

SBML Extensions: Modular Modeling

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Modular modeling is especially necessary for modeling and simulating larger biological systems and for connecting different models. The most important gains of a modular approach are:

1. The whole (complex) system is divided into **comprehensible modules** that are easier to understand and to debug. The system as a whole is described by interactions of a few modules, not by the interactions of hundreds of substances and reactions. This is especially crucial for working towards whole cell models which can only be generated in a collective approach whereby different contributors work on parts of the system.
2. Modules make it possible to **separate interface (structure) and implementation (equations)** of a model. As interfaces we are using so called *terminals*, which represent signals (mostly concentrations) or substance flows inside the network. Normally there are connections between the different modules on one level of the hierarchy. Unconnected terminals are then propagated as terminals of the subsystem for connections on a higher level. In Figure 1 these principles are shown.

A module in a larger system's context may have multiple different implementations with the same interface. This makes it easier to understand the system, because the structure of the interactions (in the sense of connected terminals) remains the same. With modularity one can easily change the implementation of a module without bothering about the surrounding context. Gene expression, for example, can be described by a detailed PDE submodel relying on polymerase movement, but this can be simplified using a time delay for transcript formation or by deriving transcriptions frequency simply from initiation frequency. Especially in larger systems this is necessary to adapt the detail level of the model to its purpose.

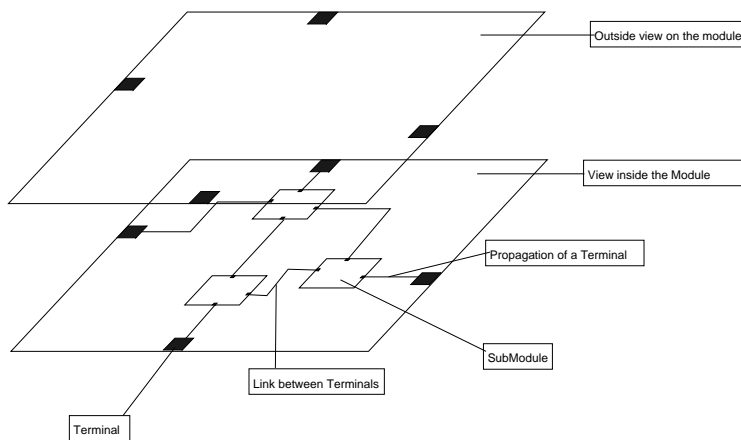


Figure 1: Hierarchical structuring of modules and connections

3. Using **standardized abstract modules** for different common parts of the metabolic and signal transduction network can improve the understanding of larger models very much. These modules form modeling knowledge bases or **libraries** that enable the reuse of modules and thus reduce the users' efforts for establishing the common and well understood parts of his model.

Accordingly, for upcoming extensions of SBML, there should be a concept for the definition of abstract, named modules with explicit interfaces (terminals). These modules should have the ability of being (multiply) instantiated, connected and parametrized in the system-model under consideration.

For the implementation of these features into SBML, we suggest the following extensions to the proposals given in [1]:

1. Definition of a `<listofTerminals>` environment for the definition of each module's (`<model>`) interfaces in analogy to the `<listofSpecies>` environment for the reactants.
2. Definition of a `<listofLinks>` environment for specifying the connections between the named terminals and / or species. Each connection would be described via `<link> link definition </link>`.
3. A `<terminalReference terminal=terminal name>` command is proposed for referencing to terminals similar to the `<specieReference specie=specie name>` command used for reactants. This could be used in the following environments: `<listofReactants>`, `<listofProducts>` and `<listofLinks>`.

References

- [1] Andrew Finney. Possible extensions to the Systems Biology Markup Language. *Internal Discussion Document*, Version of November 27, 2000.