

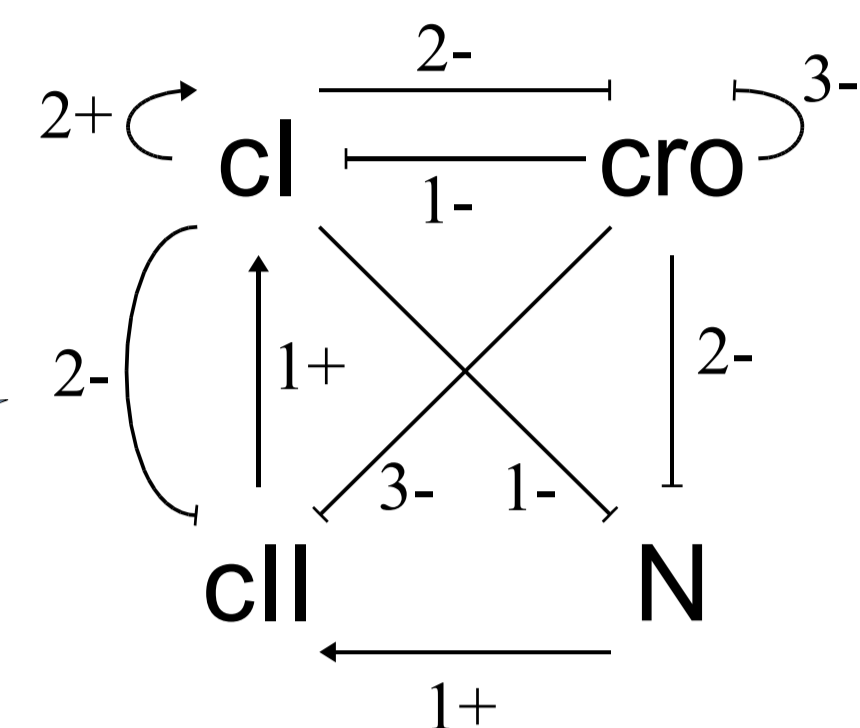
# Determining constraints in models of genetic regulatory networks using symbolic analysis

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## A regulatory network: Immunity control in bacteriophage lambda

Thieffry, Thomas, Kaufman, 1995, Bull Math Bio 57(2)



Threshold and sign of the interaction

## Dynamics of the system depends on unknown logical parameters

A logical parameter is associated with each gene and each set of its regulators:

$K_{cl}(\{cro, cII\})$  is the value towards which evolves  $cl$  when  $cro$  and  $cII$  are below their threshold.

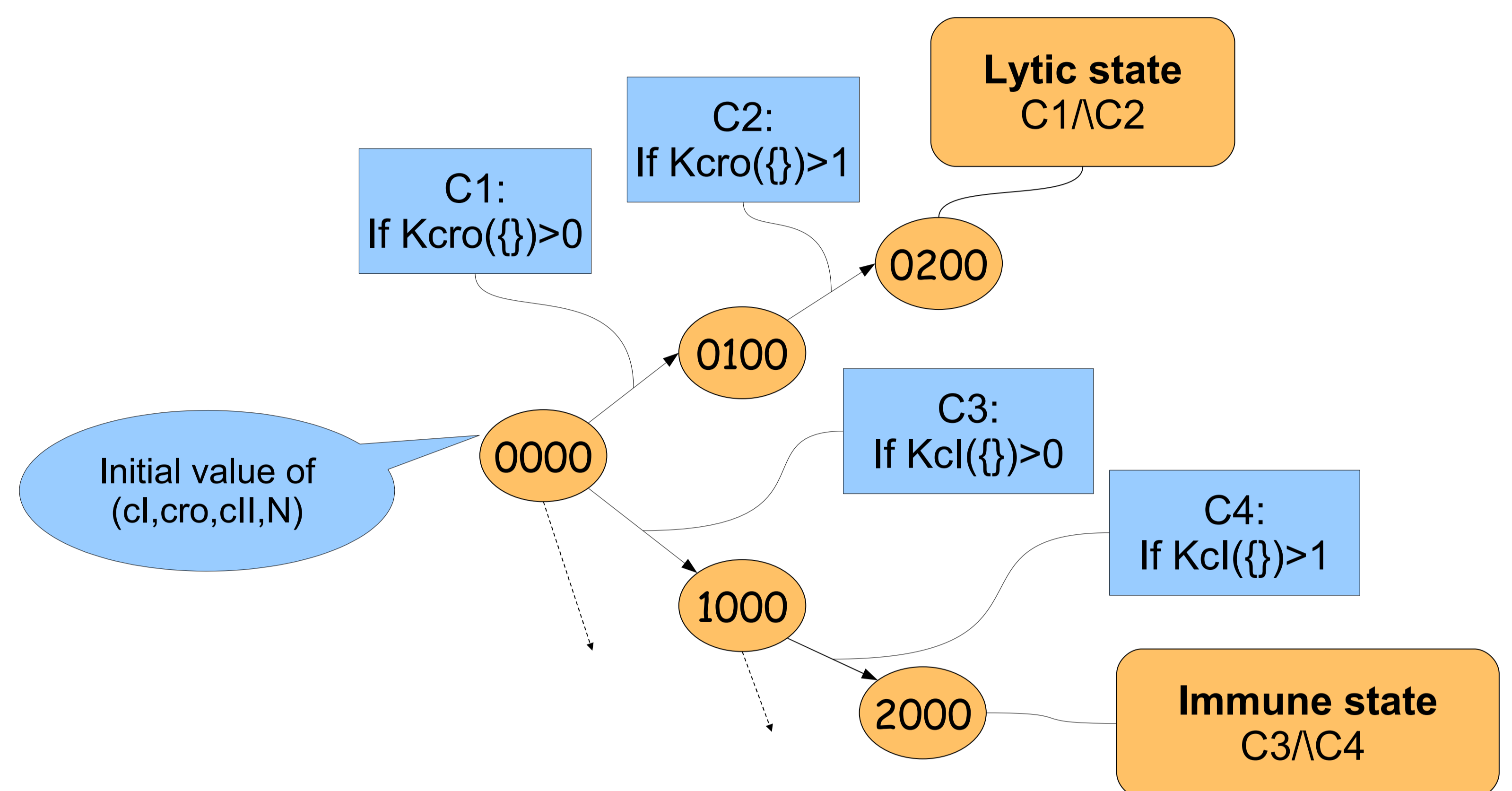
There are 24 logical parameters, corresponding to **6 879 707 136** logical models.

## Symbolic analysis

A **Symbolic Transition System** represents the set of logical models: it is not necessary to know the integer value of the parameters.

### Symbolic execution:

- constructs a tree of all the possible behaviors;
- each path is associated with a constraint on the parameters.



## Discovering unknown logical parameters by means of behavioral hypotheses given by experimental results:

- expected properties are translated into LTL formulas;
- paths corresponding to the specification are selected by model-checking methods.

Bacteria infected by bacteriophage lambda can display two behaviors: lytic response (and the cell is killed) or lysogenic response (the cell survive and carry lambda genome). These two behaviors can be translated into the LTL formulas:  $init \wedge F(\text{immune})$  and  $init \wedge F(\text{lytic})$  (from the initial state, where viral proteins are absent, an immune state can Finally (F) be reached, and a lytic state can Finally be reached). The constraints associated with the selected paths give the logical parameters corresponding to the specified behaviors.

