

Sources of signaling data

Signaling
pathway
resources

Dénes Türei

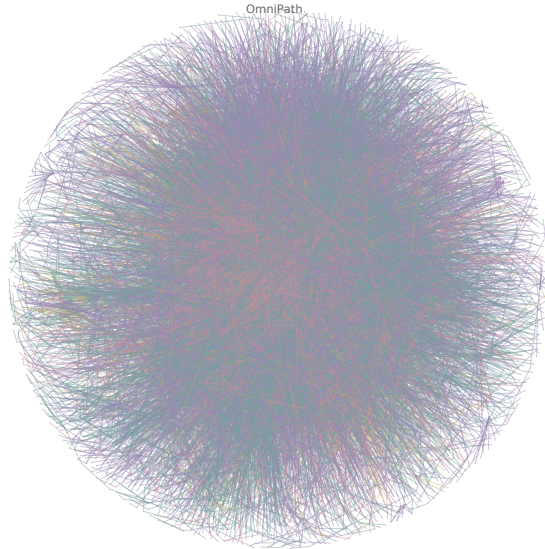
Resources

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Annotations

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Dénes Túrei

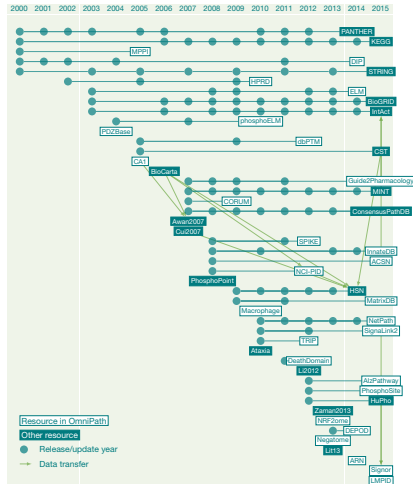
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Protein interaction
databases

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

Dénes Türei

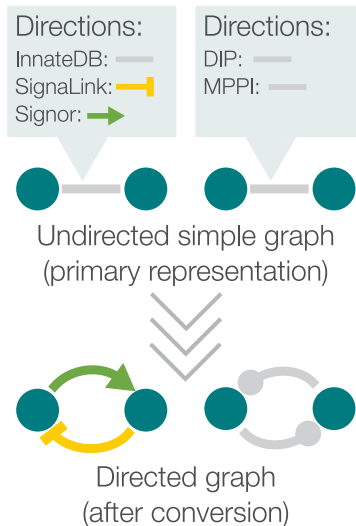
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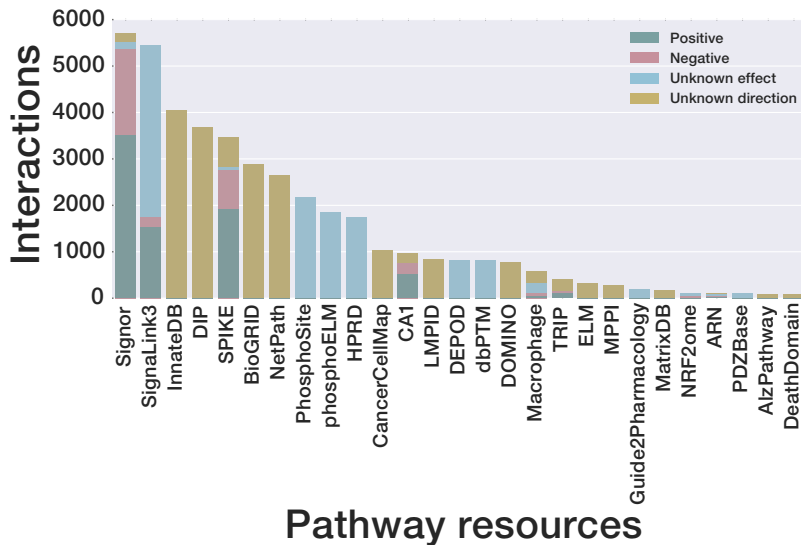
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Directions and effects



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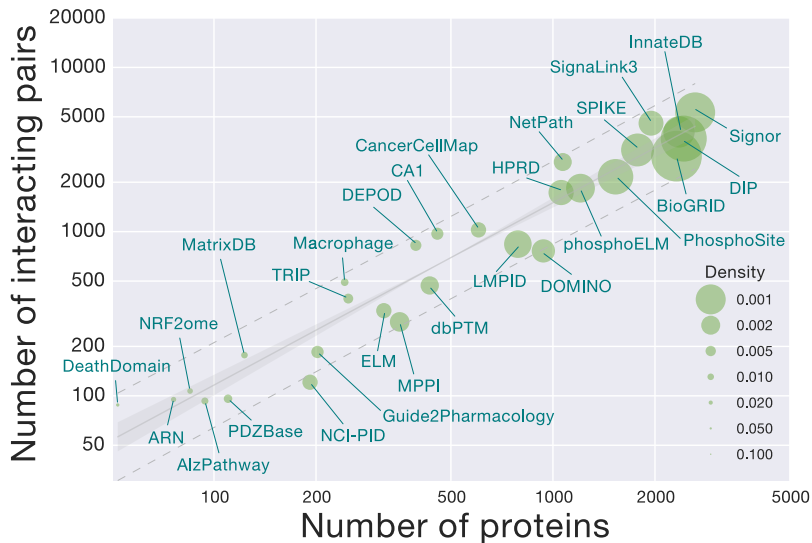
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Boundaries of our knowledge



Boundaries of our knowledge

Signaling
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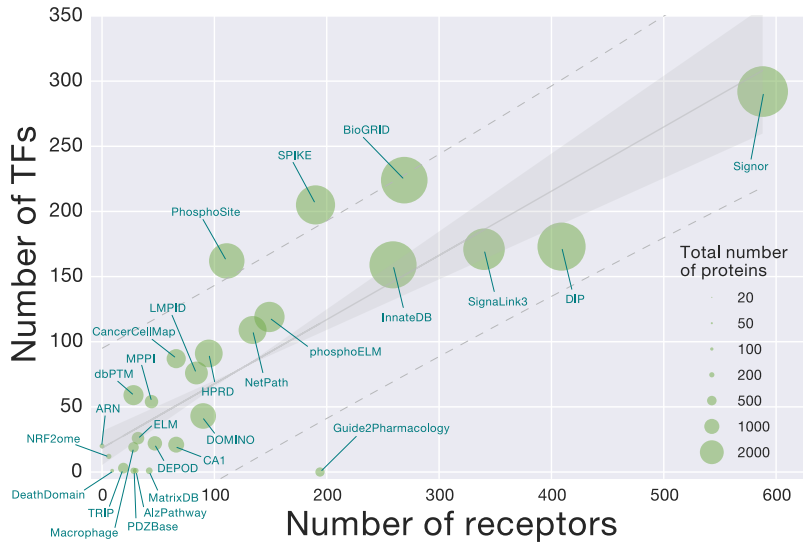
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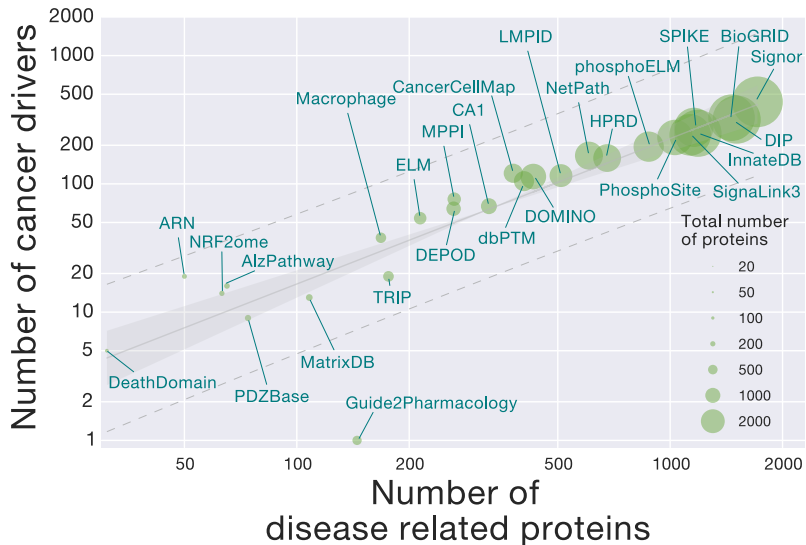
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Boundaries of our knowledge



Boundaries of our knowledge

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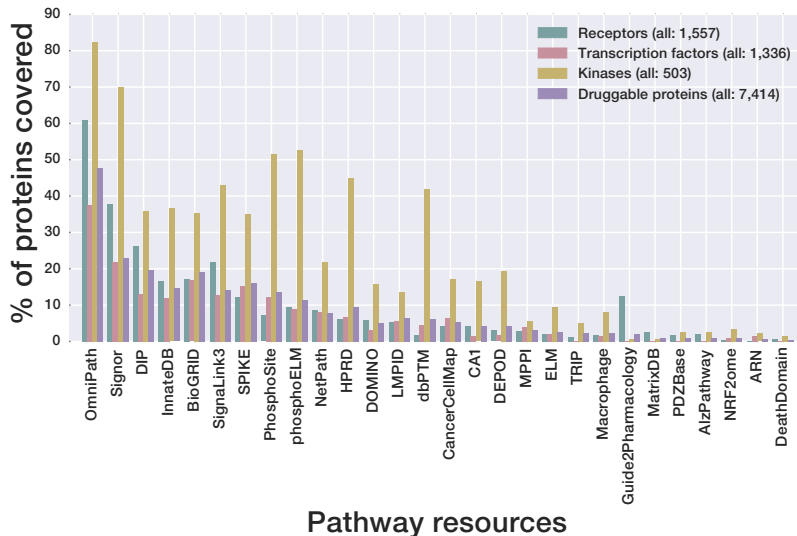
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Boundaries of our knowledge

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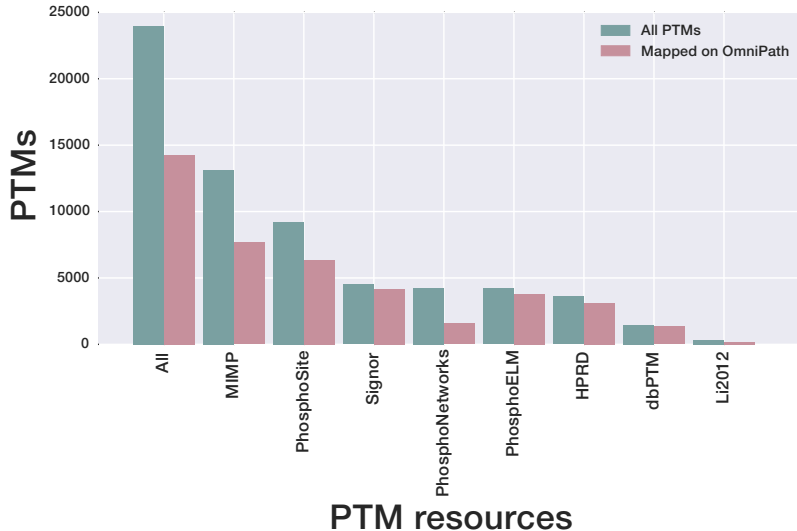
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Applications

Tedious work of curators

Signaling
pathway
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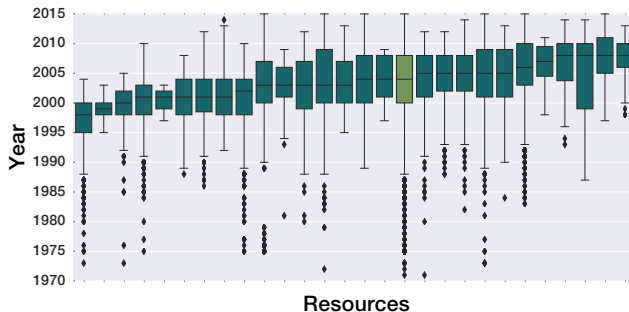
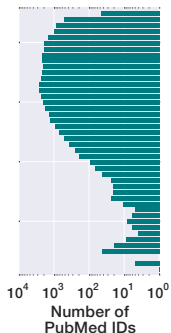
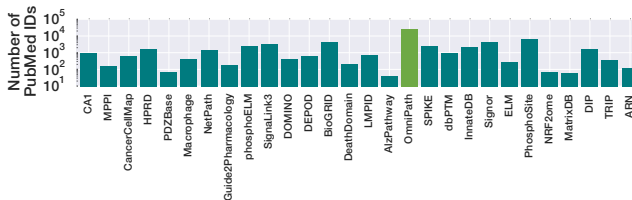
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Data integration

Signaling pathway resources

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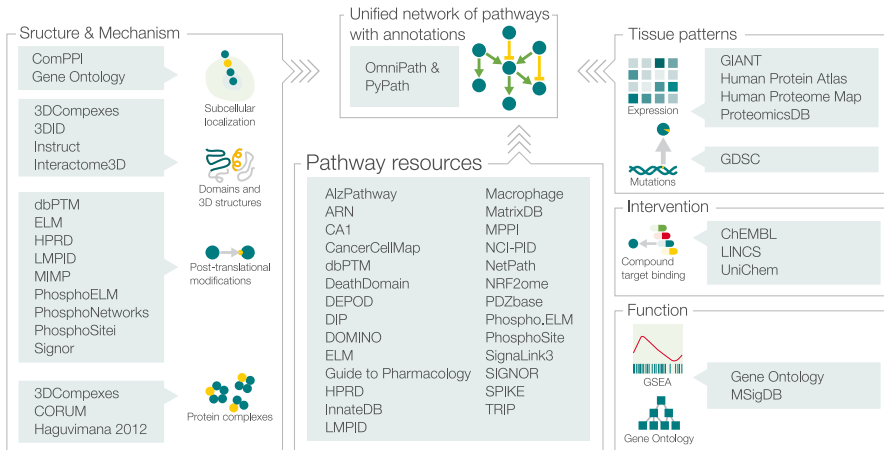
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Localization

Signaling
pathway
resources

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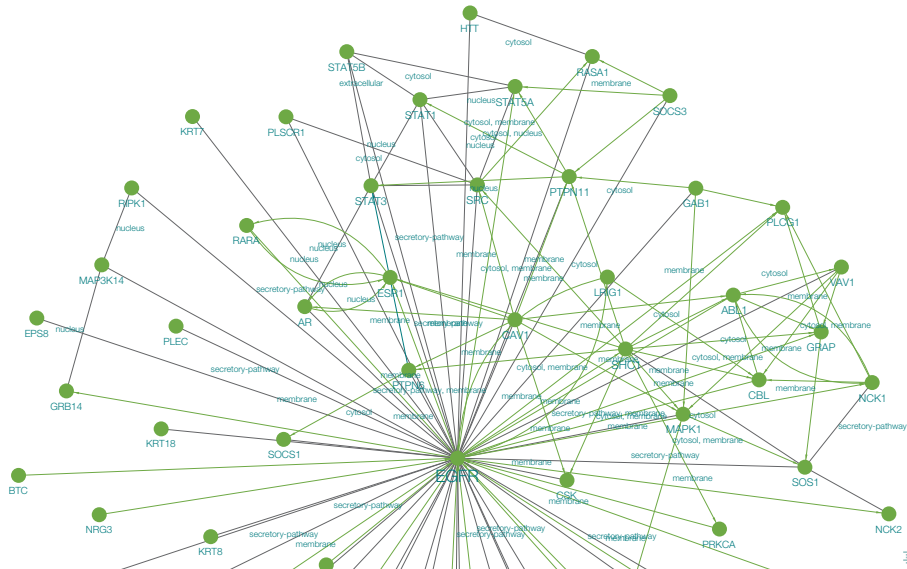
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Signaling pathway resources

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

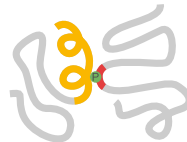


PhosphoSite
phosphoELM
iELM
Pepcyber
Domino

PISA
3DID
3DComplexes



Residue level



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



PhosphoSite
phosphoELM

Applications I. – PKN for logic models

Signaling
pathway
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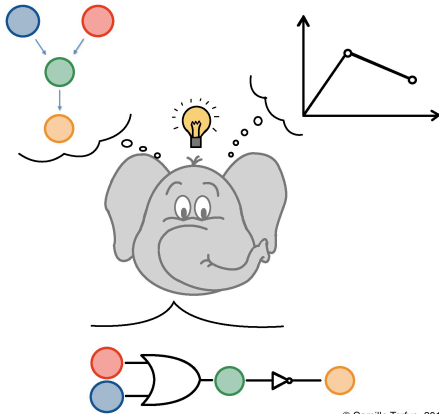
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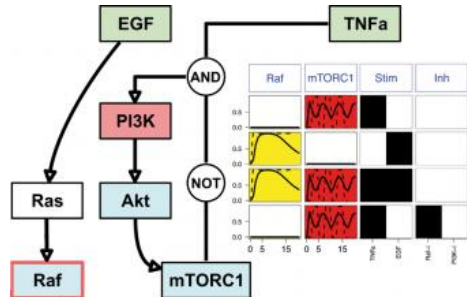
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Applications II. – Network topological methods

Signaling
pathway
resources

Dénes Túrei

Resources

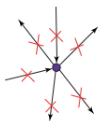
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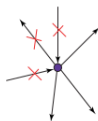
Applications

(a) Complete knockout

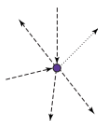


(b) Partial inactivation of several targets

(i) Partial knockout

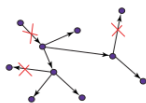


(ii) Attenuation

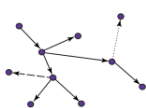


(c) Distributed system-wide attack

(i) Distributed knockout



(ii) Distributed attenuation

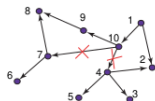


(d) Calculation of network efficiency

(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 | - |

$$E = 0.181$$

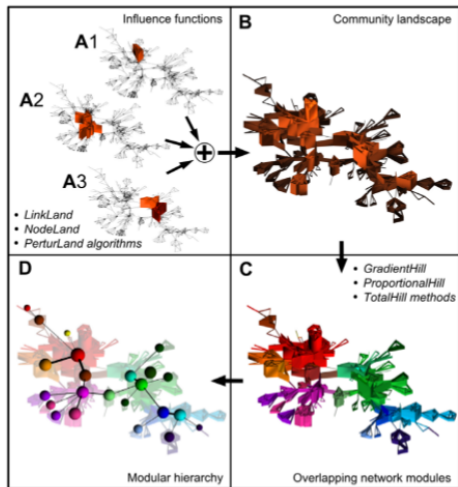
$$E_{\text{ox}} = 0.104 \text{ (57.5\%)}$$

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

Dénes Türei

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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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Link Group, Semmelweis University, Budapest, Hungary