From quantitative SBML to boolean networks
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SBML is the de facto standard to encode and exchange models of biological systems in various formalisms. More than 300 curated SBML models of the repository Biomodels are quantitative. We aim at automatically converting these SBML models into a set of compatible Boolean networks. Here, we present our pipeline SBML2BN, which consists in extracting the model structure from the input SBML model and to retrieve the dynamics of the model by deterministic simulation. The structure and dynamics are then used to synthesise a set of compatible BNs. Finally, the obtained BNs are evaluated. We have tested SBML2BN on 200 models for which we show that it is overall efficient and successful.

SBML2BN Pipeline

Quantitative Model

\[
\text{De facto standard} \\
\text{Network of reactions} \\
S + E \xrightarrow{k_{on} / k_{off}} \text{ES} \\
\text{ES} \xrightarrow{k_{cat}} \text{E} + \text{2P} \\
\]

TS Extraction = simulation + discretisation

\[
S \xrightarrow{X} \text{E} \xrightarrow{Y} G \text{if } \exists \text{ a reaction in which:} \\
\bullet \text{X a reactant or activator, and Y} \downarrow \\
\bullet \text{X an inhibitor and Y} \uparrow \\
\]

PKN Extraction

\[
X \rightarrow Y \in G \text{ if } \exists \text{ a reaction in which:} \\
\bullet \text{X a reactant or activator, and Y} \downarrow \\
\bullet \text{X an inhibitor and Y} \uparrow \\
\]

(Set of) Boolean Network(s) + Quality Check

\[
f_{as} := S \\
f_{D} := ES \\
f_{s} := ES \\
f_{I} := -S \\
\]

Compatable structure

\[\text{iff IG} \subseteq \text{PKN}\]

Compatable dynamics

\[\text{iff TS} \subseteq \text{general async. STG or good "coverage proportion"}\]

Boolean Networks Synthesis

Ideally: only BNs compatible with the given PKN and with the best coverage of the TS as possible

TS PKN assumptions

REVEAL & Best-Fit binarized complete \(\checkmark\) unsigned time unit = 1

caspo-TS [2] numeric \(\checkmark\) partial signed \(\checkmark\) local-monotony

ASKeD-BN [3] numeric \(\checkmark\) complete \(\checkmark\) signed \(\checkmark\)

Answer-Set Programming + Python

Evaluation of the Coverage

\[
\text{Median coverage median = 0.77} \\
\text{Coverage variance of 0, even when > 1 BN synthesised, except for 12 models (red circles in the figure on the right)}
\]

Models not “well-formed” [3]?

Example: BIOMD n°44 has reaction kinetics using components not listed in the reactants nor modifiers
\(\rightarrow\) PKN not complete (missing parents)
\(\rightarrow\) 1 BN generated with a coverage of 0.55

Models not “well-formed” [3]?

References:
[1] Fages et al. 2012 hal-00723554