

# Description Model of Gene Regulatory Networks for Simulation and Analysis

Tetsuya Maeshiro<sup>1,\*</sup>, Shin-ichi Nakayama<sup>1</sup>

1. School of Lib. and Info. Sci., Univ. of Tsukuba, Tsukuba, Japan

\*E-mail: maeshiro@slis.tsukuba.ac.jp

Regulation of gene transcription has fundamental role in biological activities at genetic level. We present a diagram for the simulation and analysis of gene regulatory networks. The diagram is based on hypergraph with extensions adequate for the analysis of gene regulatory networks, its principal application. The diagram is also effective to visualize key components in simulations that involve gene regulatory networks.

Key elements of the diagram are the target gene whose transcription is regulated, regulators that activate or repress the target gene, substances that act as signals, and functional relationships among them. The diagram is able to represent following gene transcription and regulation mechanisms. (i) Concurrent regulation (activation or repression), where independent signals control each regulator. (ii) Different sets of regulators control alternatively the target gene. (iii) Regulators grouped in different sets control different target genes. (iv) Different regulation pattern or activity when the regulator is in isolated form and in complex form bound with other substances. (v) Recruitment of a regulator from another regulator, i.e., time sequence of regulation. (vi) Transcription level of ground state, where no regulators are bound to the promoter region of DNA. (vii) Strength of control (regulation) on the transcription of target gene.

The diagram consists of nodes and hyperlinks. Nodes represent any substance, for instance RNA, proteins, peptides or any other chemical substances. Three types of hyperlinks exist. (i) Substance complex; (ii) Quantitative control (regulation); and (iii) Trigger control.

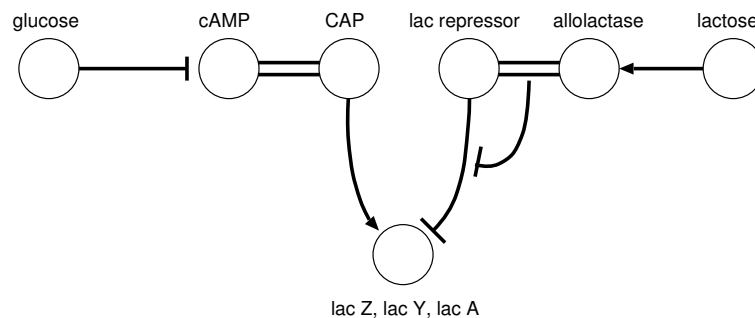


Figure 1: Diagram of lac operon

Figure 1 is the diagram of lac operon. Nodes represent proteins and other substances that participate in the regulation of lac genes (lacZ, lacY and lacZ). Arrows denote positive control or regulation over the target. For instance, increase of lactose quantity results in increase of allolactase quantity. Links ending with perpendicular short line denote negative control or regulation. For instance, increase of glucose quantity decreases cAMP quantity. Double line links represent complex, for instance cAMP–CAP complex and lac repressor–allolactase

complex. Figure indicates that lac repressor functions as a repressor over transcription of lac genes, but when in complex state bound with allolactase, this negative regulation is repressed.

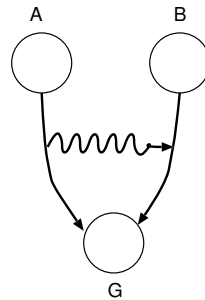


Figure 2: Diagram of a regulation with recruitment

Figure 2 is a diagram of a gene regulation involving recruitment. The diagram indicates that the regulation of A over G should initiate first, and only after that B can regulate G. Recruitment is common in gene regulation, and the figure represents a time sequence events.

The diagram is able to represent other regulatory mechanisms that have been elucidated so far.

Our diagram belongs to the class of hypergraph, thus theorems and algorithms developed for hypergraph are valid for our diagram. This property is particularly significant for the structural analysis of gene regulatory networks. Currently the diagram is being used to visualize the results of simulations of gene regulatory networks and to set simulation parameters, and to analyze DNA microarray data.