

# GINsim: a software for the qualitative modelling, analysis and simulation of genetic regulatory networks

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## 1. Motivation

Recent developments in functional genomics have generated large amounts of data on gene expression and on the underlying regulatory mechanisms. This has resulted in the progressive mapping of complex regulatory networks. As these networks usually include numerous intertwined feedback circuits, gaining an understanding of their spatio-temporal behaviour defies the intuition of the biologists. In this respect, formal modelling and simulation tools become a necessary complement to experimental tools. As precise information on molecular mechanisms and the value of kinetic parameters are currently difficult to establish, qualitative methods offer an attractive approach to model and analyse essential properties of genetic regulatory networks. Among such qualitative approaches, we have adopted the discrete, logical formalism initially proposed by R. Thomas ([3, 1] and references therein). GINsim (**G**ene **I**nteraction **N**etwork **s**imulation) allows the user to specify a model of a genetic regulatory network in term of asynchronous, multivalued logical functions, and to simulate and/or analyse its qualitative dynamical behaviour.

## 2. GINsim capabilities

**Model definition:** A graphical interface allows the definition of the regulatory graph, where nodes represent genes (or regulatory products) and arcs represent interactions. In addition to the topology of the graph, the user may modify the default parameter values of the model: the number of significant qualitative levels of expression for each gene, the condition under which an interaction is operating on its target, the logical parameters which represent the effects of incoming interactions.

**Simulation:** Given a logical regulatory graph, GINsim allows the user to launch the construction of a state transition graph representing the dynamical behaviour of the model. Several options are available to reduce the size of this new graph: restricting the number of states considered, cutting some trajectories, defining priorities between transitions, etc.

**Analysis:** As the state transition graphs may be too large for a visual analysis, the user can ask GINsim to identify the attractors (terminal strongly connected components), a shorter path between two states, etc. Forthcoming options of GINsim include a systematic analysis of the regulatory circuits as well as the possibility to use a symbolic model checker such as NuSMV.

**Additional features:** GINsim provides means to store the logical regulatory graphs and their associated transition graphs using a dedicated XML format, namely GINML. Moreover, GINsim provides export facilities to SVG, Graphviz, and Petri net formats.

## 3. Availability

GINsim is freely available from <http://gin.univ-mrs.fr/GINsim>. It is developed in Java and is thus platform-independent. The web site also provides a model repository.

## References

- [1] C. Chaouiya and E. Remy and B. Mossé and D. Thieffry (2003). Qualitative analysis of regulatory graphs: a computational tool based on a discrete formal framework. *LNCIS* **294**: 119-26.
- [2] A. G. Gonzalez, A. Naldi, L. Sanchez, D. Thieffry, C. Chaouiya (2006). GINsim: A software suite for the qualitative modelling, simulation and analysis of regulatory networks. *Biosystems* **84**(2):91-100.
- [3] R. Thomas (1991). Regulatory networks seen as asynchronous automata: A logical description. *JTB* **153**: 1-23.