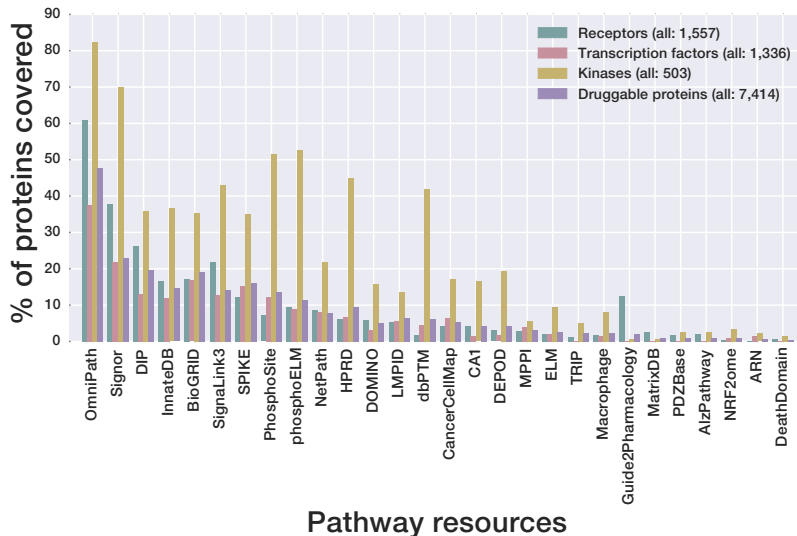
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Boundaries of our knowledge

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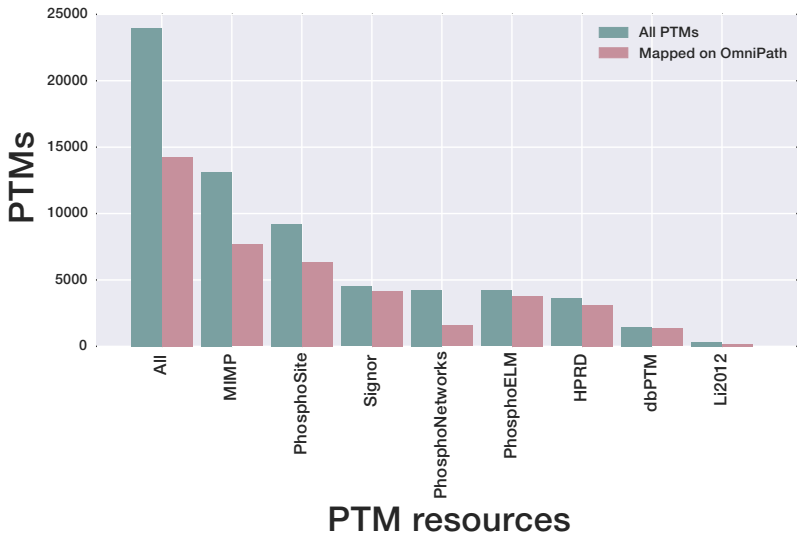
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Applications

Tedious work of curators

Signaling
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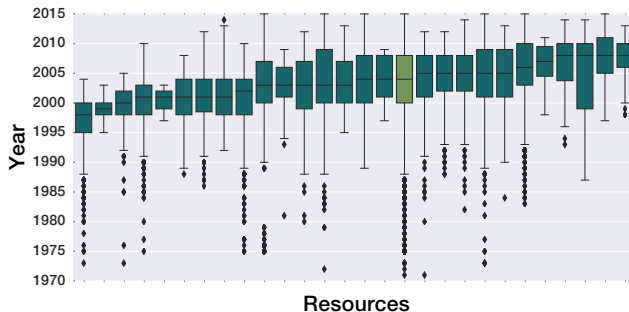
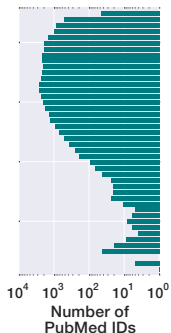
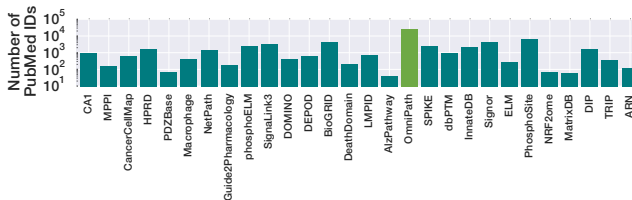
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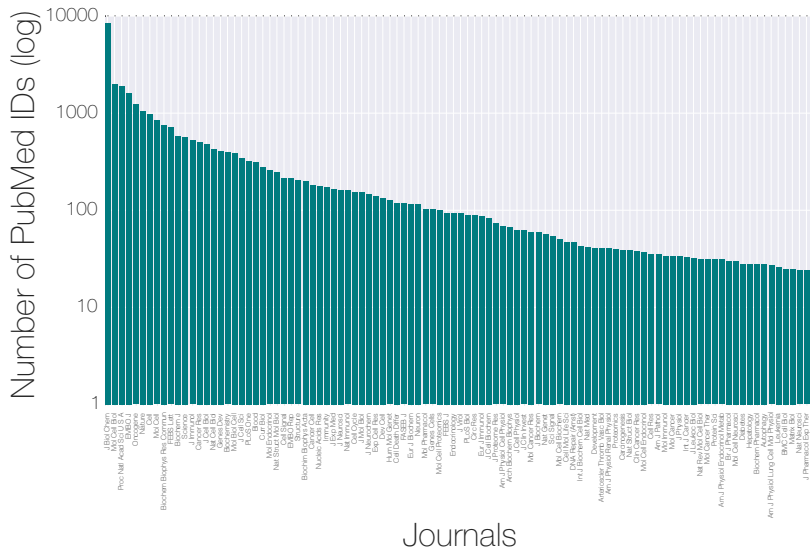
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Data integration

Signaling pathway resources

Dénes Türei

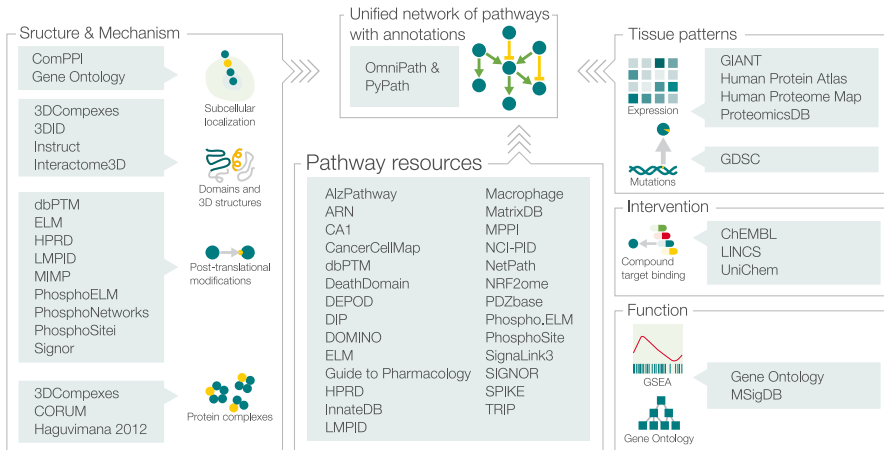
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Localization

Signaling
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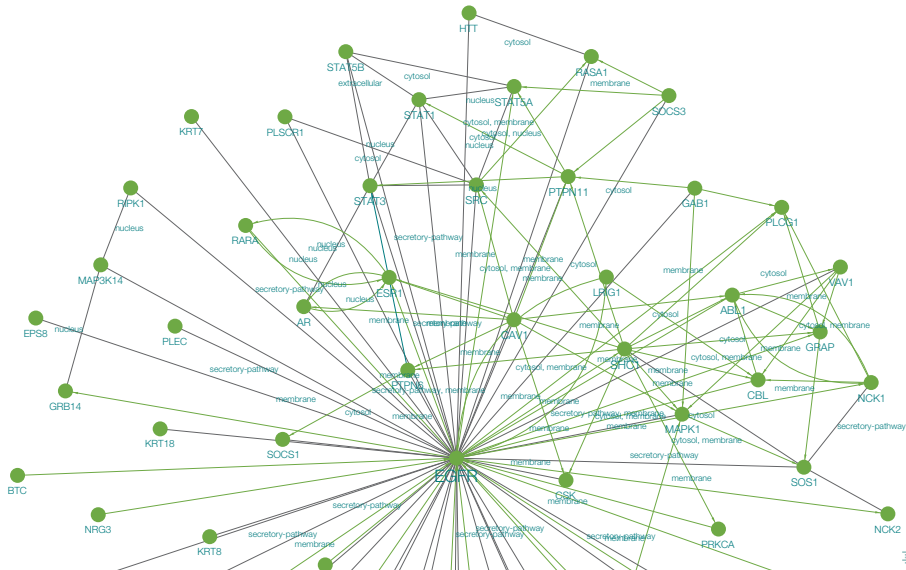
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Dénes Türei

Signaling pathway resources

Structure data

Signaling pathway resources

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3DID
Instruct
Domino
3DComplexes



Domain-domain
for 1,381 interactions



Domain-motif
for 6,168 interactions

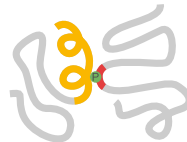


PhosphoSite
phosphoELM
iELM
Pepcyber
Domino

PISA
3DID
3DComplexes



Residue level



PTMs: 33,051 PTMs,
in 6,046 interactions;
3,355 phosphorylations
in 954 interactions



PhosphoSite
phosphoELM

Signaling pathway resources

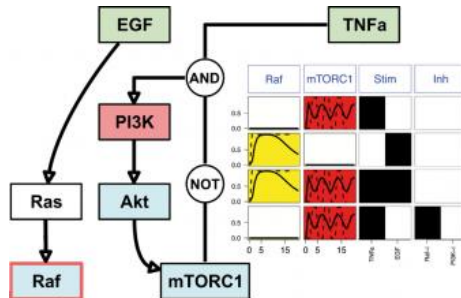
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Applications II. – Network topological methods

Signaling
pathway
resources

Dénes Túrei

Resources

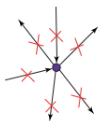
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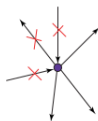
Applications

(a) Complete knockout

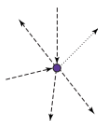


(b) Partial inactivation of several targets

(i) Partial knockout

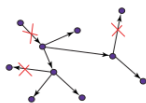


(ii) Attenuation

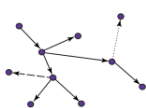


(c) Distributed system-wide attack

(i) Distributed knockout



(ii) Distributed attenuation

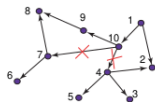


(d) Calculation of network efficiency

(i)

$$\text{Efficiency } E = \frac{\sum_{i \neq j} \frac{1}{d_{ij}}}{N(N-1)}$$

(ii)



(ii) d_{ij} matrix

	1	2	3	4	5	6	7	8	9	10
1	-	1	3	2	3	3	2	3	2	1
2	-	-	-	-	-	-	-	-	-	2
3	-	-	-	-	-	-	-	-	-	3
4	1	1	1	-	-	-	-	-	-	4
5	-	-	-	-	-	-	-	-	-	5
6	-	-	-	-	-	-	-	-	-	6
7	-	-	-	-	1	-	1	-	-	7
8	-	-	-	-	-	-	-	-	-	8
9	-	-	-	-	-	-	1	-	-	9
10	-	2	2	1	2	2	1	2	1	-

$$E = 0.181$$

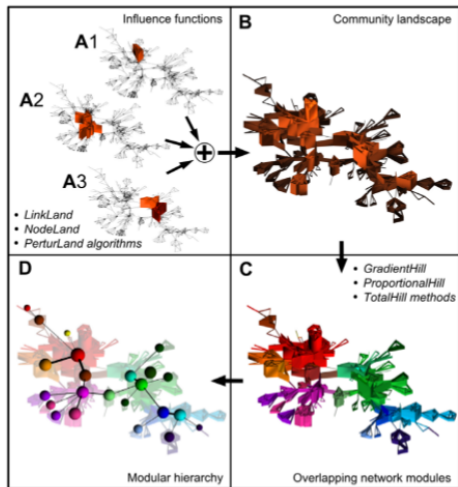
$$E_{\text{ox}} = 0.104 \text{ (57.5\%)}$$

TRENDS in Pharmacological Sciences

The efficiency of multi-target drugs: the network approach might help drug design

Péter Csermely¹, Vilmos Ágoston² and Sándor Pongor^{2,3}

Applications III. – Community detection methods



Steps of the ModuLand method family

Community Landscapes: An Integrative Approach to Determine Overlapping Network Module Hierarchy, Identify Key Nodes and Predict Network Dynamics

István A. Kovács^{1,2}, Robin Palotai¹, Máté S. Szalay¹, Peter Csermely^{1*}

Applications IV. – Perturbation propagation in networks

Signaling
pathway
resources

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OPEN ACCESS Freely available online



Perturbation Centrality and Turbine: A Novel Centrality Measure Obtained Using a Versatile Network Dynamics Tool

Kristóf Z. Szalay, Peter Csermely*

Department of Medical Chemistry, Semmelweis University, Budapest, Hungary

Acknowledgements

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Systems Biomedicine Group, EMBL-EBI, Hinxton

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NetBiol Group, Eotvos University, Budapest, Hungary
Link Group, Semmelweis University, Budapest, Hungary

Resources I.

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Applications

Data analysis, programming

<http://stackoverflow.com/>

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

Graph analysis software

<http://igraph.org/>

<https://graph-tool.skewed.de/>

<http://networkx.github.io/>

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

<http://www.linkgroup.hu/modules.php>

<http://turbine.hu/>

<http://www.traag.net/>

<https://github.com/vtraag/louvain-igraph>

<http://www.maths.qmul.ac.uk/~gbianconi/>

Resources II.

Signaling pathway resources

Dénes Túrei

Pathway resources

<http://signor.uniroma2.it/>

<http://signalink.org/>

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

<http://wodaklab.org/ws/>

<http://www.ebi.ac.uk/~denes/54b510889336eb2591d8beff/resources.html>

<http://dp.univr.it/~laudanna/LCTST/downloads/>

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

<http://ccsb.dfci.harvard.edu/web/www/ccsb/>

<http://www.barabasilab.com/>

<http://linkgroup.hu/>

<http://pandeylab.igm.jhmi.edu/>

<http://moleculargenetics.uniroma2.it/bcb/>

<http://www.cancer-systemsbiology.org/>

IPython notebook for today:

http://www.ebi.ac.uk/~denes/networks_pathways.ipynb