

Computational modeling of biased signaling in G protein-coupled receptors

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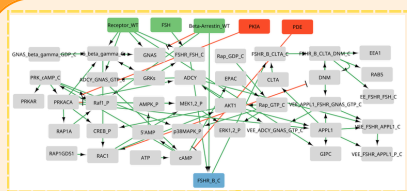
Why?

G protein-coupled receptors (GPCRs) regulate a wide range of cellular responses, and their pharmacological complexity enables selective control of signaling pathways through a process known as biased signaling. It is challenging to decipher these complex signaling networks with the use of traditional methods.

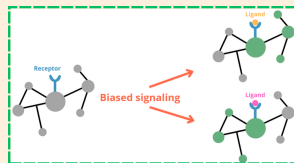
What?

This project aims to develop computational models of GPCR-dependent signaling using Boolean formalism (BNs) and Answer Set Programming (ASP).

How?



Biased signaling



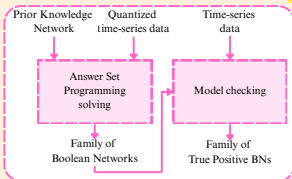
Network analysis

Expert knowledge

Time-series data

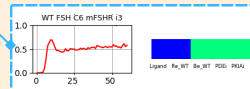
Data preprocessing

Infers GPCR signaling Boolean networks [1].



Caspo-ts

Multi-valued networks

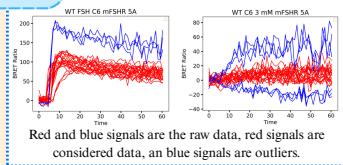


Results

Network analysis

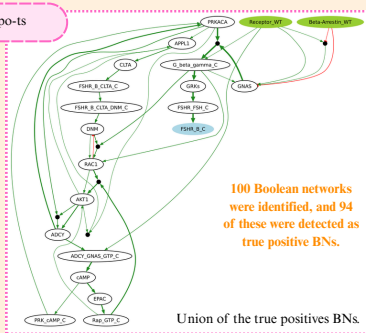
PKA plays a central role in the signaling pathways, as it obtained the highest values in closeness centrality, betweenness centrality, and degree.

Data preprocessing



Red and blue signals are the raw data, red signals are considered data, and blue signals are outliers.

Caspo-ts



100 Boolean networks were identified, and 94 of these were detected as true positive BNs.

Union of the true positives BNs.

Future work

Continue working on multi-valued networks (MVNs).

Test using simulated data.

Incorporate more expert knowledge, and datasets.

Analyze the biological relevance of the inferred Boolean networks.

Analyze biased signaling: how specific network nodes influence pathway selection.

References

[1] M. Razzaq, et al. Computational discovery of dynamic cell line specific boolean networks from multiplex time-course data. PLoS computational biology, 14(10):e1006538, 2018.