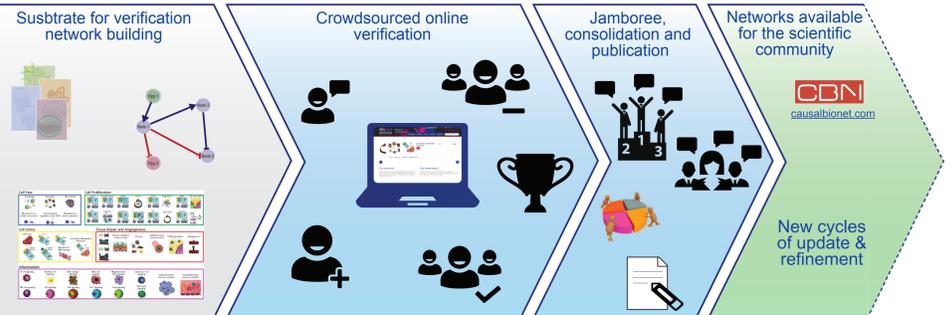




Network Verification Challenge



sbv IMPROVER project

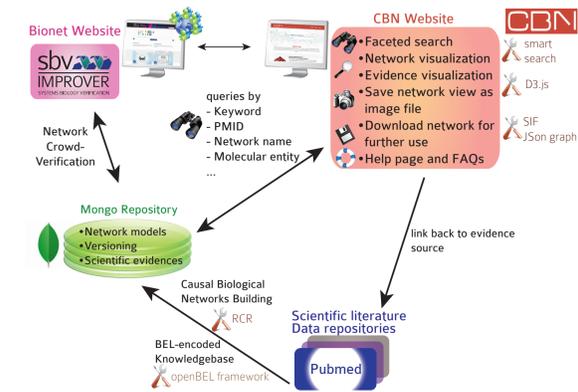
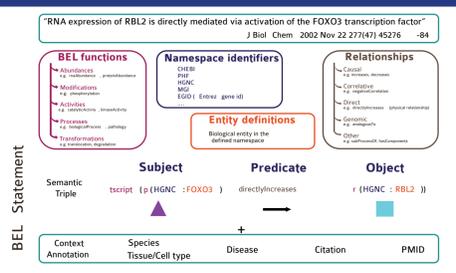
- Complements the classical peer review system
- Rigorous scrutiny of scientific research based on communities involvement
- A crowd sourcing approach of challenge-based evaluation of scientific methods
- A collaborative effort led and funded by PMI Research and Development
- Many contributors with independent methods / knowledge

Bionet - a platform with:

- Challenge explanation
- Network visualization
- Evidence visualization
- Comment and vote on evidence
- Create new edge / new supporting evidence
- Leaderboard / badges
- Activity feed

Verification and Sharing Platforms

Biological Expression Language (BEL)



A web-based crowdsourcing platform provides an easy way to share the network models allowing frequent updates by the scientific community. The platform is meant to facilitate the collaborative review of networks and is part of the sbvIMPROVER Network Verification Challenge (NVC) (<https://sbvimprover.com/>).

The CBN Database Web site (<http://causalbionet.com/>) offers an interface that accesses different versions of the network models, ranging from the 98 original non-diseased models (version 1.0, 98) to the consolidated COPD-relevant models (version 1.1), and to the crowd-verified network models during the first iteration of the NVC (version 1.2) and the second iteration of the NVC (version 2.0).

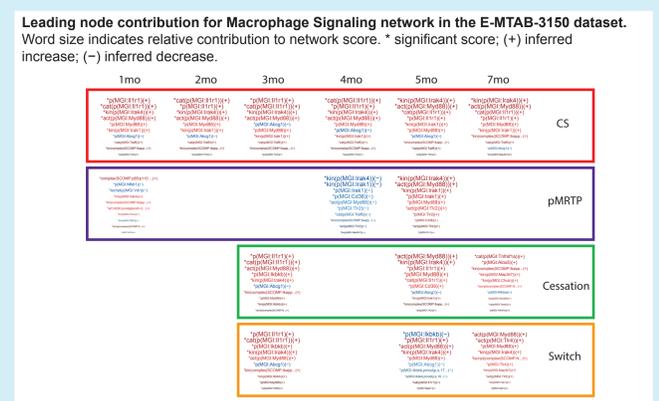
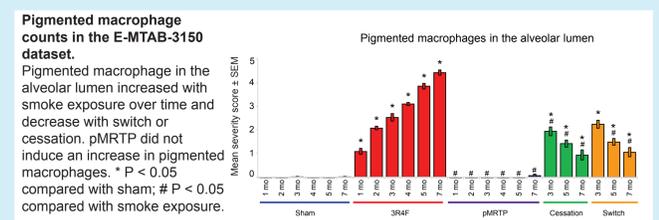
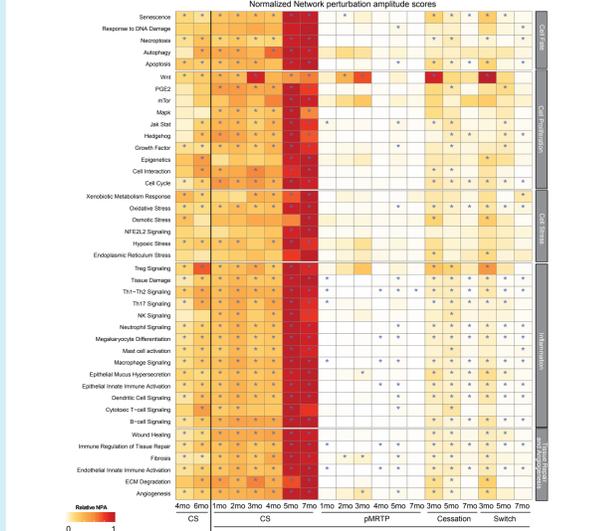
Network Statistics and Example Application

Network statistics for the Network Verification Challenge (NVC) v1.1 and v2.0 Bionet networks

Category	Network	Nodes	Edges	Mean Node Weight	Max degree	Mean path length	Clustering	Modularity
Cell Fate	Sensory-210	209	313	1.5	10	2.5	0.7	0.8
	Response to DNA Damage-11	205	324	1.6	12	2.4	0.7	0.8
	Response to DNA Damage-210	203	324	1.6	12	2.4	0.7	0.8
	Neurogenesis-210	179	129	1.4	12	2.5	0.7	0.8
	Neurogenesis-11	168	89	1.0	9	1.9	0.7	0.8
	Neurogenesis-210	132	220	1.6	15	2.5	0.7	0.8
	Apoptosis-210	105	244	2.3	11	2.0	0.7	0.8
	Apoptosis-11	105	244	2.3	11	2.0	0.7	0.8
	Apoptosis-210	105	244	2.3	11	2.0	0.7	0.8
	Apoptosis-11	105	244	2.3	11	2.0	0.7	0.8
Cell Proliferation	Wnt-210	84	134	1.6	12	2.5	0.7	0.8
	PCG2-210	73	84	1.1	10	1.9	0.7	0.8
	PCG2-11	68	72	1.0	10	1.9	0.7	0.8
	Nuclear Receptor-210	41	43	1.0	10	1.9	0.7	0.8
	Nuclear Receptor-11	38	43	1.1	10	1.9	0.7	0.8
	Noto-210	19	19	1.0	10	1.9	0.7	0.8
	Noto-11	19	19	1.0	10	1.9	0.7	0.8
	mTOR-11	14	14	1.0	10	1.9	0.7	0.8
	MAPK-11	14	14	1.0	10	1.9	0.7	0.8
	MAPK-210	14	14	1.0	10	1.9	0.7	0.8
Cell Stress	Cell Death-210	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-11	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-210	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-11	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-210	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-11	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-210	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-11	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-210	85	89	1.0	10	1.9	0.7	0.8
	Cell Death-11	85	89	1.0	10	1.9	0.7	0.8
Inflammation	Xenobiotic Metabolism Response-210	203	214	1.0	10	2.0	0.7	0.8
	Xenobiotic Metabolism Response-11	200	214	1.0	10	2.0	0.7	0.8
	Chemokine Response-210	100	100	1.0	10	2.0	0.7	0.8
	Chemokine Response-11	100	100	1.0	10	2.0	0.7	0.8
	Chemokine Response-210	100	100	1.0	10	2.0	0.7	0.8
	Chemokine Response-11	100	100	1.0	10	2.0	0.7	0.8
	Chemokine Response-210	100	100	1.0	10	2.0	0.7	0.8
	Chemokine Response-11	100	100	1.0	10	2.0	0.7	0.8
	Chemokine Response-210	100	100	1.0	10	2.0	0.7	0.8
	Chemokine Response-11	100	100	1.0	10	2.0	0.7	0.8
Immune Response	Reg Signaling-210	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-11	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-210	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-11	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-210	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-11	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-210	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-11	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-210	86	78	1.0	10	2.0	0.7	0.8
	Reg Signaling-11	86	78	1.0	10	2.0	0.7	0.8

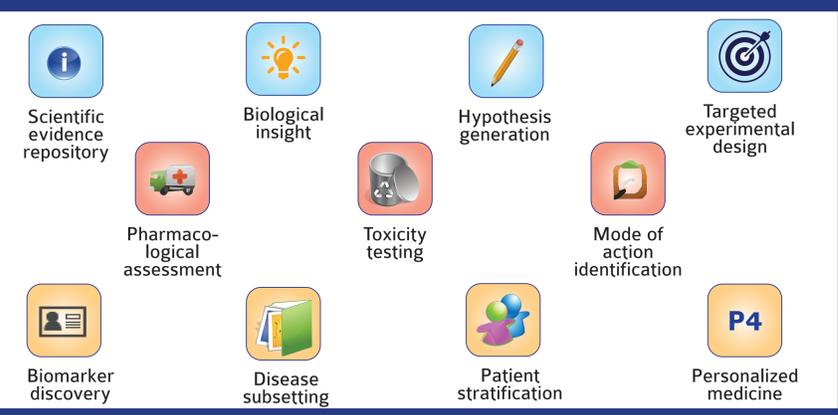
Quantification/comparison of toxicity in two related datasets using the network suite

Heatmap of network scores comparing the impact of cigarette smoke exposure, pMRTP aerosol exposure and cessation in the E-MTAB-3150 and GSE52509 datasets. Each treatment is compared to fresh air at the same time point. Scores are normalized to the maximum scores for each network. A network is considered impacted if, in addition to the significance of the score with respect to the experimental variation, the two companion statistics (O and K) derived to inform the specificity of the score with respect to the biology described in the network, are significant. * O and K statistic p-values below 0.05 and NPA significantly non-zero.



Community-reviewed Biological Network Models for Toxicology and Drug Discovery Applications. Gene Regulation and Systems Biology, 2016.

Foreseen Applications



Key References

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- A network-based approach to quantifying the impact of biologically active substances. Drug Discov Today, 2012.
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- A computable cellular stress network model for non-diseased pulmonary and cardiovascular tissue. BMC Syst Biol, 2011.
- Construction of a computable cell proliferation network focused on non-diseased lung cells. BMC Syst Biol, 2011.
- A modular cell-type focused inflammatory process network model for non-diseased pulmonary tissue. Bioinform Biol Insights, 2013.
- A 7-month cigarette smoke inhalation study in C57BL/6 mice demonstrates reduced lung inflammation and emphysema following smoking cessation or aerosol exposure from a prototypic modified risk tobacco product. Food and Chemical Toxicology, 2015

The sbv IMPROVER project, the website and the symposia are part of a collaborative project designed to enable scientists to learn about and contribute to the development of a new crowd sourcing method for verification of scientific data and results. The current challenges, website and biological network models were developed and are maintained as part of a collaboration among Philip Morris International, Selventa, OrangeBus, and ADS. The project is led and funded by Philip Morris International. For more information on the focus of Philip Morris International's research, please visit www.pmisce.com.