

PSF calculation on MAPK signaling pathway: a use case

The following options and rules were applied for PSF calculation on the MAPK signaling pathway model used by Nelander *et al* [1], as described in the manuscript. These options are adopted from a previously published Pathway Signal Flow algorithm [2]

Node data

Node data is in the form of fold change values – the ratios of absolute protein phosphorylation levels between the studied condition and the reference. For each of the six experiments described in the manuscript, one node was downregulated and assigned *fc* value of 0.1, while the rest of the nodes were assigned *fc* values of 1.0.

Simple rules

The network should contain two edge types: e.g. activation and inhibition, with the following rules:

EdgeTypes config file:	Rule config file:
<code>activation *</code>	<code>* source * target</code>
<code>inhibition /</code>	<code>/ 1/source * target</code>

Multiple input and output edge rules

The signal is split according to relative fold change values of multiple source nodes.

Signal split rule: *Proportional*

Split signal on: *Incoming edges*

The signals coming from multiple sources are added to each other to generate the signal at the target node:

Multiple signal

processing rule: *Addition*

The order of edges does not matter:

Signal processing

order: *None*

Multiple input and output edge rules

Signal split rule

☐ None ☒ Proportional ☐ Equal

☐ Supplied weights

Split signal on

☒ Incoming edges ☐ Outgoing edges

Multiple signal processing rule

☐ Updated node scores

☐ Multiplication ☒ Addition

Signal processing order

☒ None ☐ Edge ranks

Loops:

The **loops** option is set to “*Iterate until convergence*” mode, with convergence threshold set to 1 %.

References

1. Nelander S, Wang W, Nilsson B, *et al*: Models from experiments: combinatorial drug perturbations of cancer cells. *Mol Syst Biol*. 2008; **4**: 216.
2. Arakelyan A, Aslanyan L, Boyajyan A: High-throughput Gene Expression Analysis Concepts and Applications. Sequence and Genome Analysis II – Bacteria, Viruses and Metabolic Pathways. *iConcept Press*. 2013; ISBN: 978-1-480254-14-5.