Visualizing Rule-based Models

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***Short Abstract* — Rule-based models are a useful framework to represent reaction biochemistry. Combinatorial complexity in such models prevents circuit diagrams of such models as being useful for visualization and communication. Several recent approaches have targeted visualization conventions, either for biochemistry in general or for a limited rule-based syntax. Here we provide a systematic approach to visualizing a rule-based model using information extracted from the model: the bipartite transformation graph and the bipartite rule graph. The approaches are grounded in the general and flexible BioNetGen syntax. We also provide an algorithm to coarse-grain from the bipartite graphs to intuitive signal-flow diagrams.**

***Keywords* — rule-based modeling, visualization, reaction networks, signal flow diagrams, combinatorial complexity, contact map**

I. Motivation

VISUALIZATION diagrams are important tools to communicate the structure and features of biochemical models. Network-based conventions such as SBGN:PD[1] and SBGN:ER[1] are hindered by combinatorial complexity[2], where the number of explicit states is an extremely large number of combinations of a few implicit states. Signal-flow diagrams (e.g. SBGN:AF[1]) with ambiguous conventions are the most widely used in the literature to convey "how a model or system works".

Rule-based modeling (BioNetGen[3], Kappa[4]) uses a structural abstraction to create classes of reactions that implicitly represent a reaction network. This has not only increased the scope of models being constructed (e.g. [5]), but it has also enabled new visualization techniques (contact map[4], and the rule influence graph[6]). These graphs are automatically generated and useful for modeling, but they are poor representations of signal flow.

The Kohn molecular interaction map[7] and the Extended Contact Map[8] focus on the correspondence between model and biochemistry by assigning graphical conventions to commonly known biochemical processes. These maps are manually constructed with expert knowledge and their relationship to the model structure is not immediately obvious. The extended contact map thus recommends an Annotated Model Guide[8] to be used alongside, where the reaction rules used to model a particular interaction are explicitly annotated.

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Rxncon[9] uses a restricted rule-based syntax which facilitates visualization. The rxncon reaction graph[9] is a bipartite graph representing model states and processes and the connections between them. The reaction graph is a good indicator of signal flow in a model and it will be useful to have a bipartite state/process graph visualization for BioNetGen models that is automatically generated from model structure. Here we generalize the reaction graph approach to general BioNetGen syntax and provide a coarse-graining method to automatically extract signal flow information from rule-based models.

II. Work

A. Bipartite Transformation Graph

The bipartite transformation graph is the equivalent of the rxncon reaction graph, but incorporating general BioNetGen syntax and using BioNetGen conventions such as reaction center and reaction context[10]. Conventions are defined to systematically extract information from BioNetGen objects that are equivalent to "states" and "reactions" in rxncon. We also demonstrate a scalable layout using lists instead of alternating levels for the bipartite nodes.

B. Bipartite Rule Graph

The bipartite rule graph is an extension of the bipartite transformation graph that accommodates the flexibility of BioNetGen syntax such as simultaneous transformations, multiple components, etc.

C. Coarse-grained Model Visualization

The coarse-graining approach uses two complementary techniques: (1) aggregating a set of nodes into a single node and (2) converting bipartite graphs into unipartite graphs by eliminating a node-type. The input is the information extracted from the model for the bipartite transformation graph. The output of the coarse-graining process is information at a level of detail similar to SBGN:AF and other signal-flow diagrams.

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