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From Quantitative SBML to Boolean Networks

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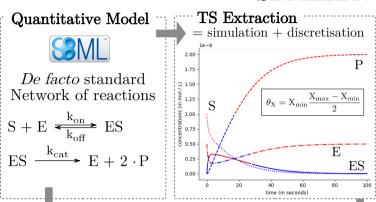
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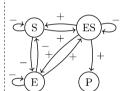


SBML is the de facto standard to encode and exchange models of biological systems in various formalisms. More than 300 curated SBML models of the repository Biomodels are quantitative. We aim at automatically converting these SBML models into a set of compatible Boolean networks. Here, we present our 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



PKN Extraction



 $X \xrightarrow{-} Y \in \mathcal{G}$ if \exists a reaction in which:

- X a reactant or activator, and Y\
- X an inhibitor and Y ≥

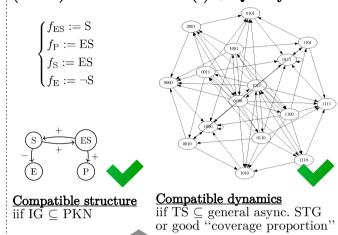
 $X \stackrel{+}{\rightarrow} Y \in \mathcal{G}$ if \exists a reaction in which:

- X a reactant or activator, and Y/
- X an inhibitor and Y\

Implementation uses:



$(Set ext{ of})$ Boolean Network(s) + Quality Check



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 &	binarized	unsigned	$\overline{\text{time unit} = 1}$
Best-Fit	complete \checkmark	unsigned	
caspo-TS [2]	numeric \checkmark	signed \checkmark	local-monotony
	partial		
ASKeD-BN [3]	numeric \checkmark	signed ✓	
ADICED DIN [9]	complete \checkmark	signed v	
<u> </u>			
	Answer-Set	Programmi	ng + Python

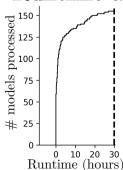
Models for the Evaluation

Curated branch of Biomodels release 31 (June 2017)

- 640 models in total
- 369 complete quantitative models = those with a PKN and a TS
- 209 models evaluated = models with all the components having less than 10 parent nodes. They have from 1 to 70 components



Runtime and # BN Synthesised



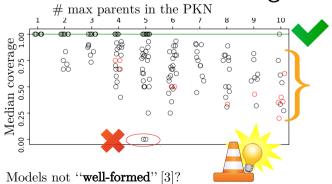
155 models processed in \leq 30 hours \sim half processed in < 30 mins

106 models w/ a unique BN synthesised

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

 \rightarrow Overall, the pipeline is good

Evaluation of the Coverage



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

References:

- Fages et al. 2012 hal-00723554
- Ostrowski et al. 2016 doi:10.1016/j.biosystems.2016.07.009
- 3 Vaginay et al. 2021 doi:10.1007/978-3-030-85672-4_12











