Network Enrichment Analysis: Method, Software, And Web-Site For Functional Interpretation Of 'Omics' Data In Global Networks

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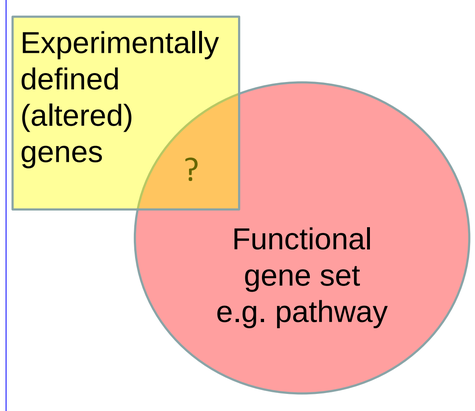
Network enrichment analysis: the concept

The overall goal of our tools for network enrichment analysis (NEA) is functional exploration of experimental data in either hypothesis-driven or hypothesis-free manner. Similarly to any biological observation, statistical significance of network patterns should always be estimated. This is done by comparing the network connectivity score either between or within gene sets to that expected by chance.

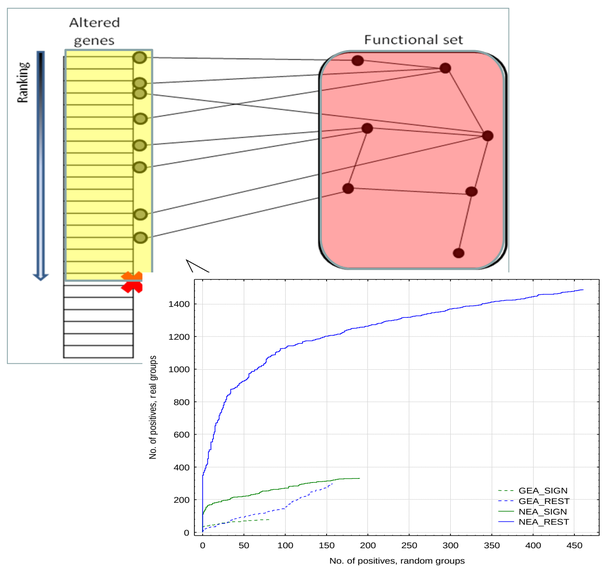
The method extends the gene set enrichment analysis (GSEA) into the network domain. The output and interpretation of NEA are similar to those of GSEA, but the sensitivity of NEA is higher ~5-10-fold. In addition, NEA is applicable to both gene sets and single genes, including those lacking any GO and pathway annotations.

Comparison to state-of-the-art method

Gene set enrichment analysis

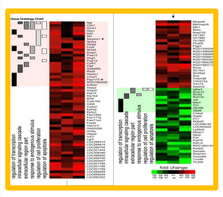


Network enrichment analysis

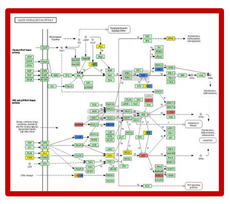


Alexeyenko A., Lee W., … Pawitan Y. **Network enrichment analysis: extension of gene-set enrichment analysis to gene networks.** *BMC Bioinformatics, 2012*

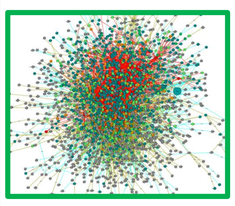
Three inputs to NEA



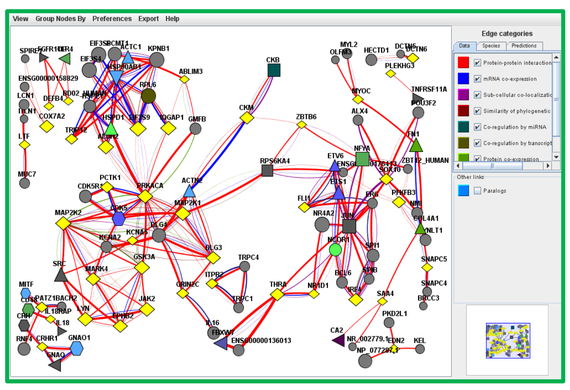
1) Your gene/protein set: mutations, rare variants, candidate disease genes, differentially expressed genes.



2) A collection of previously known functional sets: pathways, Gene Ontology terms etc.



3) A global network of interactions and relations between genes and proteins (known and/or predicted)

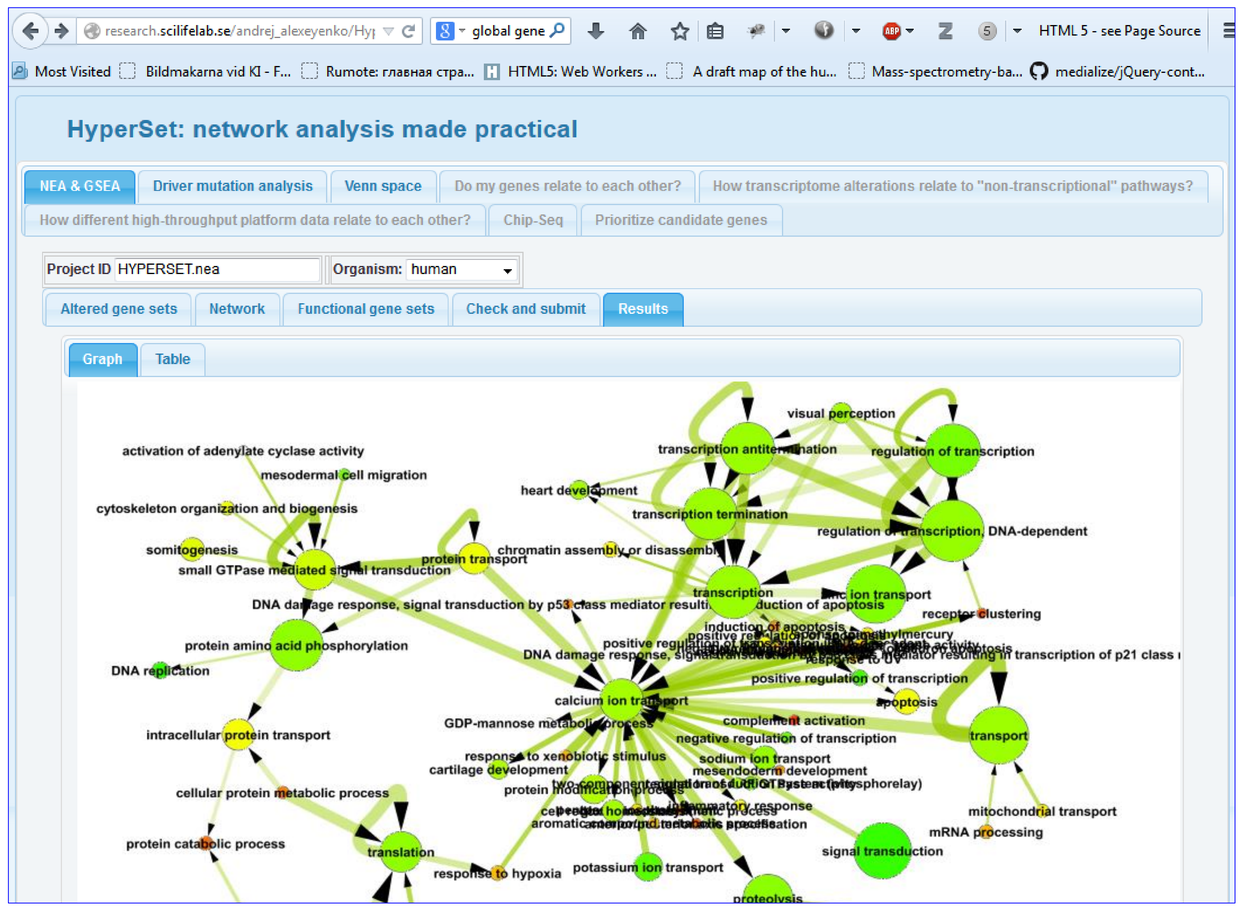


Alexeyenko A. and Sonnhammer E. **Global networks of functional coupling in eukaryotes by comprehensive data integration** *Genome Research, 2009*

NEA can also accommodate any custom/proprietary network

User-friendly implementation on-line

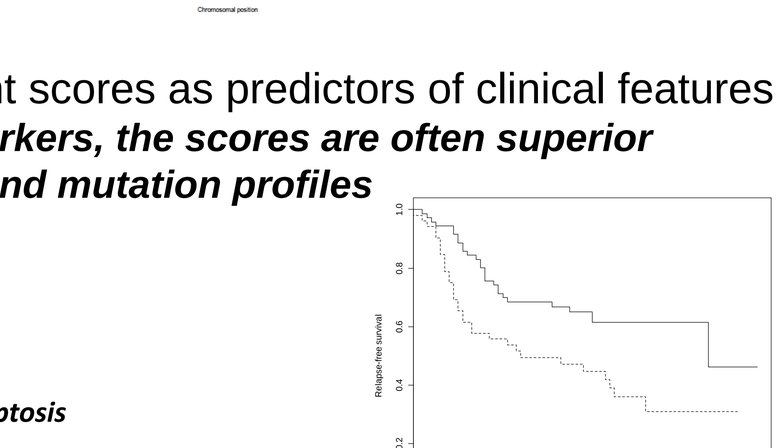
https://www.evinet.org/



Example applications

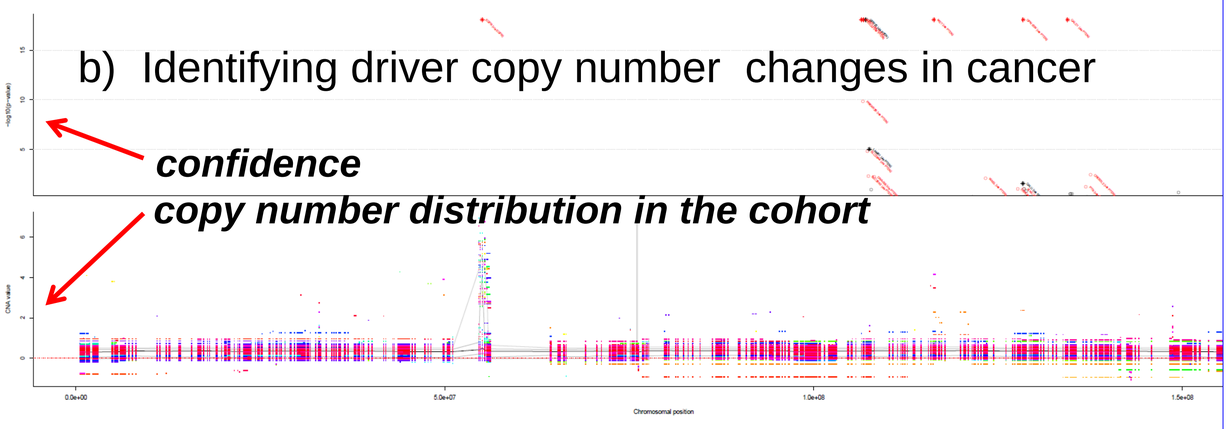
a) Distinguishing between driver and passenger cancer mutations

Red: drivers
Black: passengers



b) Identifying driver copy number changes in cancer

confidence
copy number distribution in the cohort



c) Network enrichment scores as predictors of clinical features

When used as biomarkers, the scores are often superior to gene expression and mutation profiles

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