

# BioNetCAD1.1 tutorial

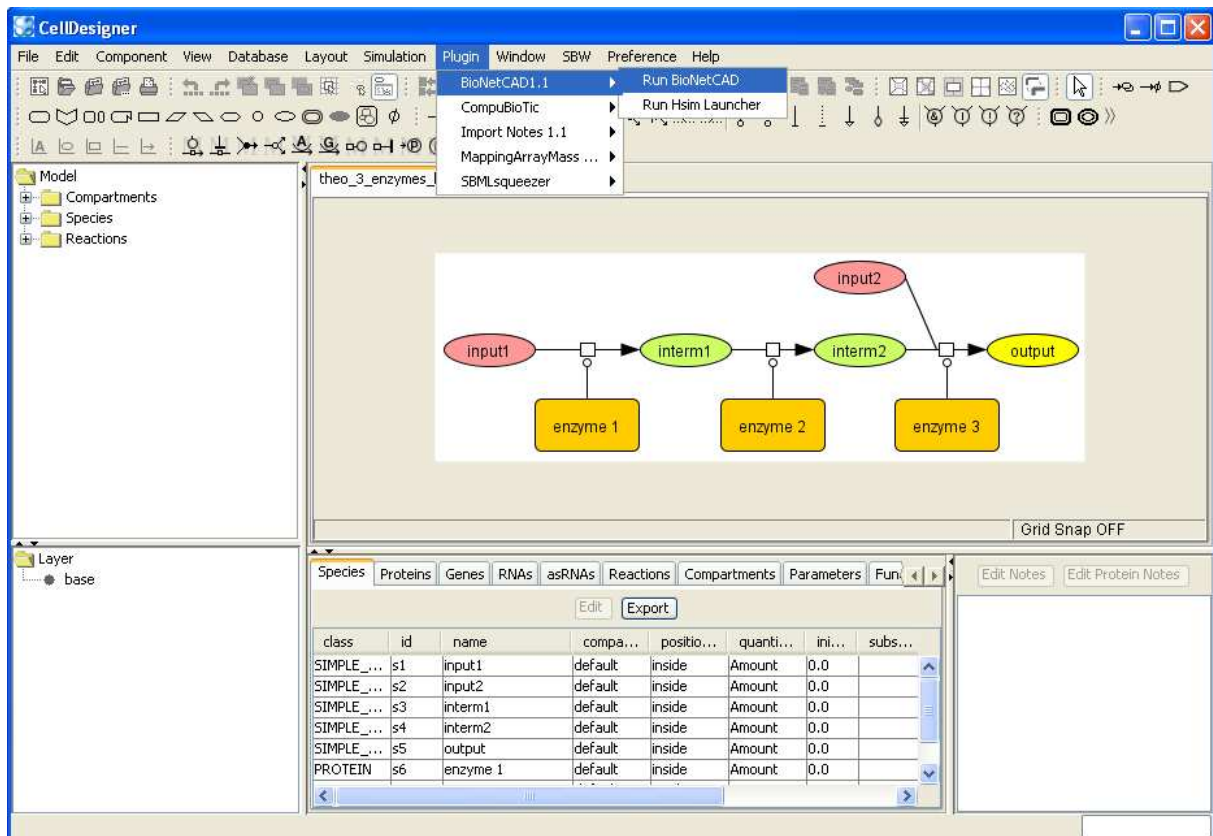
Version: 1.1

Date: 04/15/2010

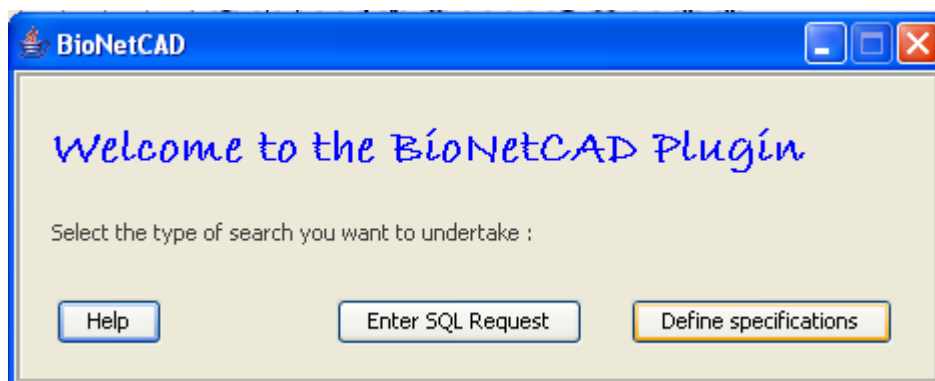
## 1. IMPLEMENTATION OF BIOCHEMICAL NETWORKS

### A Logic “AND” gate

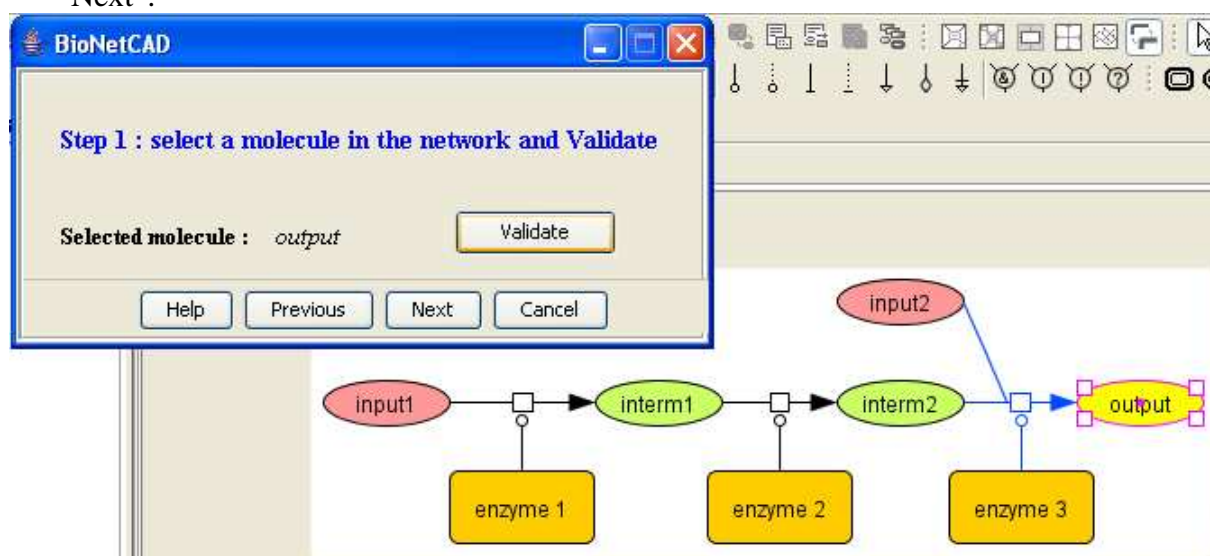
1. Open file in *CellDesigner*: theo\_3\_enzymes\_logic\_gate.xml
2. Once a model is opened in *CellDesigner*, go to menu Plugin and choose BioNetCAD1.1, and click on “Run BioNetCAD”.



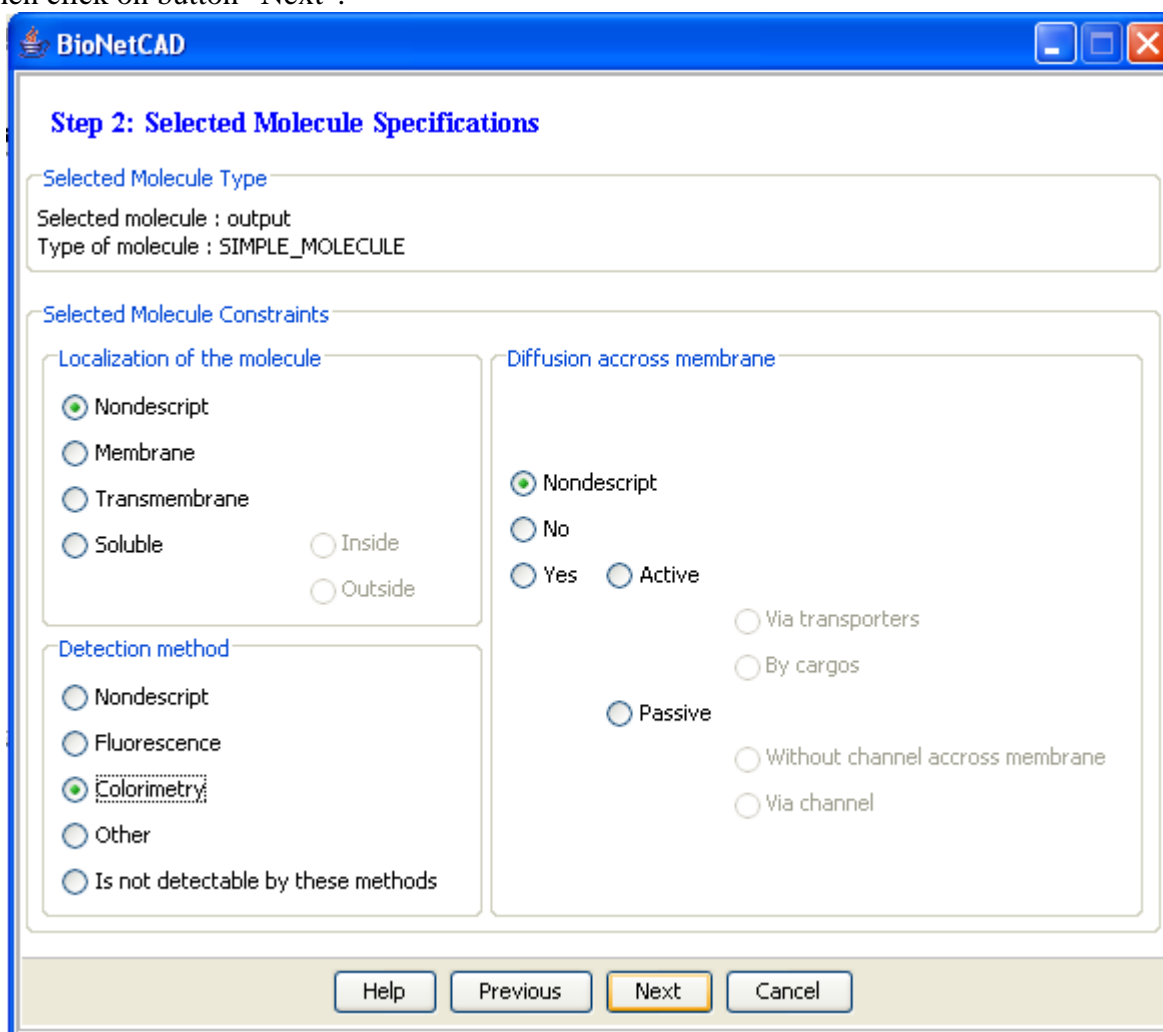
3. The BioNetCAD interface opens and asks you to choose between writing an SQL query and defining specifications about the network.  
Choose “Define specifications”.



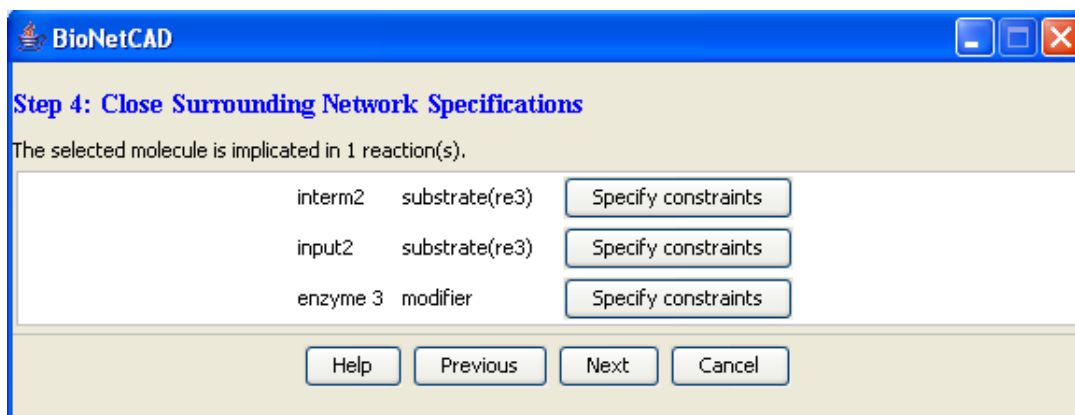
4. Click on the schema of “output” in the *CellDesigner* model in order to select it and then click on button “Validate” in the BioNetCAD interface to validate your choice. Then click on button “Next”.



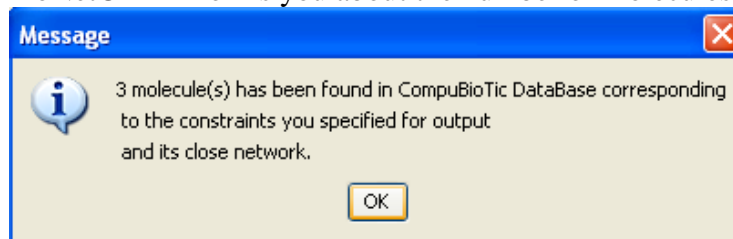
5. Next interface allows you to specify constraints about the molecule you have selected (“output” in this case).  
Choose “Colorimetry” in the “Detection method” section.  
Then click on button “Next”.



6. BioNetCAD proposes you to specify constraints about molecules directly linked to the selected molecule by reactions.  
Here, no constraints will be specified. Thus, click on “Next”.



7. Now BioNetCAD performs a research on the database taking into account the constraints you specified for the selected molecule, the constraints about the network’s molecules, and the topology of the network drawn under *CellDesigner*.  
After the research, BioNetCAD informs you about the number of molecules found. Click “Ok”.



8. The results of the research on CompuBioTicDB are displayed. Choose one combination by *CellDesigner* reaction, by selecting a radio button: for instance, select SM00050 with hydrogen peroxide as implementation of “interm2”. Once your choice is made, click on “Update the network”.

**BioNetCAD**

**Results**

3 molecule(s) has been found in CompuBioTic DataBase corresponding to the constraints you specified for output and its close network.

SELECT \* FROM real\_molecule, small\_molecule WHERE idMOL=RM\_idMOL8 AND (rmDetection

Molecule ID	Molecule Name	Close Network															
SM00016	O-dianisidine (oxidised)	<p>re3</p> <p>Reaction 3 : Donor + H(2)O(2) = oxidized donor + 2 H(2)O</p> <table border="1"> <thead> <tr> <th>interm2</th> <th>input2</th> <th>new product</th> <th>enzyme 3</th> <th></th> </tr> </thead> <tbody> <tr> <td>Hydrogen peroxide</td> <td>O-dianisidine (reduced)</td> <td>water</td> <td>Peroxidase</td> <td><input type="radio"/></td> </tr> <tr> <td>O-dianisidine (reduced)</td> <td>Hydrogen peroxide</td> <td>water</td> <td>Peroxidase</td> <td><input type="radio"/></td> </tr> </tbody> </table>	interm2	input2	new product	enzyme 3		Hydrogen peroxide	O-dianisidine (reduced)	water	Peroxidase	<input type="radio"/>	O-dianisidine (reduced)	Hydrogen peroxide	water	Peroxidase	<input type="radio"/>
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SM00050	2,2-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid, ABTS oxidised	<p>re3</p> <p>Reaction 53 : ABTS + H(2)O(2) = oxidized ABTS + 2 H(2)O</p> <table border="1"> <thead> <tr> <th>interm2</th> <th>input2</th> <th>new product</th> <th>enzyme 3</th> <th></th> </tr> </thead> <tbody> <tr> <td>2,2-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid, ABTS</td> <td>Hydrogen peroxide</td> <td>water</td> <td>Peroxidase</td> <td><input type="radio"/></td> </tr> <tr> <td>Hydrogen peroxide</td> <td>2,2-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid, ABTS</td> <td>water</td> <td>Peroxidase</td> <td><input checked="" type="radio"/></td> </tr> </tbody> </table>	interm2	input2	new product	enzyme 3		2,2-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid, ABTS	Hydrogen peroxide	water	Peroxidase	<input type="radio"/>	Hydrogen peroxide	2,2-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid, ABTS	water	Peroxidase	<input checked="" type="radio"/>
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SM00064	nitrophenol	<p>re3</p> <p>Reaction 5 : A phosphate monoester + H(2)O = an alcohol + phosphate</p> <table border="1"> <thead> <tr> <th>interm2</th> <th>input2</th> <th>new product</th> <th>enzyme 3</th> <th></th> </tr> </thead> <tbody> <tr> <td>nitrophenylphosphate</td> <td>water</td> <td>Phosphate</td> <td>Alkaline phosphatase</td> <td><input type="radio"/></td> </tr> <tr> <td>water</td> <td>nitrophenylphosphate</td> <td>Phosphate</td> <td>Alkaline phosphatase</td> <td><input type="radio"/></td> </tr> </tbody> </table>	interm2	input2	new product	enzyme 3		nitrophenylphosphate	water	Phosphate	Alkaline phosphatase	<input type="radio"/>	water	nitrophenylphosphate	Phosphate	Alkaline phosphatase	<input type="radio"/>
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Help Previous Update the network Make another research Create a CSV file Cancel

9. The network is implemented with the choice of molecules you have made. Click on “Make another research” to search implementations for the molecule “enzyme 2”.
10. Repeat steps 3 and 4 of the tutorial with selection of “enzyme 2”. In the “Step 2: Selected Molecule Specifications” interface, select “Enzymatic function” in the “Protein’s function” section. Then click “Next”.

**BioNetCAD**

### Step 2: Selected Molecule Specifications

Selected Molecule Type  
 Selected molecule : enzyme 2  
 Type of molecule : PROTEIN  
 Type of protein : GENERIC

Selected Molecule Constraints

**Localization of the molecule**

☒ Nondescript  
☐ Membrane  
☐ Transmembrane  
☐ Soluble ☐ Inside ☐ Outside

**Detection method**

☒ Nondescript  
☐ Fluorescence  
☐ Colorimetry  
☐ Other  
☐ Is not detectable by these methods

**Diffusion across membrane**

☒ Nondescript  
☐ No  
☐ Yes ☐ Active  
☐ Via transporters  
☐ By cargos  
☐ Passive  
☐ Without channel across membrane  
☐ Via channel

**Protein's function**

☒ Enzymatic function  
☐ Binding function

**EC Class**

☒ Nondescript  
☐ EC1 - Oxidoreductases - ☐ EC4 - Lyases -  
☐ EC2 - Transferases - ☐ EC5 - Isomerases -  
☐ EC3 - Hydrolases - ☐ EC6 - Ligases -

Help Previous Next Cancel

11. Click on “Specify constraints” for the molecule “Hydrogen peroxide”. Click “Validate” on the next interface.

**BioNetCAD**

### Step 4: Close Surrounding Network Specifications

The selected molecule is implicated in 1 reaction(s).

interm1	substrate(re2)	Specify constraints
Hydrogen peroxide	product(re2)	Specify constraints

Help Previous Next Cancel

**BioNetCAD - Network component constraints**

### Step 3: Linked Molecule Molecule Specifications

**Linked Molecule Molecule Type**  
 Linked Molecule molecule : Hydrogen peroxide  
 Type of molecule : SIMPLE\_MOLECULE

☒ **Direct entry of the molecule (if you know it)**

**Direct entry**  
 Enter one or more of the following :  
 CheBI Identifier  
 Linked Molecule Molecule name  
 Formula

Hydrogen peroxide

☐ **Specify constraints of the molecule**

**Linked Molecule Molecule Constraints**

**Localization of the molecule**

☒ Nondescript  
☐ Membrane  
☐ Transmembrane  
☐ Soluble      ☐ Inside  
☐ Outside

**Diffusion across membrane**

☒ Nondescript  
☐ No  
☐ Yes      ☐ Active  
☐ Via transporters  
☐ By cargos  
☐ Passive  
☐ Without channel across membrane  
☐ Via channel

**Detection method**

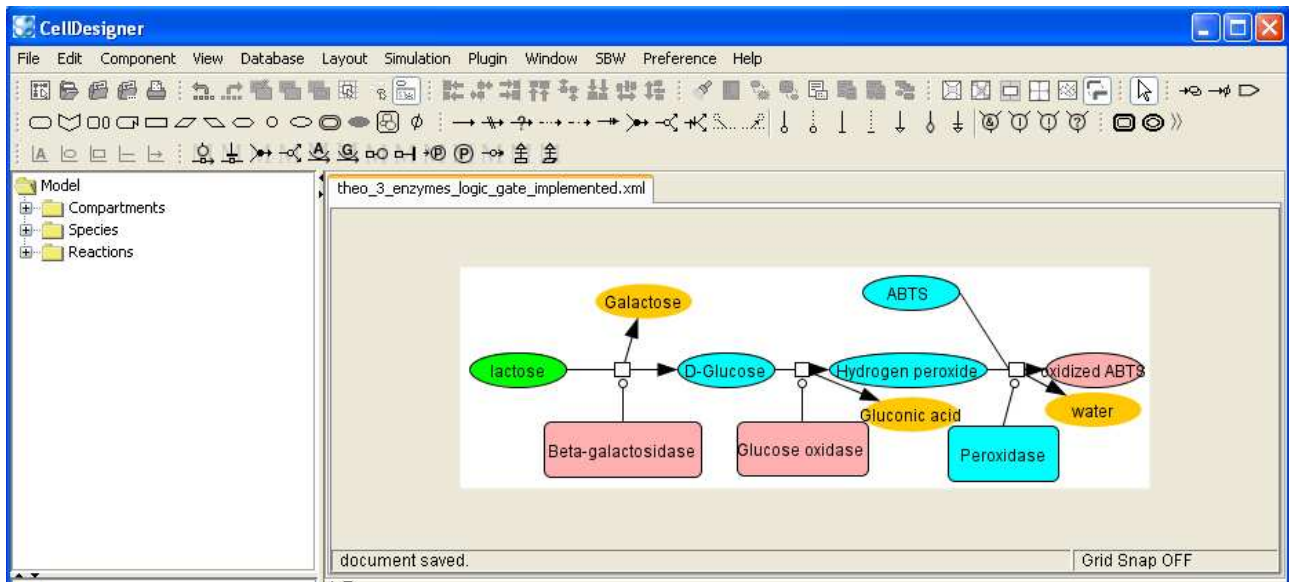
☒ Nondescript  
☐ Fluorescence  
☐ Colorimetry  
☐ Other  
☐ Is not detectable by these methods

Help   Validate   Close

BioNetCAD will search for enzymes having hydrogen peroxide as product.

12. Again, results are displayed. Choose “glucose oxidase” with D-glucose as implementation of interm1. Repeat tutorial steps 9 to 11. For the last search, choose “enzyme 1” as firstly selected molecule and specify constraints about the D-glucose in the close network.

13. Finally, an implemented network is obtained.



## 2. HSIM SIMULATIONS

1. Open theo\_3\_enzymes\_logic\_gate\_implemented.xml or theo\_3\_enzymes\_logic\_gate.xml after implementation in Section 1 of the present tutorial.
2. In the Plugin menu of CellDesigner and choose BioNetCAD1.1, and click on "Run Hsim launcher".
3. Hsim launcher interface asks for several parameters needed for the Hsim configuration file.

As an example, enter the following parameters:

Geometry settings: cell height:200; cell width: 200

Reactions parameters settings:

Re3

kcat=736

Hydrogen peroxide kM=0.005

ABTS kM=0.18

Re2

Kcat=0.3

D-glucose kM=31.8

Re3

Kcat=60

Lactose kM=1.4

Initial quantities settings:

Water 0

Peroxidase 0.3

ABTS 2.5

Oxidized ABTS 0

Gluconic acid 0

Hydrogen peroxide 0

Glucose oxidase 0.09

Galactose 0

Lactose 250

D-glucose 0

Beta-galactosidase 0.011

When all the parameters are specified, click on "Launch Hsim".



**BioNetCAD - Hsim launcher**

Welcome to the BioNetCAD HsimLauncher Plugin

**Geometry settings**

cell height  cell width

**re2**

kcat =

D-Glucose KM (mM) =

**re1**

kcat =

lactose KM (mM) =

Peroxidase	<input type="text" value="0.3"/>
ABTS	<input type="text" value="2.5"/>
oxidized ABTS	<input type="text" value="0"/>
Gluconic acid	<input type="text" value="0"/>
Hydrogen peroxide	<input type="text" value="0"/>
Glucose oxidase	<input type="text" value="0.09"/>
Galactose	<input type="text" value="0"/>
lactose	<input type="text" value="250"/>
D-Glucose	<input type="text" value="0"/>
Beta-galactosidase	<input type="text" value="0.011"/>