

Visual Tools for Modeling and Simulation of Cell Signaling Networks

Adam M. Smith^α, Wen Xu^α, Yao Sun^α, James R. Faeder^β, G. Elisabeta Marai^α

^αDepartment of Computer Science ^βDepartment of Computational and Systems Biology

University of Pittsburgh

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MOTIVATION: CELL SIGNALING

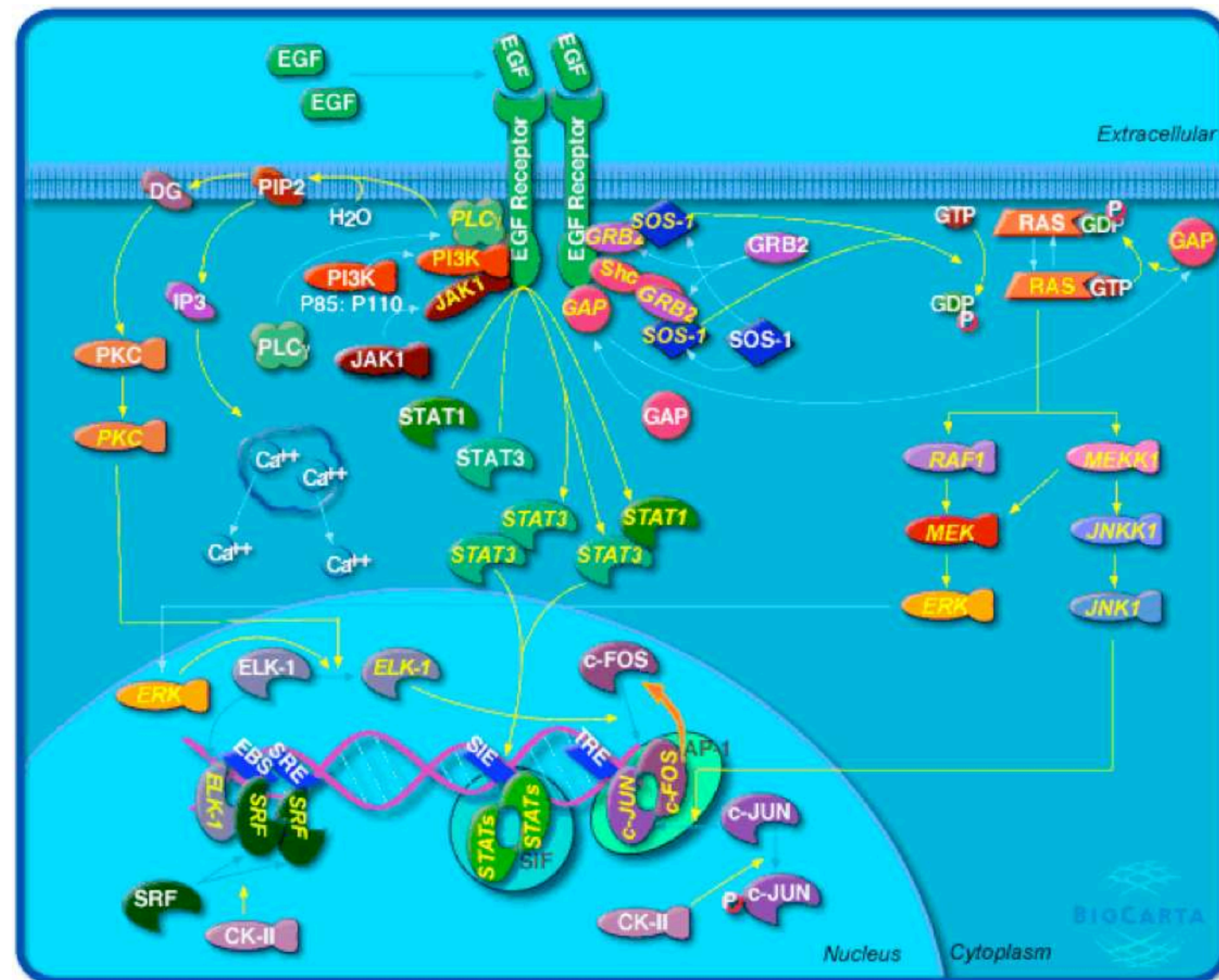


Figure 1: Hand drawn diagram of cell signaling network.

- *Cell Signaling* is the propagation of chemical messages through molecular networks.
- Figure 1 shows an example of a complex network of biological interactions.
- Studying cell signaling pathways leads to drug discovery and possible treatment for maladies such as cancer, diabetes, and genetic disorders

RULE-BASED MODELING AND SIMULATION

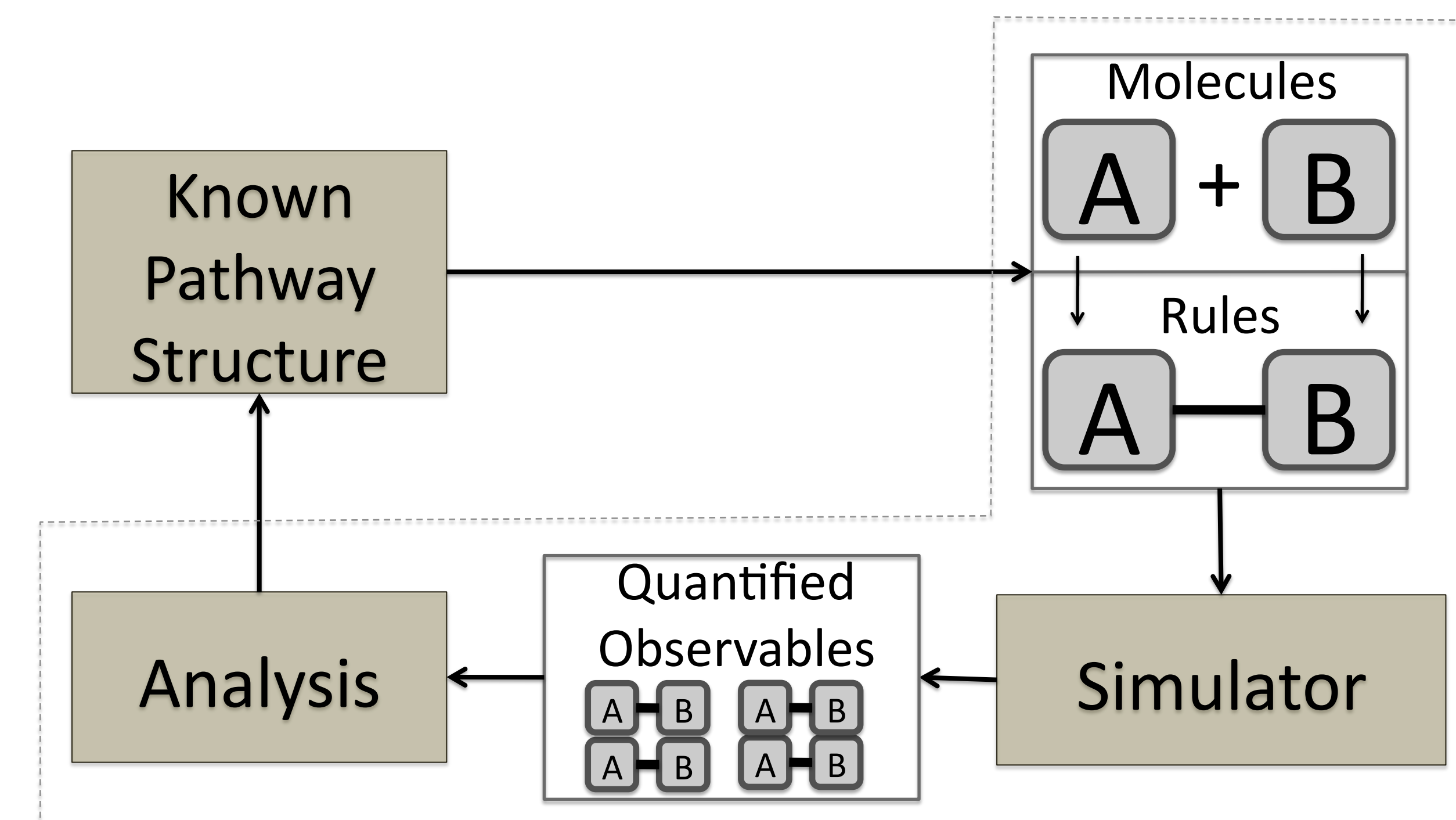


Figure 2: Rule-based modeling and simulation rely on known network structure, and can offer predictions for future experimental analysis.

- Traditionally, researchers use chemical experiments in order to observe reactions and build upon the existing knowledge of the community.
- *Rule-based* computational models are used to supplement physical experimentation and as shown in Figure 2.
- Rules are comprised of a collection of molecules (the *reactants*) that when combined can create new molecules (the *products*) by either breaking or creating *bonds* between the molecules.
- Simulators apply rules to a starting set of molecules and then report the quantity of each type of compound in the resulting system.

BIONETGEN: RULE-BASED MODELING AND SIMULATION TOOL

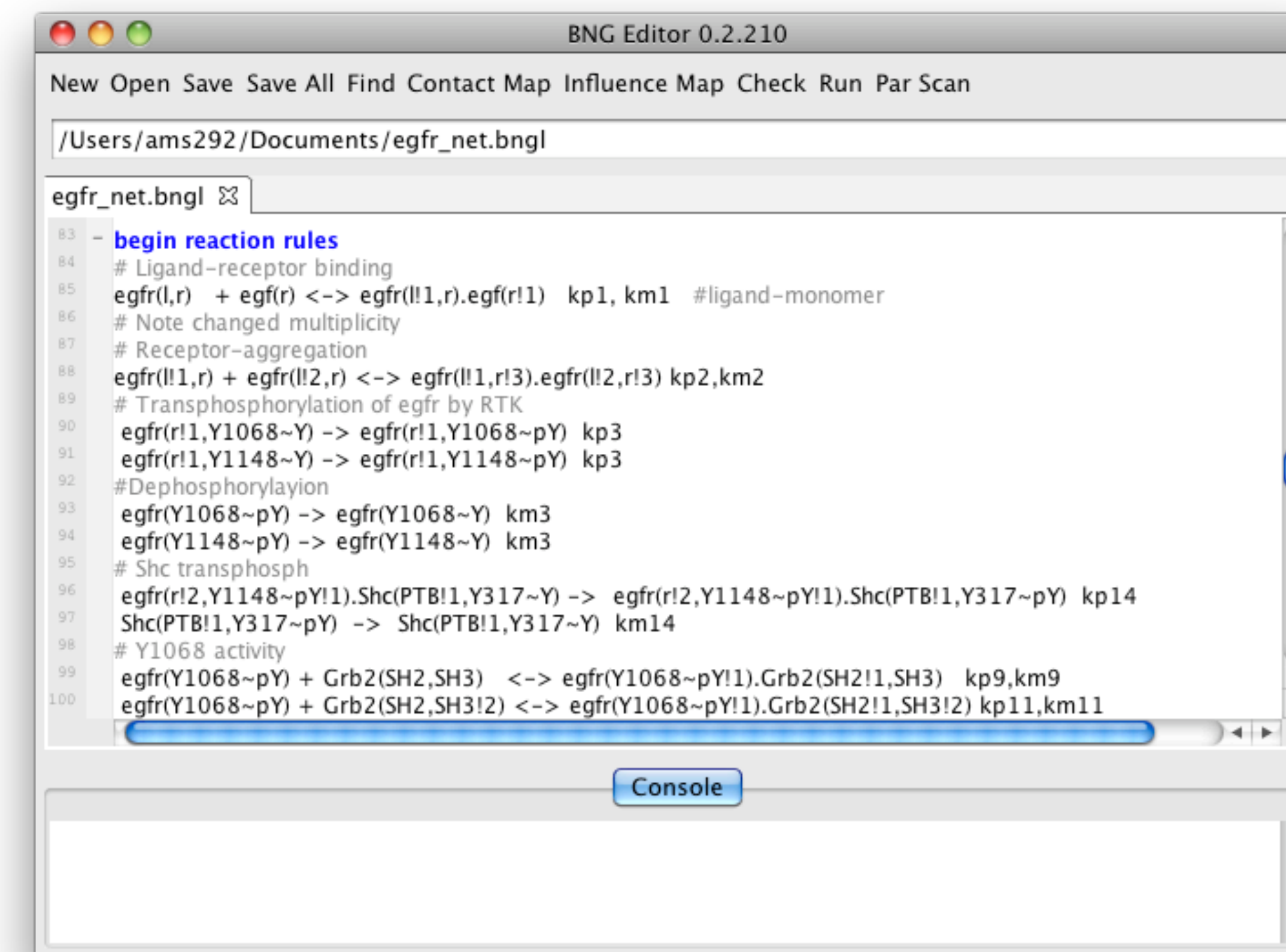


Figure 3: The main BNG Editor window.

- The BioNetGen (BNG) Language and simulator allow for model construction and simulation through a textual description of the system.
- Complexity of textual modeling may be prohibitive to biologists without programming experience.
- We are developing the BNG Editor: an Integrated Development Environment (IDE) that aims to decrease the difficulty of rule-based modeling and simulation using visualization, syntax highlighting, model syntax checking, and integrated execution in order to aid in the construction and analysis of networks.

VISUAL AND EXECUTABLE MODELS

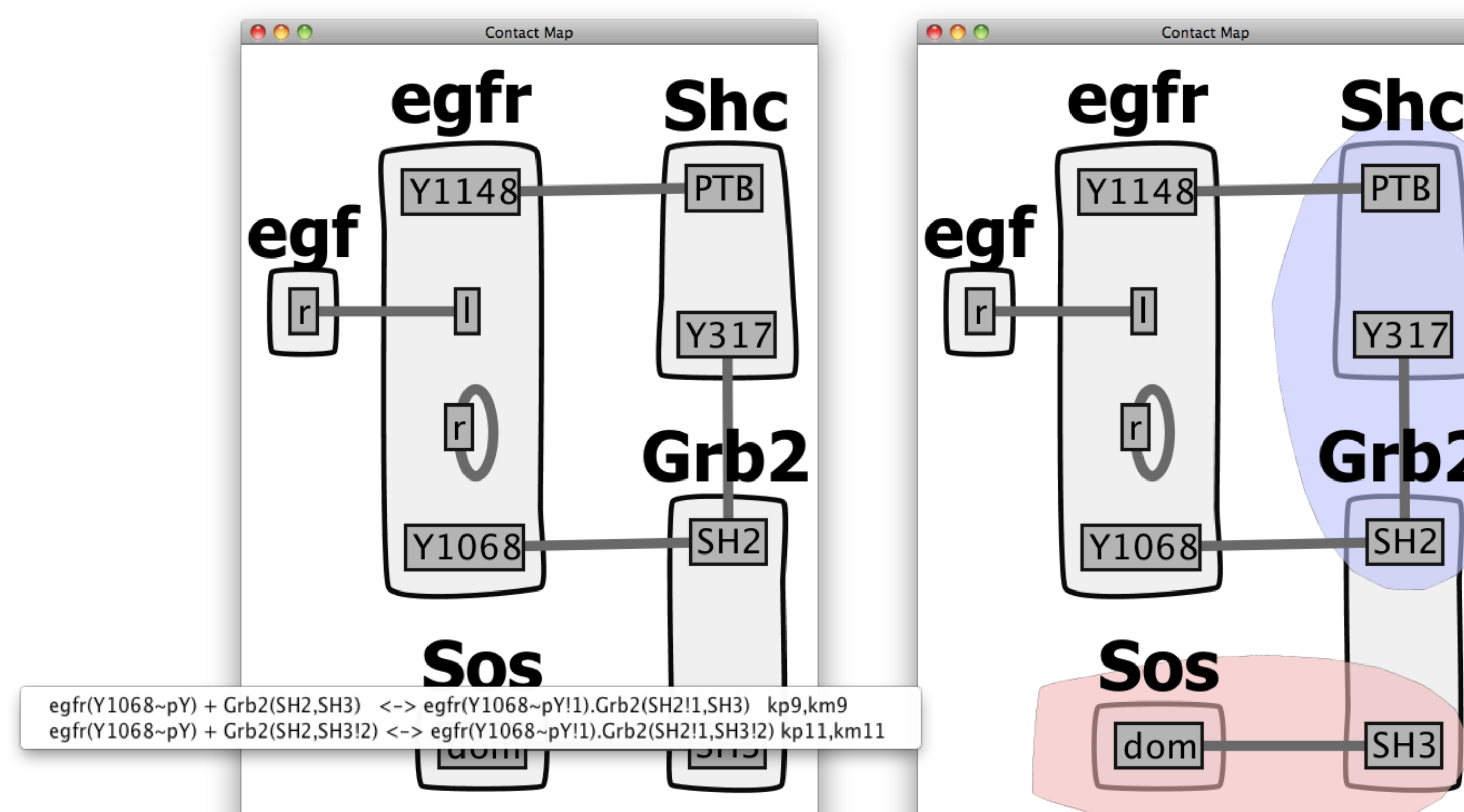


Figure 4: Left: The interactive contact map visualizes molecules and rules that may potentially affect the bonds that they create. Right: Colored overlays reveal additional rule information.

- While the user edits a model in the main window (see Figure 2), the interactive contact map visualizes molecules and the bonds that the rules affect.
- Clicking on a bond in the contact map lists the rules that may create that bond.
- Clicking on a rule renders a bubble sets overlay that shows additional rule information.

SIMULATION AND RESULTS ANALYSIS

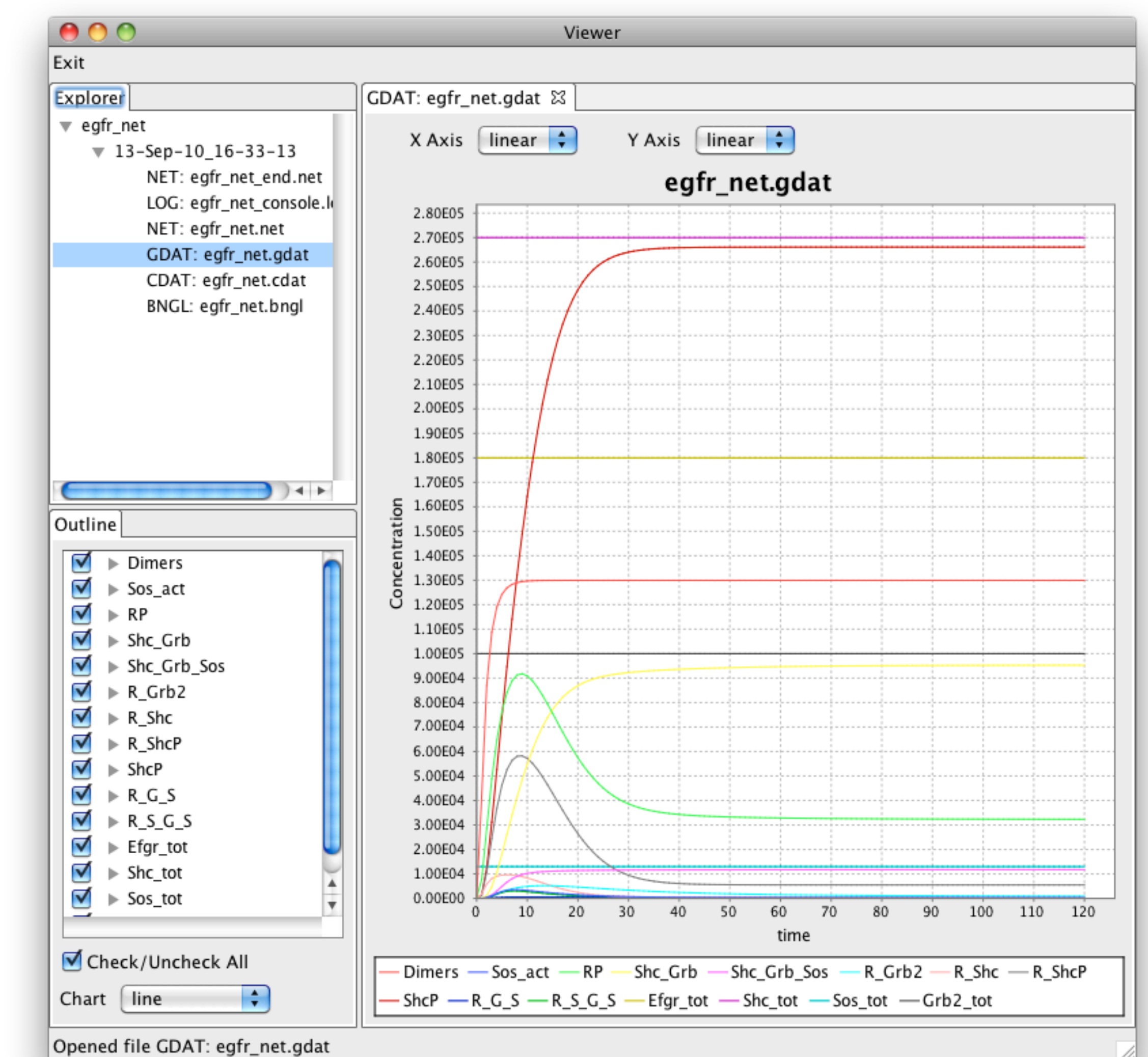


Figure 5: The results viewer displays the files that are produced by the simulator. The upper left pane allows the user to select a file to view.

- The created model is executed from the main editor window.
- Text file results are shown with syntax highlighting and navigation shortcuts.
- The middle pane of Figure 4 shows the concentrations of observables are displayed as line charts in linear or log scale.
- Graph-based models of observables, similar to the contact map, are displayed by selecting an observable from the pane in the lower left of Figure 4.
- Multiple simulation runs can be compared in order to analyze the effects of changing the model.
- Parameter scanning allows the researcher to see the effects of varying the value of a single rule parameter.

CONCLUSIONS AND FUTURE WORK

- We are implementing the BNG Editor: a rule-based modeling and simulation GUI.
- BNG Editor simplifies construction, simulation, and analysis of cell signaling networks through graphical user interfaces and interactive visualization.
- The interactive contact map allows for visual debugging and exploration of the executable models.
- The results viewer supports analysis of simulation results and visual representations of observables.
- We plan to increase the functionality of our existing prototype by including additional data on demand and developing novel and intuitive interactive visualization.
- Long term goals include fully visual model construction.

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