

# Getting started with BatchReactor®

## Use Case 2: Simulation of bioreactions

Software & Services In Process Simulation

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ProSim




# Introduction

This document describes a method to model bioreactions using BatchReactor® software.

The challenge tied to the modeling of bioreactions results from the complexity of bioreaction schemes and kinetics. With the advanced mode available in Simulis Reactions, the user can import libraries of bioreaction kinetic models that can be easily modified and adjusted to a wide range of bioreactions.

As an example, this document showcases how to simulate the classical rate of biomass growth using the model of Monod.

Here are the steps to follow:

-  Step 1: Selection of the compounds
-  Step 2: Configuration of the bioreaction
-  Step 3: Specification of the equipment and the operating scenario

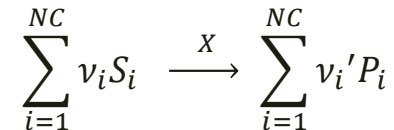
Before reading this document, it is recommended to consult “Getting Started with BatchReactor® - Use Case 1”

# Description of the model

A bioreaction corresponds to an autocatalyzed reaction, since the biomass has both roles of catalyst and product of the reaction:



The bioreaction stoichiometry can be described as follows:



With:

NC	Number of components
S	Substrates ( <i>i.e.</i> , glucose, oxygen and other limiting or non-limiting substrates...)
P	Products ( <i>i.e.</i> , biomass growth, products of interest and other by-products)
X	Biomass ( <i>e.g.</i> , micro-organisms catalysing the bioreaction)
$v_i, v_i'$	stoichiometric coefficients (positive value for products and negative value for substrates)

The global bioreaction rate can be defined as follows:

$$r_G = \frac{1}{v_i} r_{S_i} = \frac{1}{v_i'} r_{P_i}$$

With:

$r_G$	Global reaction rate of the bioreaction (positive value)
$r_{S_i}$	Specific rate of consumption of the substrate $S_i$ (negative value)
$r_{P_i}$	Specific rate of formation of the product $P_i$ (positive value)

# Description of the model

Using the advanced mode available in Simulis Reactions, the user can import a library of bioreaction kinetic models. Two different formalisms are available, where it is possible to combine elementary kinetic models ( $r(C_{Si})$ ) to take into account multiple different uptake/inhibition kinetics:

*Product of elementary kinetic models (Option 1):* 
$$r_G = \left( \alpha \cdot \mu_{max} \prod_{i=1}^{NLS} r(C_{Si}) + \beta \right) \cdot C_X$$

*Sum of elementary kinetic models (Option 2):* 
$$r_G = \left( \alpha \cdot \sum_{i=1}^{NLS} \mu_{max,i} \cdot r(C_{Si}) + \beta \right) \cdot C_X$$

With:

$\alpha$	The growth-related coefficient
$\beta$	The non-growth-related coefficient
$\mu_{max}$	The maximum growth rate
$C_{Si}, C_X$	Substrate, inhibitor or biomass concentration

The elementary kinetic models  $r(C_{Si})$  are selected from a standard list that can be enriched by the user



Model index	Description	Equation of the term $r(C_{Si})$
1	Monod	$\frac{C_S}{K_S + C_S}$
2	Hill	$\frac{C_S^N}{K_S^N + C_S^N}$
3	Contois	$\frac{C_S}{K_S C_X + C_S}$
Etc...	...	...

# Description of the model

**APPLICATION EXAMPLE:** this simple application example is based on the modeling of biomass growth, corresponding to the following equation:



The bioreaction stoichiometry can be described as follows:  $S \xrightarrow{X} X$

The global rate of bioreaction is represented by the model of Monod:

$$r_G = \mu \cdot C_X = \mu_{max} \left( \frac{C_S}{K_S + C_S} \right) C_X$$

With:

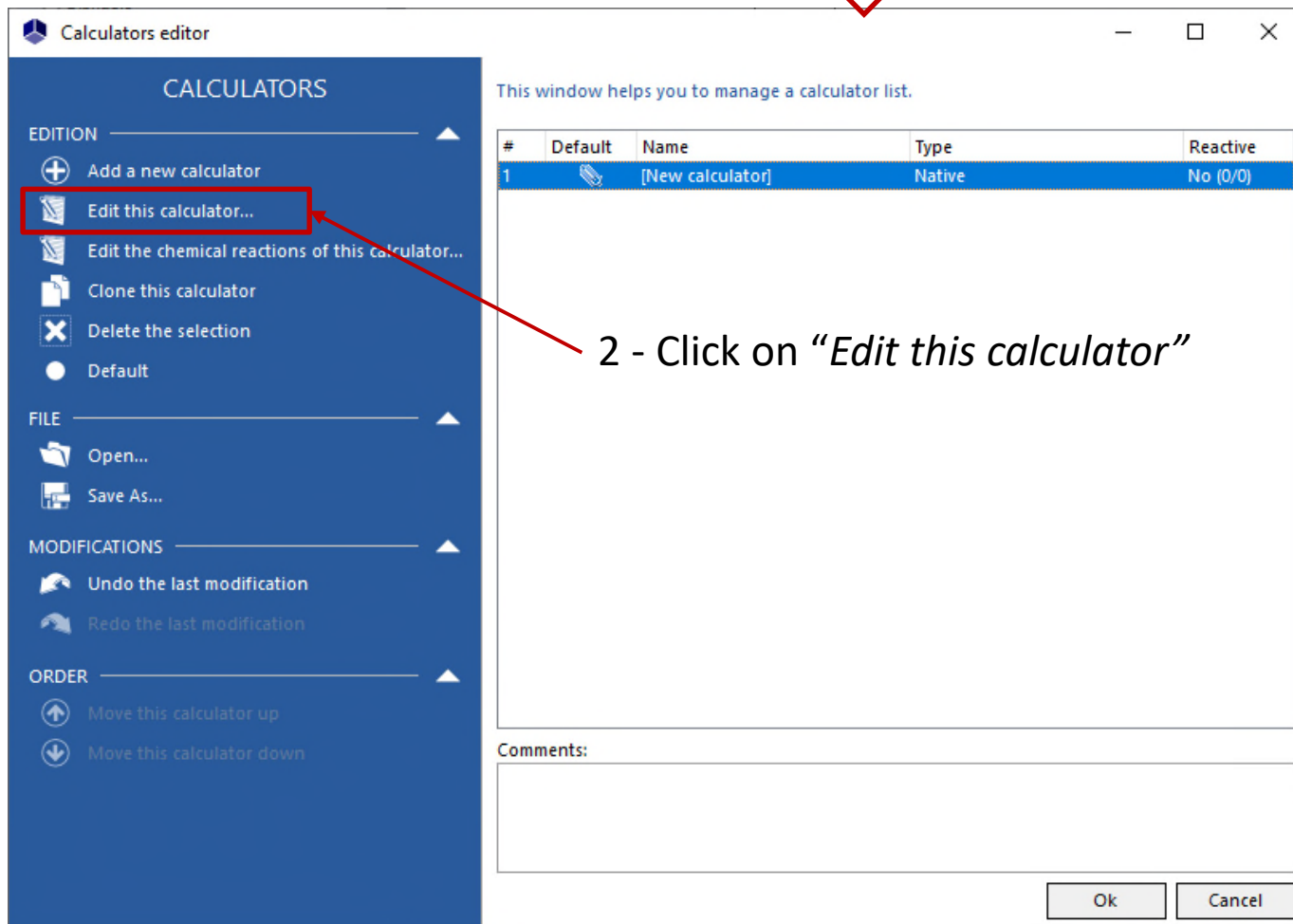
Model parameters	Definition	Value
$\mu_{max}$	Maximum growth rate	$4.10^{-5} \text{ s}^{-1}$
$K_S$	Saturation constant	2.8 g/L
$C_S, C_X$	Concentration of substrate (S) and biomass (X)	Process variables



The global rate is defined here in: g of biomass/(L.s). Since the stoichiometric coefficients are provided in molar, the global molar rate is obtained with the equation:  $r_{G,molar} = \frac{r_{G, mass}}{M_{Biomass}}$

# Step 1: Selection of the compounds

1 - Click on the “*Edit the thermodynamics and compounds*” icon to access the “*Calculators editor*” window



# Step 1: Selection of the compounds

This application example requires to import the following compounds:



WATER



SUBSTRATE (modeled as “Glucose”):

- Import of the “Glucose” from the compounds database
- Modification of the name: SUBSTRATE
- Modification of the CAS number<sup>(\*)</sup>: 1111-11-1



BIOMASS (modeled as “Glucose”):

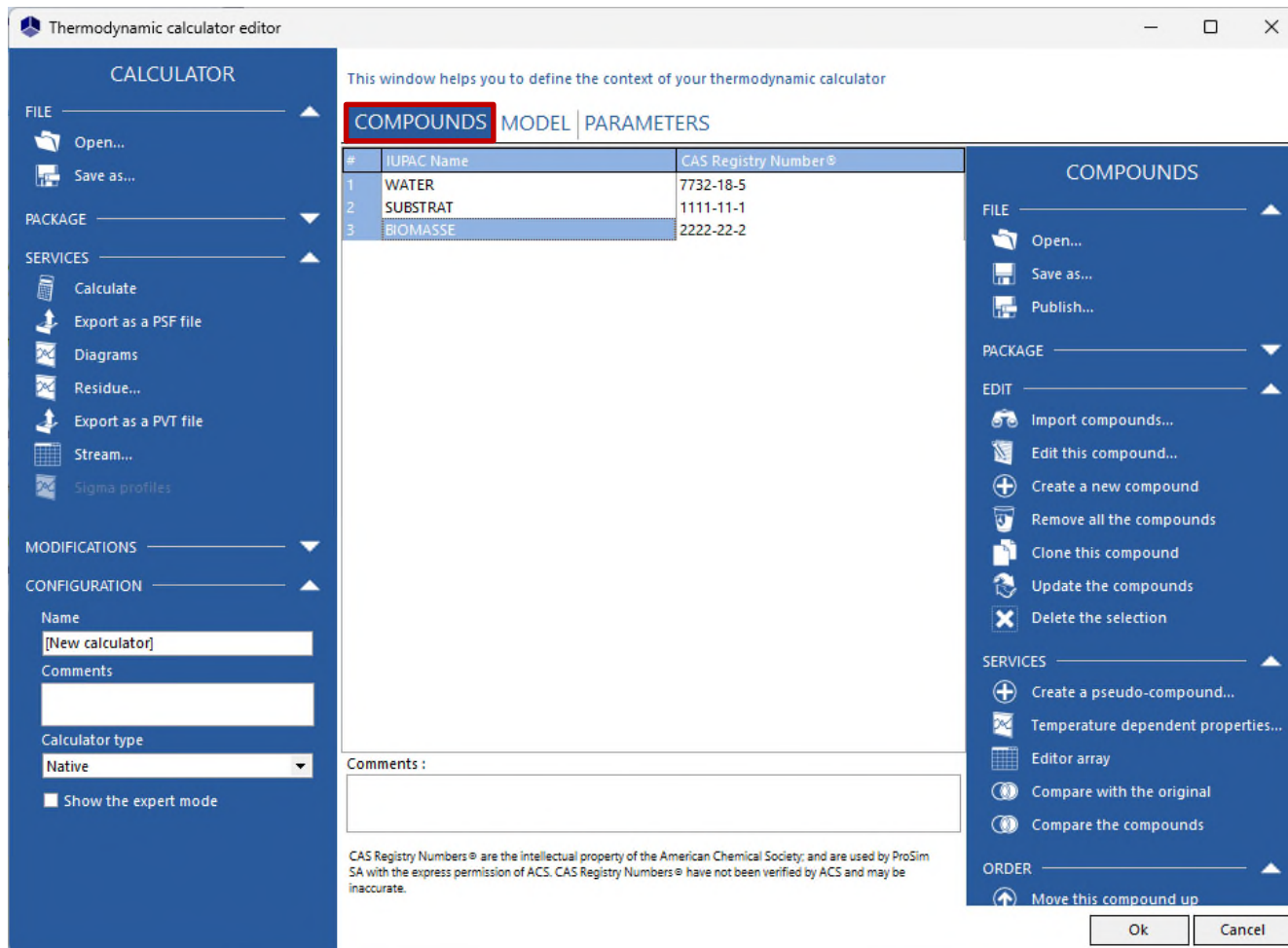
- Import of the “Glucose” from the compounds database
- Modification of the name: BIOMASS
- Modification of the CAS number<sup>(\*)</sup>: 2222-22-2

<sup>(\*)</sup>: CAS Registry Numbers® are the intellectual property of the American Chemical Society; and are used by ProSim SA with the express permission of CAS. CAS Registry Numbers® have not been verified by CAS and may be inaccurate



# Step 1: Selection of the compounds

Once this step is done, the compounds are displayed as follows in the “*Compounds*” tab:



For more information about compounds selection, please refer to “*Getting started with Simulis Thermodynamics, use case 1*”



# Step 1: Selection of the compounds

1 - In the “Model” tab, select the “ideal” thermodynamic profile:

The screenshot shows the 'Thermodynamic calculator editor' window. The 'MODEL' tab is selected and highlighted with a red box. The 'Profile' dropdown menu is also highlighted with a red box and set to 'Ideal'. Other settings include 'Approach type' as 'From activity coefficients', 'Equation of state' as 'Perfect gas', 'Activity coefficient model' as 'Ideal', and 'Pure liquid fugacity standard state' as 'Vapor pressure'. The 'Ok' button at the bottom right is also highlighted with a red box.

Thermodynamic calculator editor

This window helps you to define the context of your thermodynamic calculator

COMPOUNDS **MODEL** PARAMETERS

Name:

Category:

Profile:

Approach type:

Equation of state:

Alpha function:

Mixing rules:

Activity coefficient model:

Pure liquid fugacity standard state:

Liquid molar volume:

Transport properties:

Enthalpy calculation:

User-defined thermodynamic model:

Model index:

Comments:

THERMODYNAMIC MODEL

DOCUMENTATION

Thermodynamic assistant

Thermodynamic help

ADDITIONAL PARAMETERS

MODEL INFORMATION

WATER-HYDROCARBON

PURE WATER

Ok Cancel

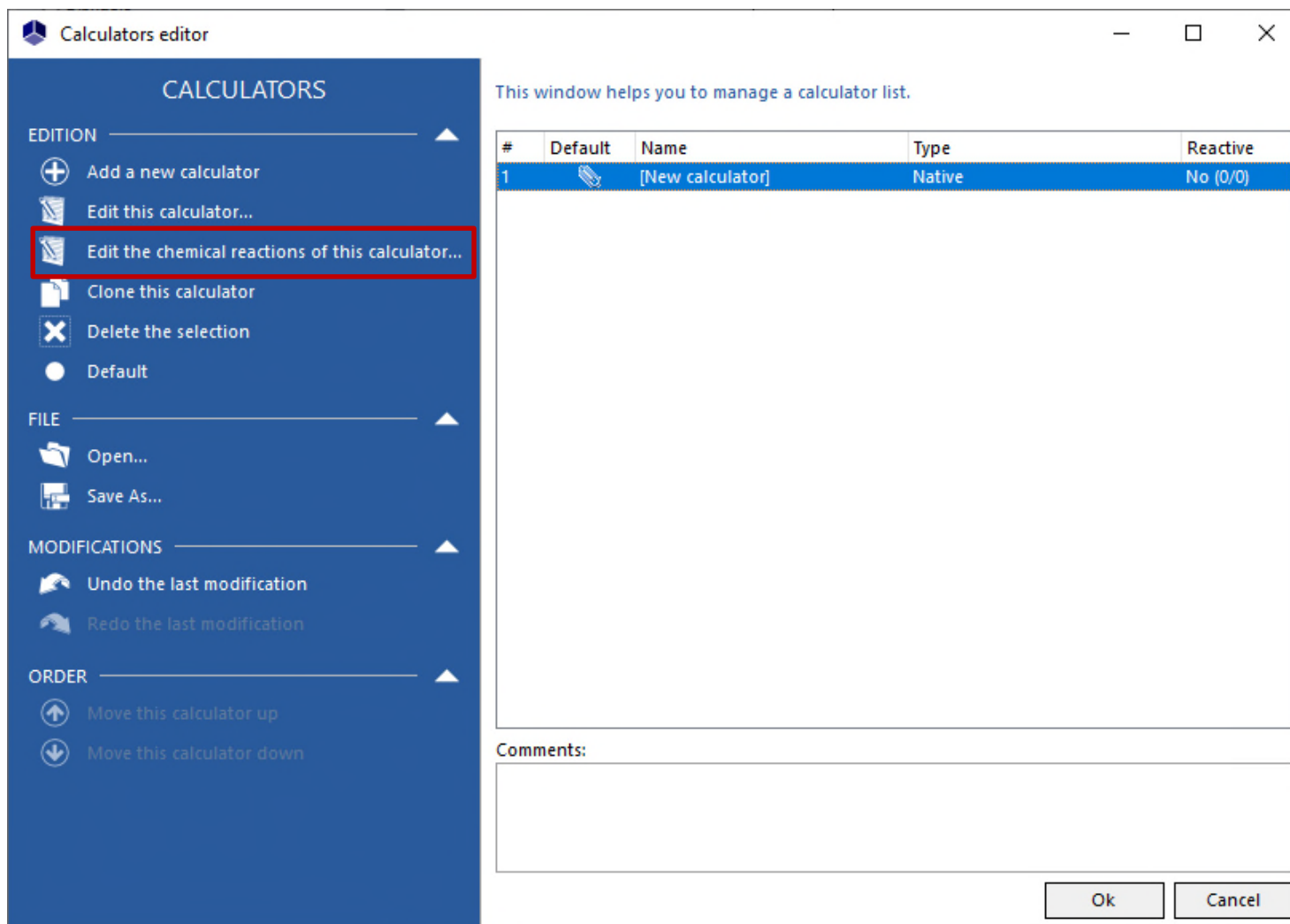
2 - Click on “Ok”  
to confirm



For more information about thermodynamic model configuration, please refer to “*Getting started with Simulis Thermodynamics, use case 1*”

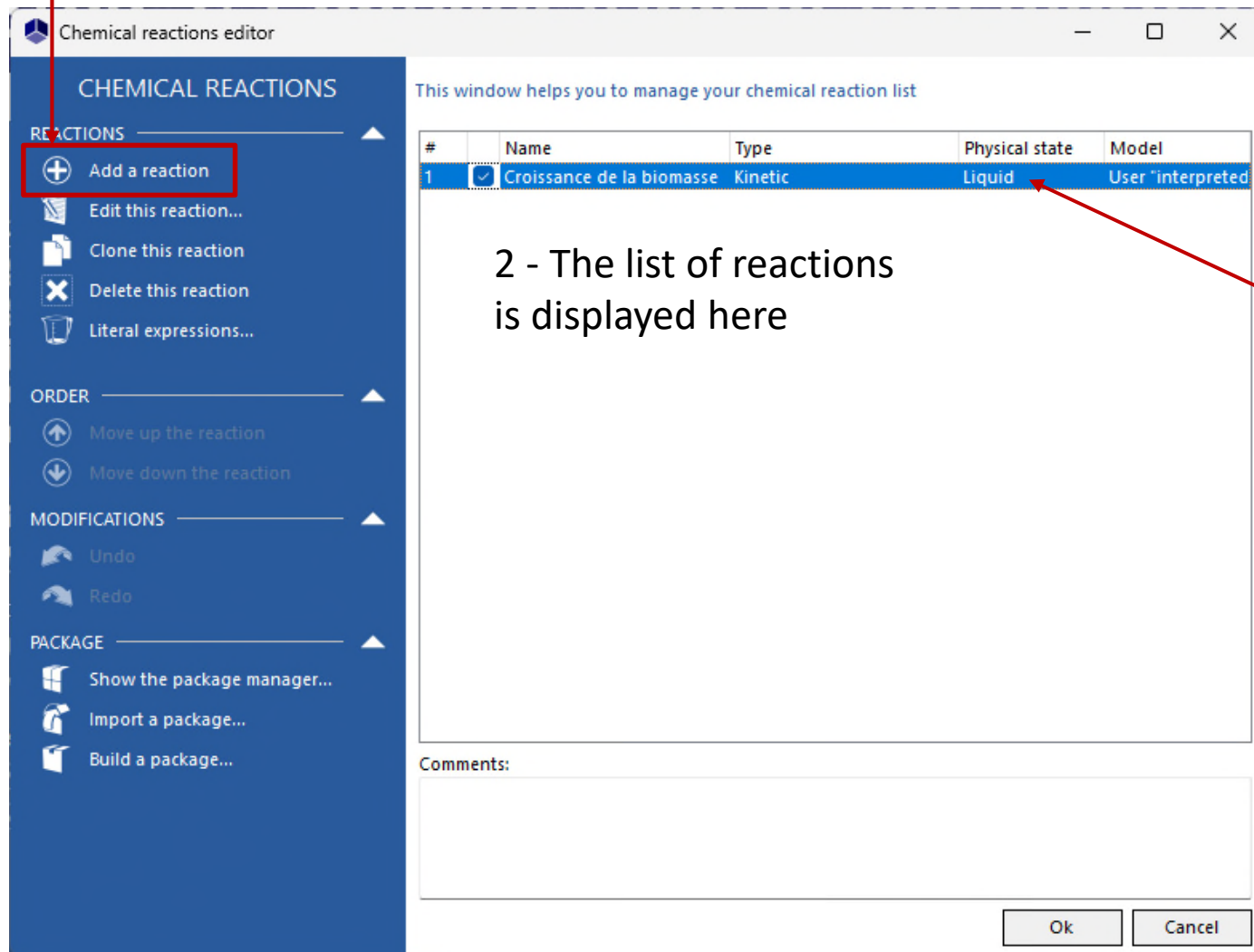
# Step 2: Configuration of the bioreaction

Back on the “*Calculators editor*” window, click on “*Edit the chemical reactions of this calculator*”



# Step 2: Configuration of the bioreaction

1 - Select "Add a reaction"



2 - The list of reactions is displayed here

3 - Double click on the new reaction to configure it

# Step 2: Configuration of the bioreaction

Chemical reaction editor

CHEMICAL REACTION

REACTION ▲

☐ Equilibrium  
☒ **Kinetic**  
☐ Instantaneous

TOOLS ▲

PDF Export (Print)

MODIFICATIONS ▲

Undo  
 Redo

HELP ▲

Technical help...

This window helps you to define the context of your chemical reaction

ID: {E2445F8E-EFD6-40A9-98BD-FA7A3277942B}

1 - Select the "General" tab

General VBScript Kinetic parameters Equilibrium constant Interface Notes

Name Croissance de la biomasse 2 - Indicate a name (optional)

User ID

Physical state Liquid 3 - Indicate the reaction phase

Reaction heat Supplied by the user 0 cal/mol

Concentration model Molar concentration

Rate model User "interpreted"

Properties		Stoichiometry and orders		
Name	CAS Registry Number® or...	Stoichiometry	Direct	Reverse
WATER	7732-18-5	0	0	0
SUBSTRAT	1111-11-1	-1	1	0
BIOMASSE	2222-22-2	1	0	0

Ok Cancel

# Step 2: Configuration of the bioreaction

Chemical reaction editor

CHIMICAL REACTION

REACTION ———— ▲

- Equilibrium
- Kinetic**
- Instantaneous

TOOLS ———— ▲

PDF Export (Print)

MODIFICATIONS ———— ▲

Undo

Redo

HELP ———— ▲

Technical help...

This window helps you to define the context of your chemical reaction

ID: {E2445F8E-EFD6-40A9-98BD-FA7A3277942B}

General VBScript Kinetic parameters Equilibrium constant Interface Notes

Name Croissance de la biomasse ☒ Activated

User ID

Physical state Liquid

Reaction heat Supplied by the user 0 cal/mol

Concentration model Molar concentration

Rate model User "interpreted"

Properties		Stoichiometry and orders		
Name	CAS Registry Number® or...	Stoichiometry	Direct	Reverse
WATER	7732-18-5	0	0	0
SUBSTRAT	1111-11-1	-1	1	0
BIOMASSE	2222-22-2	1	0	0

Ok Cancel

4 - Specify a "Reaction heat" of 0 cal/mol



# Step 2: Configuration of the bioreaction

Access the **Advanced mode** to provide a custom kinetic model for the bioreaction



It is not necessary to configure these tabs when using the advanced mode

Chemical reaction editor

CHEMICAL REACTION

REACTION ——— ▲

- Equilibrium
- Kinetic**
- Instantaneous

TOOLS ——— ▲

PDF Export (Print)

MODIFICATIONS ——— ▲

Undo

Redo

HELP ——— ▲

Technical help...

This window helps you to define the context of your chemical reaction

ID: {E2445F8E-EFD6-40A9-98BD-FA7A3277942B}

General VBScript Kinetic parameters Equilibrium constant Interface Notes

Name Croissance de la biomasse ☒ Activated

User ID

Physical state Liquid

Reaction heat Supplied by the user 0 cal/mol

Concentration model Molar concentration

Rate model User "interpreted"

Properties		Stoichiometry and orders		
Name	CAS Registry Number® or...	Stoichiometry	Direct	Reverse
WATER	7732-18-5	0	0	0
SUBSTRAT	1111-11-1	-1	1	0
BIOMASSE	2222-22-2	1	0	0

Ok Cancel

5 - Select the "User interpreted" rate model (Advanced mode)



# Step 2: Configuration of the bioreaction

Access the **Advanced mode** to provide a custom kinetic model for the bioreaction

Chemical reaction editor

CHEMICAL REACTION

REACTION ———— ▲

- Equilibrium
- Kinetic**
- Instantaneous

TOOLS ———— ▲

PDF Export (Print)

MODIFICATIONS ———— ▲

Undo

Redo

HELP ———— ▲

Technical help...

This window helps you to define the context of your chemical reaction

ID: {E2445F8E-EFD6-40A9-98BD-FA7A3277942B}

**General** VBScript Kinetic parameters Equilibrium constant Interface Notes

Name: Croissance de la biomasse ☒ Activated

User ID:

Physical state: Liquid

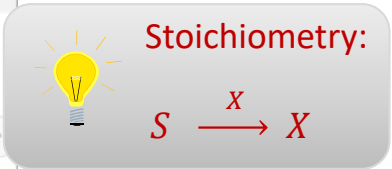
Reaction heat: Supplied by the user 0 cal/mol

Concentration model: Molar concentration

Rate model: User "interpreted"

Properties		Stoichiometry and orders		
Name	CAS Registry Number® or...	Stoichiometry	Direct	Reverse
WATER	7732-18-5	0	0	0
SUBSTRAT	1111-11-1	-1	1	0
BIOMASSE	2222-22-2	1	0	0

Ok Cancel



2 - Indicate the bioreaction stoichiometry:

- "-1" for the substrate
- "1" for the biomass

# Step 2: Configuration of the bioreaction

Access the **Advanced mode** to provide a custom kinetic model for the bioreaction

The screenshot shows the 'Chemical reaction editor' window. The left sidebar contains sections for 'CHEMICAL REACTION' (with 'Kinetic' selected), 'TOOLS' (with 'PDF Export (Print)'), 'MODIFICATIONS' (with 'Undo' and 'Redo'), and 'HELP' (with 'Technical help...'). The main area has tabs for 'General', 'VBScript', 'Kinetic parameters', 'Equilibrium constant', 'Interface', and 'Notes'. The 'VBScript' tab is active, showing a 'USER GUIDE' with instructions. Below the tabs, there are input fields for 'T=' (298,15 K) and 'P=' (101325 Pa), and a table for molar fractions of 'WATER', 'SUBSTRAT', and 'BIOMASSE'. A red box highlights the 'Technical help...' button in the sidebar, and another red box highlights the 'VBScript' tab. A red line connects the 'Technical help...' button to the 'Bioreaction rate' equation in the adjacent callout.

1 - Select the "VBScript" tab

Bioreaction rate:

$$r_G = \mu_{max} \left( \frac{C_S}{K_S + C_S} \right) C_X$$

2 - Select "Technical help" to get information about the library of kinetic models dedicated to bioreactions

# Step 2: Configuration of the bioreaction

Access the **Advanced mode** to provide a custom kinetic model for the bioreaction



Technical help...

It is necessary to look at the “*Technical help*” to get information about the suitable kinetic models for the bioreaction along with the parameters to provide

Selection of the suitable model



Bioreaction rate :

$$r_G = \mu_{max} \left( \frac{C_S}{K_S + C_S} \right) C_X$$

Selection of the model for the global rate of bioreaction



(**Option 1**):  $r_G = \left( \alpha \cdot \mu_{max} \prod_{i=1}^{NLS} r(C_{Si}) + \beta \right) \cdot C_X$

Selection of the elementary kinetic model  
 $r(C_{Si})$

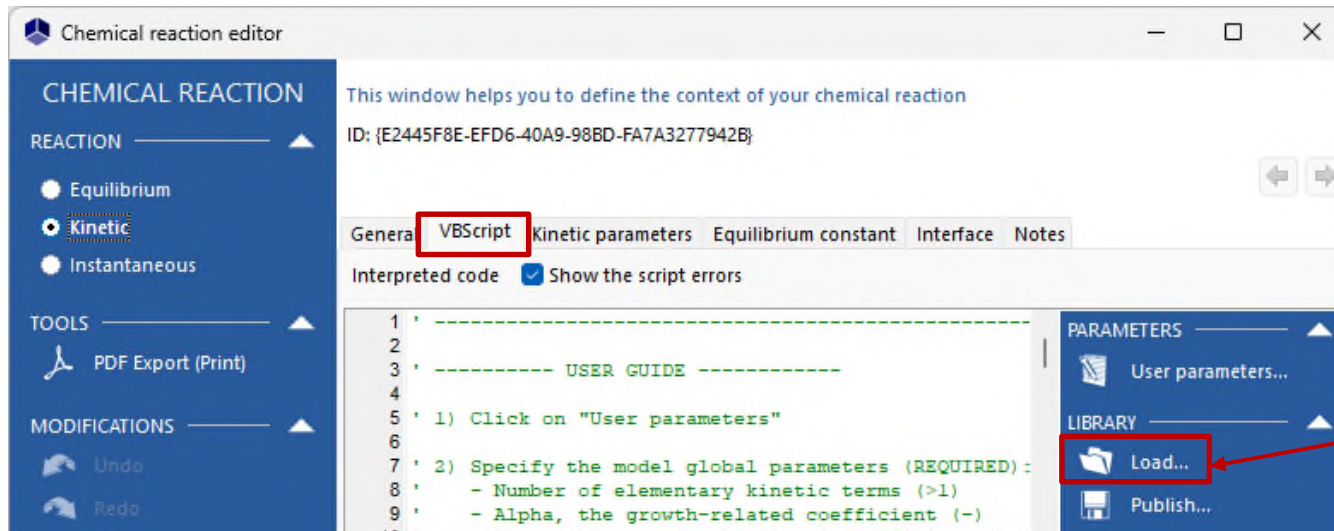
1 elementary term



Model index	Description	Equation of the term $r(C_{Si})$
1	Monod	$\frac{C_S}{K_S + C_S}$

# Step 2: Configuration of the bioreaction

Access the **Advanced mode** to provide a custom kinetic model for the bioreaction



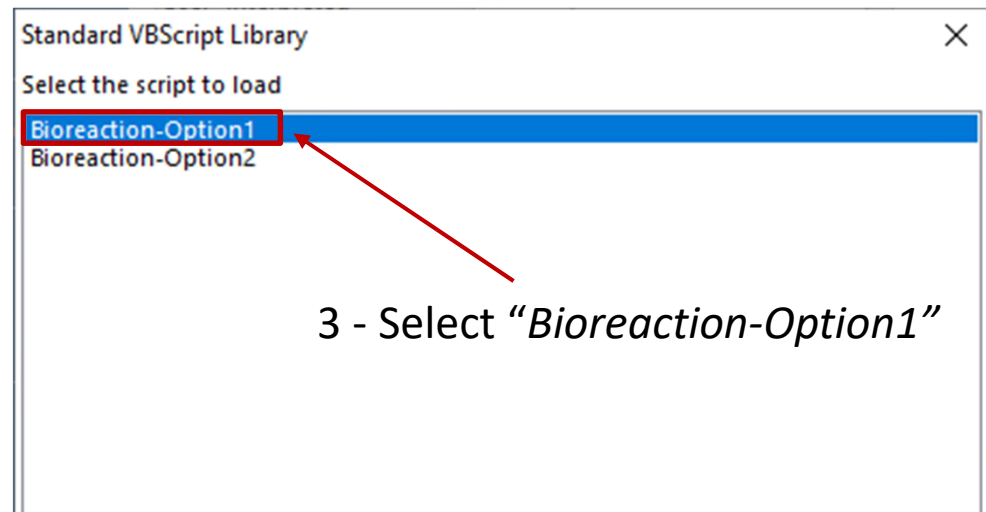
Bioreaction rate:

$$r_G = \mu_{max} \left( \frac{C_S}{K_S + C_S} \right) C_X$$

1 - Click on  
"Load"



2 - The library of available scripts  
is displayed here



3 - Select "Bioreaction-Option1"



# Step 2: Configuration of the bioreaction

Access the **Advanced mode** to provide a custom kinetic model for the bioreaction

Chemical reaction editor

CHIMICAL REACTION

REACTION ———— ▲

- Equilibrium
- Kinetic**
- Instantaneous

TOOLS ———— ▲

PDF Export (Print)

MODIFICATIONS ———— ▲

Undo

Redo

HELP ———— ▲

Technical help...

This window helps you to define the context of your chemical reaction

ID: {E2445F8E-EFD6-40A9-98BD-FA7A3277942B}

General **VBScript** Kinetic parameters Equilibrium constant Interface Notes

Interpreted code ☒ Show the script errors

```

1 ' -----
2 ' ----- USER GUIDE -----
3 ' -----
4 ' 1) Click on "User parameters"
5 ' 2) Specify the model global parameters (REQUIRED):
6 '   - Number of elementary kinetic terms (>1)
7 '   - Alpha, the growth-related coefficient (-)
8 '   - Beta, the non-growth-related coefficient (s-1)
9 '   - Maximum growth rate (s-1)
10 '   - CAS number of "X", the Biomass compound (with
11 '   - CAS number of "Reference", the reference comp
12 '
13 '

```

T= 298,15 K P= 101325 Pa

Name	Molar fraction
WATER	0,00000
SUBSTRAT	0,00000
BIOMASSE	0,00000

PARAMETERS ———— ▲

**User parameters...**

LIBRARY ———— ▲

Load...

Publish...

EDITION ———— ▲

Copy

Paste

TEST ———— ▲

Test

Ok Cancel



Bioreaction rate:

$$r_G = \mu_{max} \left( \frac{C_S}{K_S + C_S} \right) C_X$$

5 - Click on  
"User parameters"

4 - The script is loaded here

# Step 2: Configuration of the bioreaction

Access the **Advanced mode** to provide a custom kinetic model for the bioreaction

## 1 - Specify the model input parameters:

- 1 elementary kinetic term, corresponding to the model #1 (Monod)
- $\alpha = 1$
- $\beta = 0$
- $\mu_{max} = 4.10^{-5} \text{ s}^{-1}$
- $K_S = 2.8 \text{ g/L}$
- CAS number<sup>(\*)</sup> of the biomass (X) and the compound of reference: 2222222
- CAS number<sup>(\*)</sup> of the substrate (S): 1111111



Bioreaction rate :

$$r_G = \mu_{max} \left( \frac{C_S}{K_S + C_S} \right) C_X$$

User parameters

PARAMETERS

- Add
- Delete
- Move up
- Move down
- Copy
- Paste

HELP

- Technical help...

List of parameters

#	Description	Value
1	Number of terms	1
2	Alpha (-)	1
3	Beta (s-1)	0
4	Max growth rate (s-1)	4E-005
5	CAS of X	2222222
6	CAS of compound of reference	2222222
7	Term #1: Model index (OPTIONAL)	1
8	Term #1: CAS of S (OPTIONAL)	1111111
9	Term #1: CAS of I (OPTIONAL)	0
10	Term #1: Ks (g/L) (OPTIONAL)	2,8
11	Term #1: Ki (g/L) (OPTIONAL)	0
12	Term #1: N (OPTIONAL)	0
13	Term #1: Tmin (K) (OPTIONAL)	1
14	Term #1: Tmax (K) (OPTIONAL)	1000
15	Term #2: Model index (OPTIONAL)	0
16	Term #2: CAS of S (OPTIONAL)	0

Ok Cancel

2 - Click on “Ok” to confirm and go back to the main flowsheet

(\*) CAS Registry Numbers® are the intellectual property of the American Chemical Society; and are used by ProSim SA with the express permission of CAS. CAS Registry Numbers® have not been verified by CAS and may be inaccurate



# Step 3: Specification the equipment and the operating scenario

## 1 - Scenario:

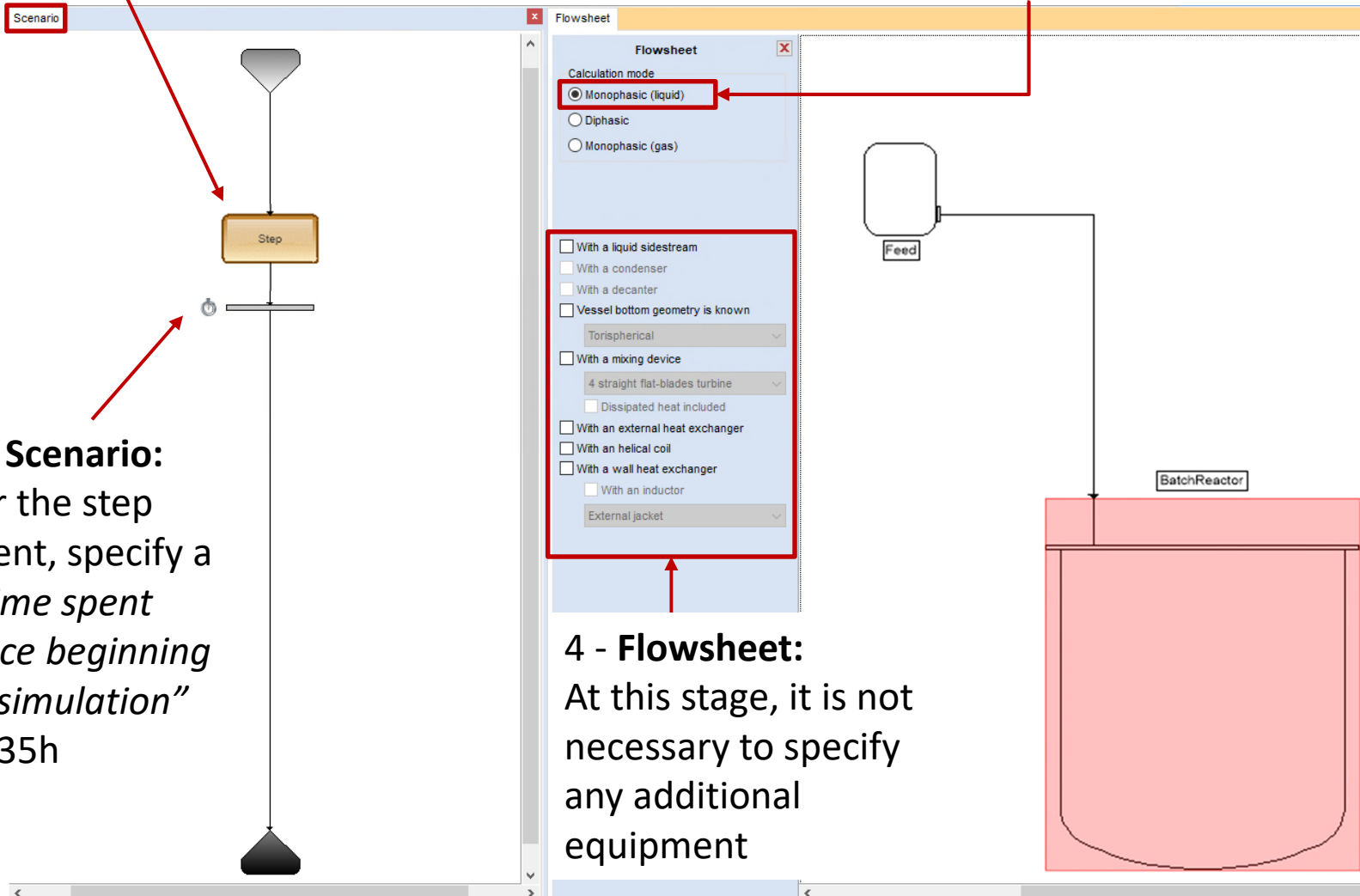
Add 1 “Constant heat duty” step

## 3 - Flowsheet:

Check the “Monophasic (liquid)” calculation mode

## 2 - Scenario:

For the step event, specify a “Time spent since beginning of simulation” of 35h

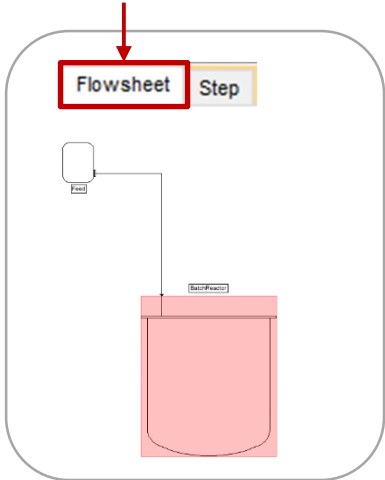


## 4 - Flowsheet:

At this stage, it is not necessary to specify any additional equipment

# Step 3: Specification the equipment and the operating scenario

1 - Select the “*Flowsheet*” tab and double click on the reactor to specify the initial conditions



The 'Reactor' configuration window is shown with the 'BatchReactor' name. The 'Parameters' tab is active. The 'Reactor temperature [TR]' is set to 'Fixed temperature' with a value of '298.15 K'. The 'Reactor pressure [PR]' is set to 'Fixed pressure' with a value of '101325 Pa'. The 'Alarms [VR]' are set to 'Minimum 1E-5 m3' and 'Maximum 1 m3'. The 'Initial load' button is highlighted with a red box, and a red arrow points from it to the 'Initial load' specification window.

The 'Initial load' specification window is shown. The 'Fractions' tab is active. The 'Mass' unit is selected. The table shows the following data:

Compound	Fraction
WATER	0.9625
SUBSTRATE	0.035
BIOMASS	0.0025

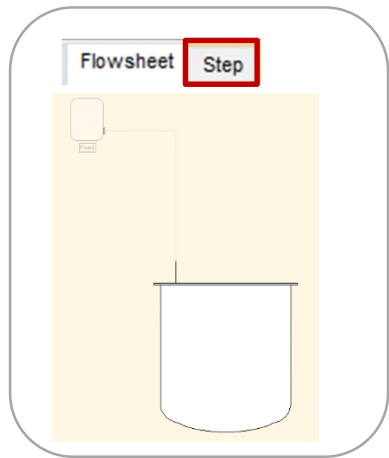
The 'Total volume load' is set to '1 l'.

2 - Specify the initial conditions:

- $T = 298.15 \text{ K}$
- $P = 101325 \text{ Pa}$
- Initial mass composition: 96.25% Water, 3.5% Substrate, 0.25% Biomass
- Initial load: 1L

# Step 3: Specification the equipment and the operating scenario

1 - Double click on the “Step” in the operating scenario or select the “Step” tab and double click on the reactor to specify the operating conditions



2 - Specify the operating conditions:

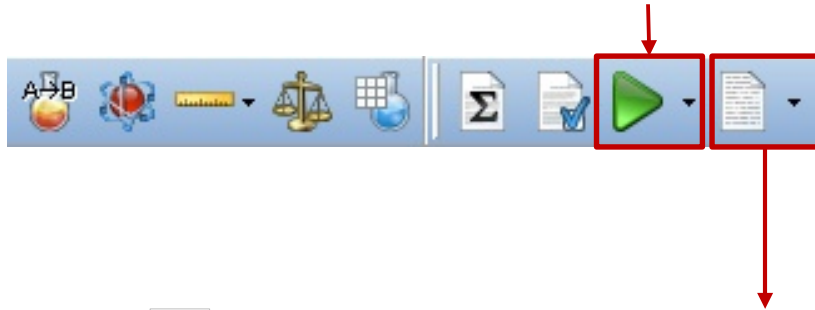
- No feed
- Heat duty = 0 J/s
- Pressure = 101325 Pa



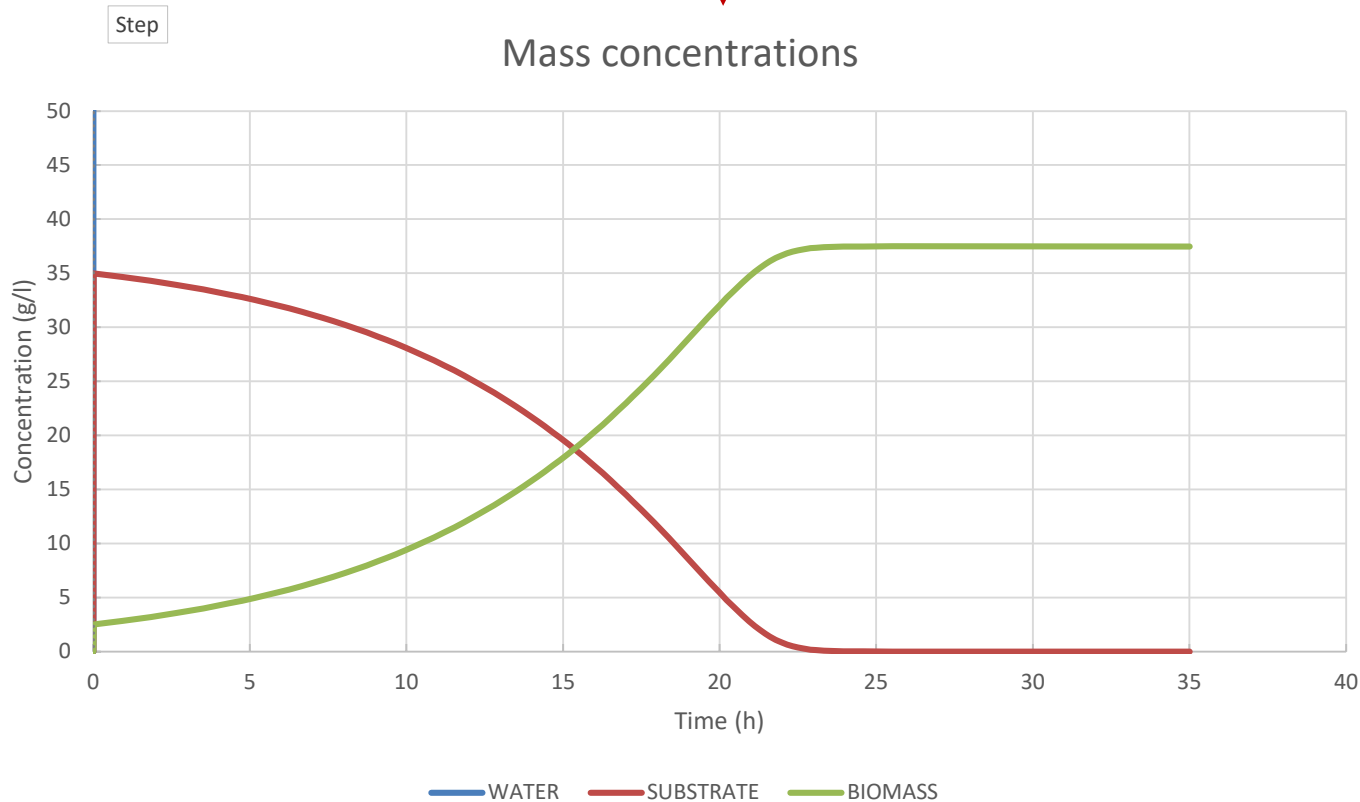
For more information about these steps, please refer to “*Getting started with BatchReactor, use case 1*”

# Results

1 - Click on the green arrow to run the simulation



2 - Once the simulation is done, click on the “Results” icon to access the simulation report



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# ProSim

Software & Services In Process Simulation

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