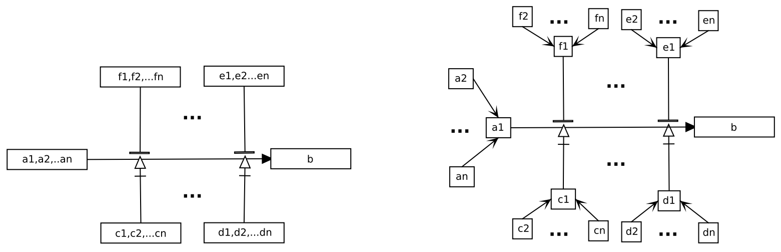
P3M User Manual

1 Calling the system

The system P3M takes as input files representing MIMs as created by PathVisio[1]. Arrow types allowed in the file are: *necessary stimulation* (—|▷), *conversion* (→), *inhibition* (⊣) and *binding* (→). This latter type of arrow is used when the left hand side of a production/activation/inhibition is a set of entities. In other terms, nodes labelled by sets of entities, like in Figure 1(a), are replaced by a set of nodes linked by the binding arrow, like shown in Figure 1(b). This makes it easier for the user to select entity types and initial values by use of the graphical interface (described below).



(a) (b)

Figure 1: Activations/Inhibitions

The system P3M is called from the command line with the following syntax:

```
p3m [<options>]
```

The possible options (shown when the system is called with the `-help` option) are:

-filename This option is followed by the name of the Pathvisio file (without the `.gpml` extension). If not set, the system tries to open the file file `example.gpml`.

-grounding This option is followed by a natural number, representing the time up to which the LTL encoding of the theory is grounded. Its default value is 0.

-query This option is followed by the query passed to the system for either graph querying or graph updating. The query is a string starting with

[1]https://github.com/PathVisio/pathvisio

either the character `+` or the character ∼. The `+` character identifies positive queries, and ∼ represents negation. The positive/negative character is followed by the name of an entity occurring in the graph and the time at which the literal (positive or negative atom) is required to hold. The integer representing time is enclosed in round brackets. All special symbols (including brackets) must be escaped (i.e. preceded by a backslash).

For instance, P3M can be called with the options:

```
-query +Galactosidase\(5\)
-query ~Galactosidase\(5\)
```

If the `-query` option is missing, P3M only checks the validity of the graph.

-assumed This option is used when the user wishes to set initial values for some variables. The option is followed by a string containing a sequence of "literals", i.e. entity names preceded by either the `+` or the ∼ character.

For instance, if one wants to set the initial value of the variable `pml` to true and that of `mdm2` to false, the system can be called with the option

```
-assumed +pml~mdm2
```

Note that the two assumptions `+pm1` and ∼`mdm2` are not separated by spaces. Default value is empty.

-false Sets all endogenous variables truth values to false at time $t = 0$. The option `-assumed` has priority over `-false`, so only values of variables not present after `-assumed` are set to false. If the option `-false` is missing and the initial value of an endogenous variable is not set by either the `-assumed` option or the initialization file (see below), it will be left unset.

-endos By default, when solving a graph querying or updating task, the system searches truth value assignments for exogenous variables only. When the values of a set $\mathcal{S}$ of endogenous variables are not defined at time $t = 0$, then the system searches an assignment of truth values to exogenous variables such that the query asked is true for all possible truth value assignments to the variables in $\mathcal{S}$. If `-endos` is used, then the system searches assignements for all unset variables, both exogenous and endogenous, in order to satisfy the query.

-graph This option is used when the graph updating task must be accomplished. Default is false.

-image When called with this option, the systems automatically saves an image of each displayed graph. Each image is a `.png` file, whose name is the same as the filename given in input, followed by digits.

-orig When looking for models to solve a query, the system may find multiple models which can be reduced to a set of simpler ones. For example, $\{(a, b, c), (\sim a, b, c)\}$ can be reduced to $\{(b, c)\}$. If `-orig` is set, the full set of models is printed before the reduced set. If unset, only the reduced models are printed. Default is false.

-noreduction If `-noreduction` is set, the reduction step described above is not performed. In fact, this step is computationally quite expensive (it often takes most of the system's time), so if the program becomes too slow, it is a good idea to try to set it. Default is false.

-no-init-vars If set, the system does not use the GUI to initialize the type of variables. Default is false.

-no-init-values If set, the system does not use the GUI to initialize the value of variables. Default is false.

-exit-after-solve If set, the system directly exits after the solver step and writes a file (with the same name as the Pathvisio input file, and extension `.time`) containing timing information. Default is false. These last three options are mainly used for benchmarking.

-debug Used only by the developers.

-cnf Write the set of initial clauses in a file, in a format close to DIMACS format.

An instance of how the system can be called is the following:[2]

```
p3m -filename lac_r -grounding 5 -query +Glucose\(5\) -image
  -graph -assumed +lacl+lacZ+CAMP~Repressor~Galactosidase~Glucose
```

Entities types and initial values can be read from an *initialization file*: if a file with extension `.ini` exists with the same name as the Pathvisio file, the system initializes entities types and values as specified in the file. Such initialization files can be created when using the graphical interface (see next section). The option `-assumed` has priority over the values present in the initialization file, which, in turn, have priority over `-false`.

2 The graphical interface

At system call, the graph is displayed to the user, and information on the classification and initial values of entities are printed to the shell.

The user can then interact by clicking on the image, in order to modify entities types and initial values. Modifications are made in two steps:

- The first set of modifications users can make concerns the classification of entities as exogenous or endogenous. This classification is shown by the font. Exogenous variables are in bold font, while endogenous variables are in regular font. By clicking on a variable, its type cyclically changes.

  This step ends when the user presses the 'g' key (this key must be pressed to proceed even when nothing has been modified).

- When entering the second modification step, the colors of the names of exogenous entities may change, according to the corresponding initial values. For instance, if the system is called on the `lac.gpml` file with the option

[2]The filenames used in this document correspond to the example files available at P3M web page.

`-assumed +lacl~Lactose`, `lacl` will be written in green and `Lactose` in red. All the other names are black (unset).

Users are now allowed to change the initial values of entities by clicking on them. When clicking on the box of one of such entities, its color cycles: from black (not set) to green (true), then to red (false), then black again.

When users have finished modifying the types and initial values of the entities, they can press the ’s’ key to save them. The system then writes such information in the initialization file, that will be read by the system at its next call (see the end of previous section).

During both modification steps, the user can also press the ’i’ key, in order to write a `png` image of the current graph.

Note that in order for key pressing to have effect, the graph must be the active window.

When the user press again the ’g’ key, the system enters the solving phase.

2.1 Graph validation

When the system is called with no `-query` option, it just checks whether the graph is consistent or not. In the first case, no output is given, otherwise the message “Inconsistent Database” is printed to the shell.

2.2 Graph querying

When the system is called with the `-query` option, and without the `-endos` option, it searches for initial values of the unset exogenous variables that would imply that the given query holds at the given time, for any possible value of the unset endogenous variables. Like explained in Section 1, if the `-endos` option is instead used, P3M tries to prove the query for all truth value assignments of any unset variable. In order to accomplish this task, it generates all the possible combinations of values for the unset variables (either endogenous only, or all the unset ones) and tests the query on them. Those that would imply the query are computed (and printed to the shell when the `-orig` option is used), and then reduced in order to obtain a set of minimal answers.

In order to illustrate the output of the system, we shall use the MIM shown in Figure 2, and assume the system is called as follows:

```
 p3m -filename lac_m -grounding 3 -orig -query +Galactosidase\(3\)
```

We moreover assume that none of the default initial values and types are modified by the user.

The solution found by the system will be written to the shell:

```
Original set:
(lacZ,true)(Repressor,true)(Lactose,true)(Glucose,false)(CAMP,true)
(lacZ,true)(Repressor,false)(Lactose,true)(Glucose,false)(CAMP,true)
(lacZ,true)(Repressor,false)(Lactose,false)(Glucose,false)(CAMP,true)
Reduced set:
(CAMP,true)(Glucose,false)(Lactose,true)(lacZ,true)
(CAMP,true)(Glucose,false)(Repressor,false)(lacZ,true)
```

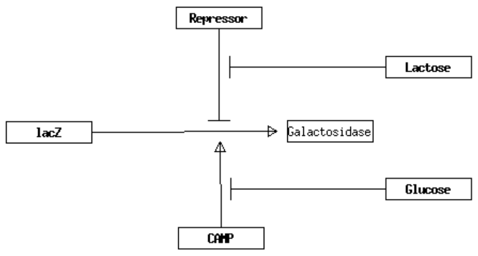


Figure 2: Sample toy graph, exogenous variables are in bold font, endogenous are in regular font

Each of the “original set” rows corresponds to a complete assignment of initial values to the exogenous variables that imply the query (i.e. Galactosidase being true at time 3). Each row in the “reduced set” corresponds to a minimal set of assumptions justifying the query. When called without the `-orig` option, P3M just shows the number of original sets, followed by the reduced sets, like above.

The values of the exogenous variables are also displayed in the graphical window: true values are in green, false values in red, and unset (or don’t care) values remain black (see Figure 3).

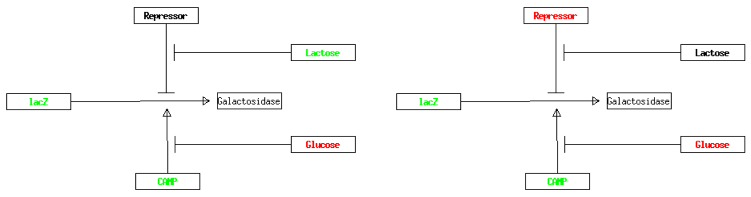


Figure 3: The two possible solutions, the colors of the exogenous variables depend on their truth values

The ’i’ key can be pressed to save an image of the current graph, the ’n’ key can be used to go to the next set of variables values, and the ’p’ key can be used to go back to the previous set. The ’g’ key exits the current step.

If the query is already a consequence of the graph encoding, the system notifies it. And it also notifies when no solution is found. These are cases where graph updating may be reasonably asked for.

2.3 Graph updating

When called with the `-graph` option, the system tries at first to find explanations for the given query without modifying the graph. If one is found, it notifies the user that there is no need to build a supergraph. Otherwise, when no solution can be found, it produces all the possible ways to obtain a new graph by adding, removing or modifying a single link. The graph querying task is then invoked on each of them, and, when a solution can be found, the new graph is displayed along with the assumptions on initial values that can explain the query.

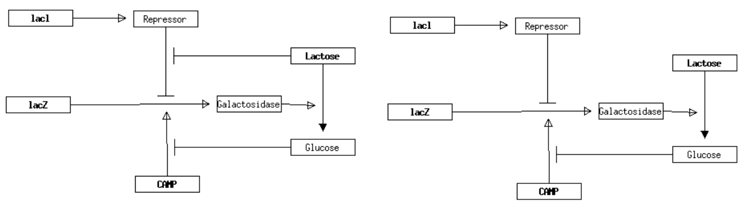


Figure 4: The lac operon graph (left side), and the same graph without the inhibition link (right side)

To explain the behaviour of the system for graph updating, we are going to use the correct form of the graph representing the lac operon, but with one inhibition missing (see Figure 4). In order for P3M to perform graph updating, it can be called as follows:

```
p3m -filename lac_r -grounding 3 -query +Glucose\(3\) -graph
    -assumed +lacl+lacZ+CAMP~Repressor~Galactosidase~Glucose
```

The users can ask the system to save the image by pressing the ’i’ key, before proceeding. When they press the ’g’ key, the system goes on computing other possible graphs that might be solutions. Two results among the 144 possible ones are displayed in Figure 5.

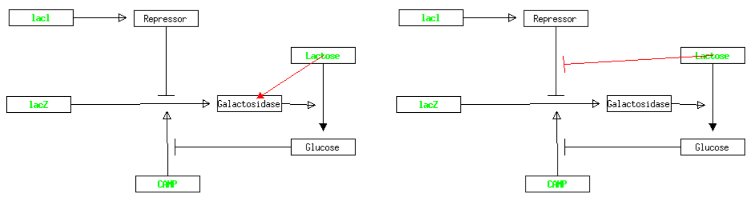


Figure 5: Two solutions proposed by the system, the “correct” one is on the right.