

Constraint-driven optimization approach to build a Petri Net defense response model in plants

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Biologists have been investigating the plant defense response to virus infections for a considerable time. However, individual research groups usually focus their experimental work on a subset of the entire system, and the global defense response network in plants has not been developed so far. When building a model of such a complex biological network, three issues need to be addressed: the definition of appropriate modeling formalism, the extraction of network structure and the determination of network parameters.

Following this approach, different formalisms were studied and consequently the model was represented by means of a Hybrid Functional Petri Net formalism [1]. Next, the network structure was manually constructed and curated by biology experts. Finally, the network parameters, such as initial values and reaction speeds, were to be estimated.

Due to the complexity of the plant defense and the lack of experimental data, the manual estimation of model parameters was unattainable. Therefore, we have developed an automatic method based on differential evolution algorithm [2]. This enables us to estimate the model parameters that violate the minimal number of constraints. The constraints are provided by the experts and represent relations between the model variables. If the simulation results do not match expert expectations, the network structure and the constraint definition are revised and the optimization parameter search is repeated.

Finally, the system yields both simulation results and optimized model parameters, which provide an insight into the biological system.

Our constraint-driven optimization approach allows for an efficient exploration of the dynamic behavior of the biological models and also increases their reliability.

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[1] Cell Illustrator 4.0 software [<http://www.cellillustrator.com/>]

[2] Storn et al., "Differential Evolution - a Simple and Efficient Adaptive Scheme for Global Optimization over Continuous Spaces" , Technical Report TR-95-012, ICSI, 1995