Getting started with Simulis Reactions®

Use Case 2: Modeling of bioreactions using the advanced mode

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Introduction

This document describes a method to model bioreactions using the advanced mode of Simulis Reactions.

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 model 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 model

Before reading this document, it is recommended to consult "*Getting Started with Simulis Reactions - 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:

$$Substrates + Biomass \rightarrow More\ Biomass + Products$$

The bioreaction stoichiometry can be described as follows:

$$\sum_{i=1}^{NC} \nu_i S_i \xrightarrow{X} \sum_{i=1}^{NC} \nu_i' P_i$$

With:

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

The global bioreaction rate can be defined as follows:

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

With:

r_G	Global reaction rate of the bioreaction (positive value)
r_{Si}	Specific rate of consumption of the substrate S_i (negative value)
r_{Pi}	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 ($\boldsymbol{r(C_{Si})}$) to take into account multiple different uptake/inhibition kinetics:

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

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

With:

α	The growth-related coefficient
β	The non-growth-related coefficient
μ_{max}	The maximum growth rate
C_{Si}, C_X	Substrate, inhibitor or biomass concentration

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

Model index	Description	Equation of the term $\boldsymbol{r(C_{Si})}$
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:

$$Substrate + Biomass \rightarrow More\ Biomass$$

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

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

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

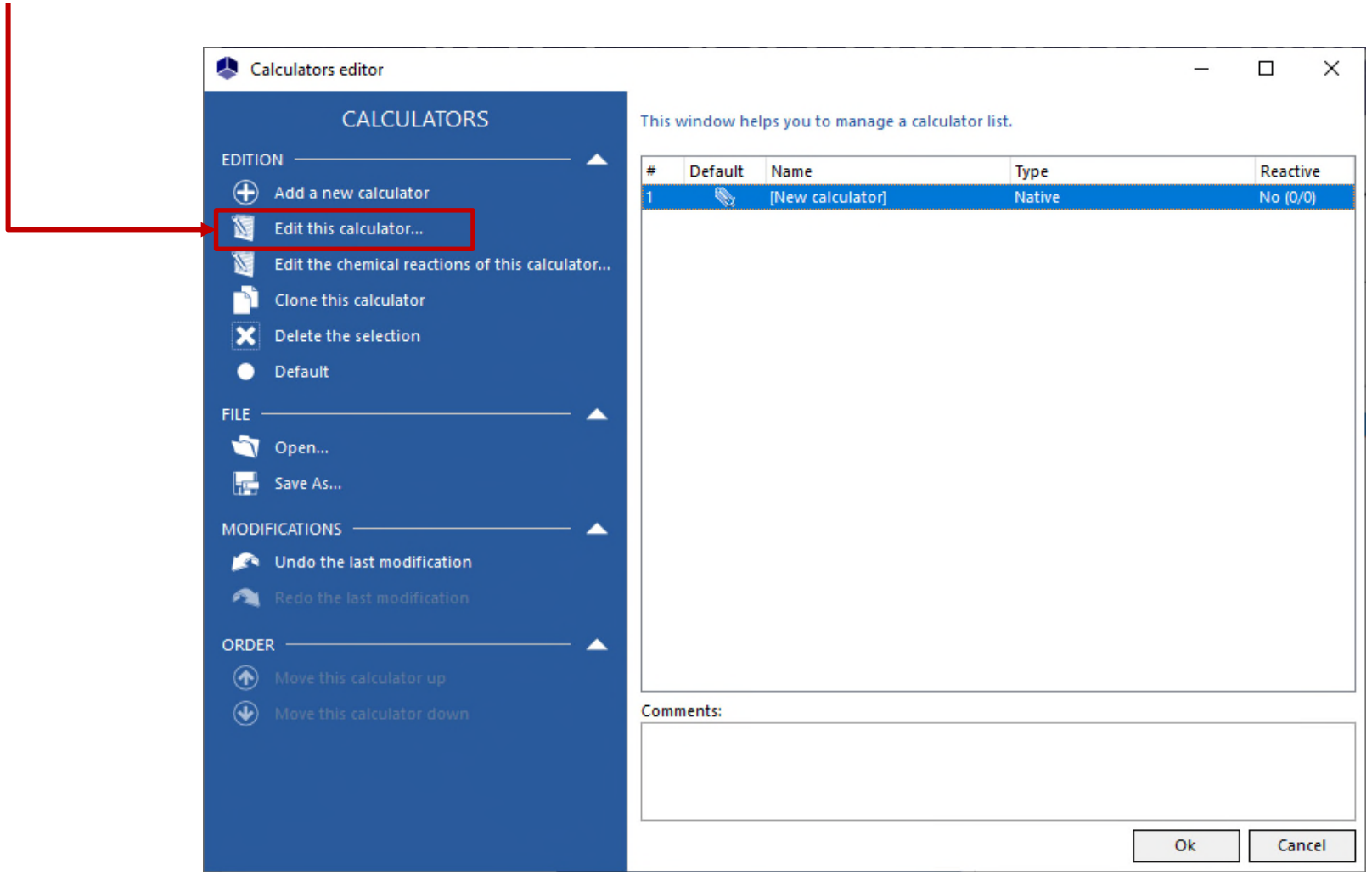
With:

Model parameters	Definition	Value
$\boldsymbol{\mu_{max}}$	Maximum growth rate	4.10^{-5} s^{-1}
$\boldsymbol{K_S}$	Saturation constant	2.8 g/L
$\boldsymbol{C_S, C_X}$	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

From the "*Calculators editor*" window, select "*Edit this calculator*"



Step 1: Selection of the compounds

This application example requires to import the following compounds, with the modifications described hereafter:

- WATER

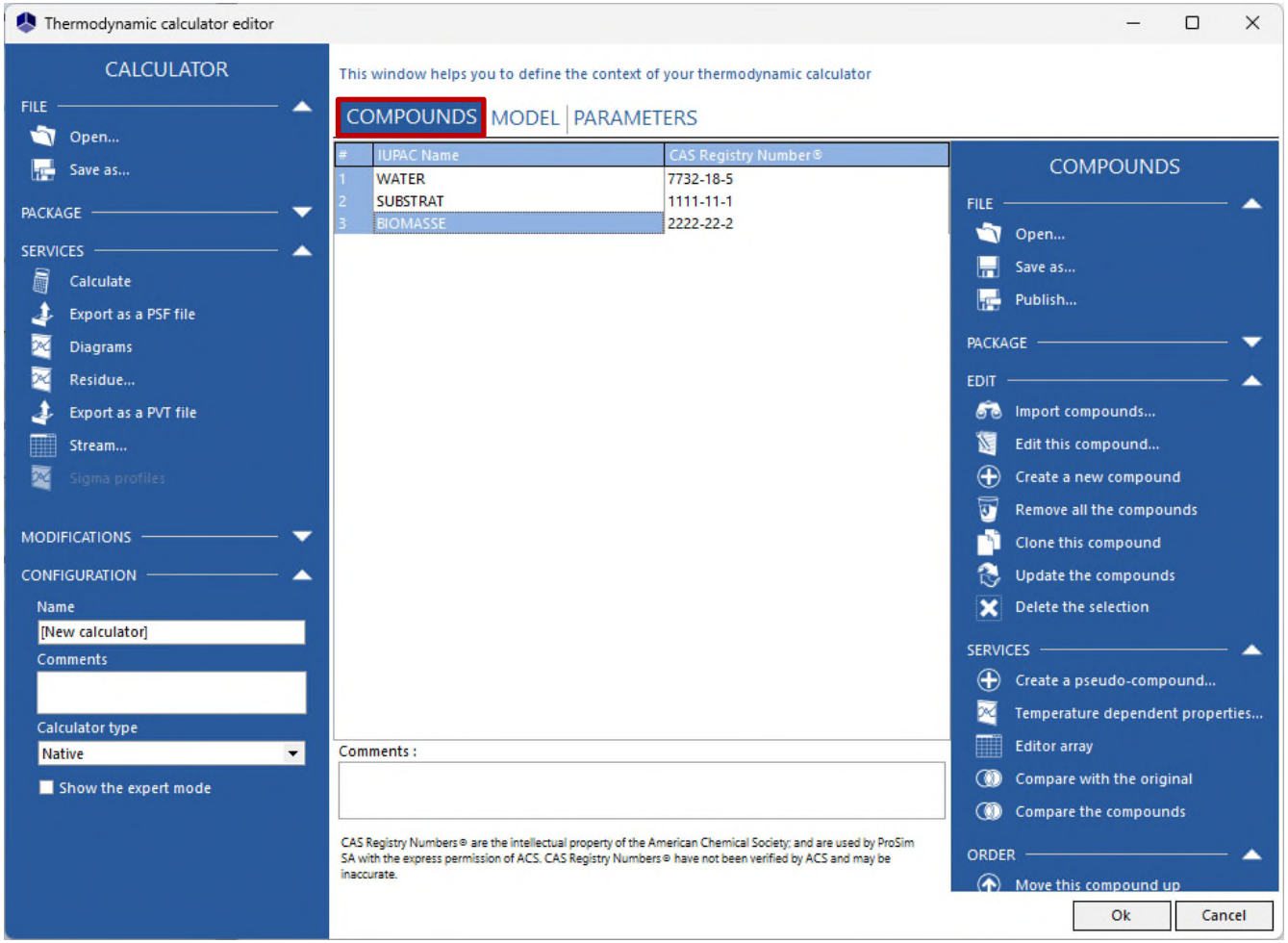
- SUBSTRATE (modeled as “Glucose”):
  - Import of the “Glucose” from the compounds database
  - Modification of the name: SUBSTRATE
  - Modification of the CAS number(*): 1111-11-1

- BIOMASS (modeled as “Glucose”):
  - Import of the “Glucose” from the compounds database
  - Modification of the name: BIOMASS
  - Modification of the CAS number(*): 2222-22-2

(*): 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

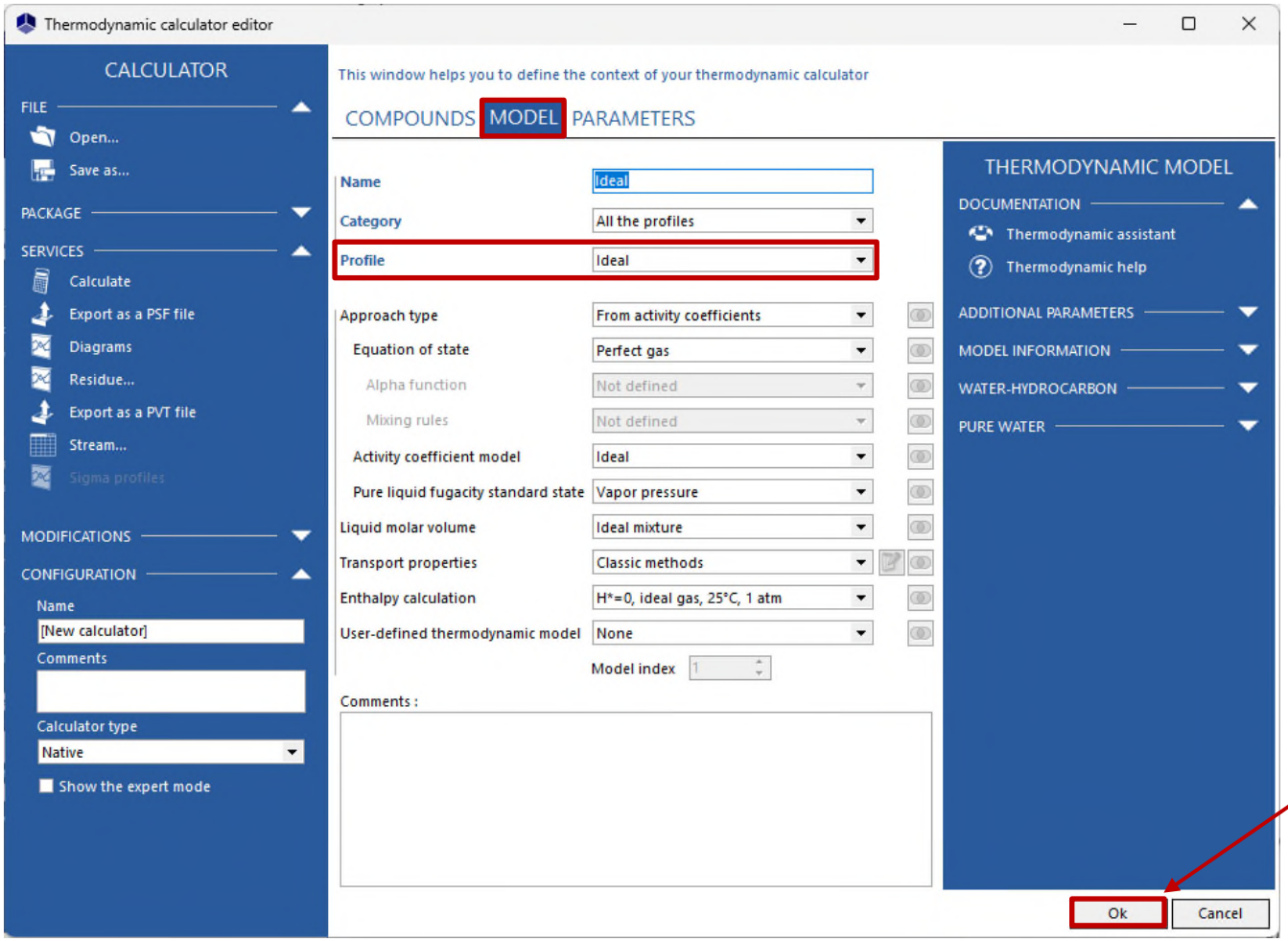
Once this step is done, the compounds are displayed as follows in the "*Compounds*" tab:



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:

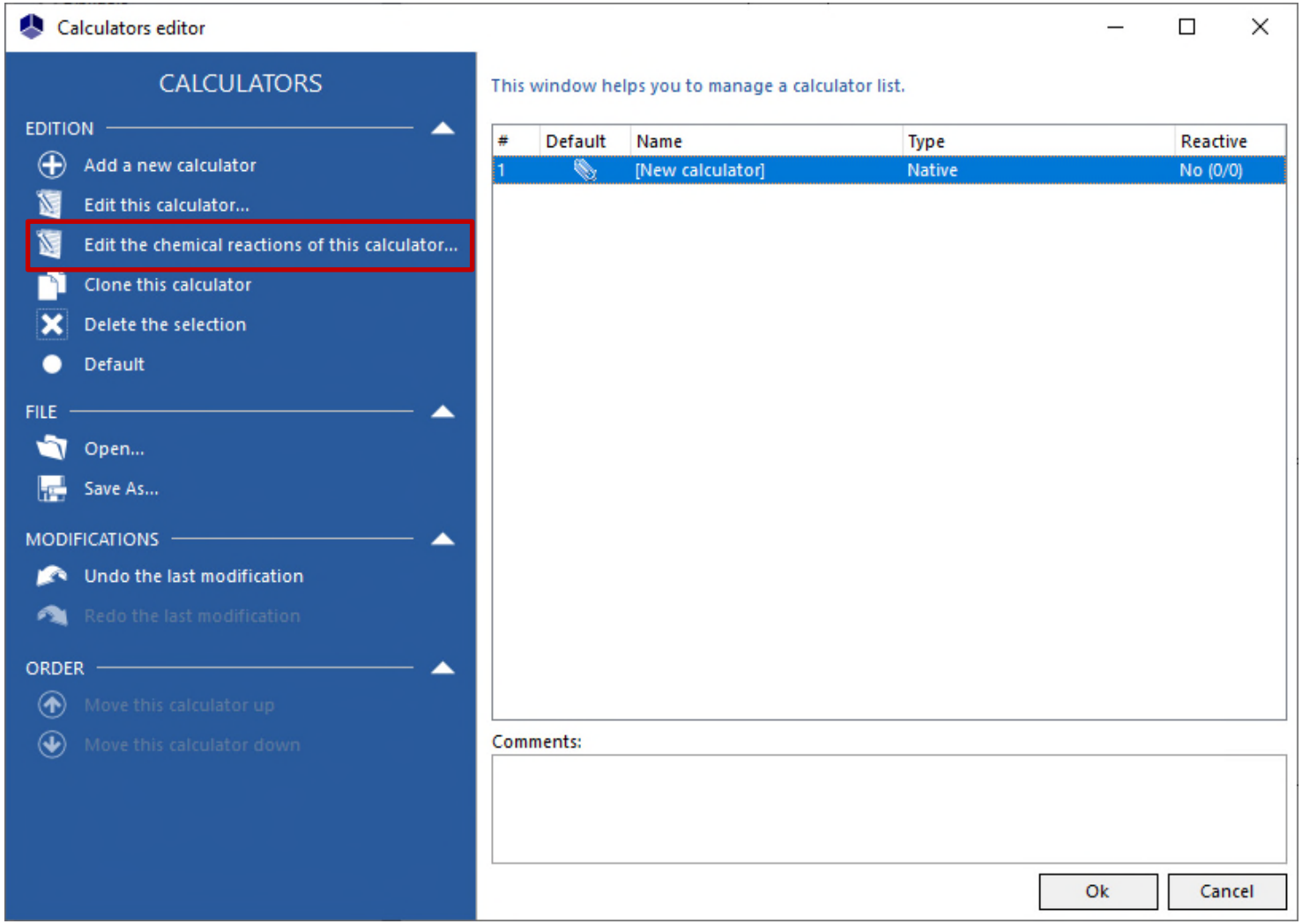


2 - Click on "*Ok*" to confirm

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

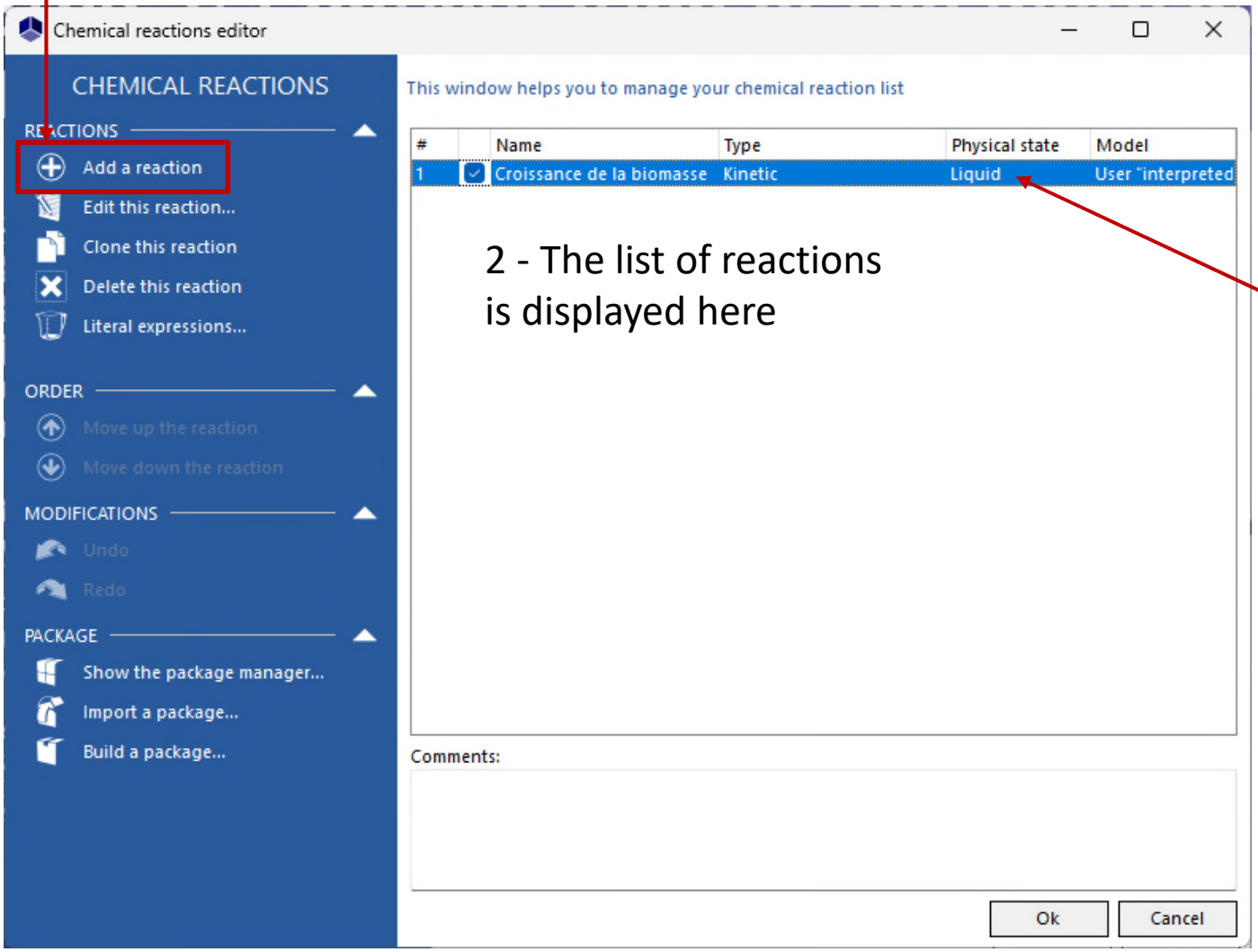
Step 2: Configuration of the bioreaction model

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



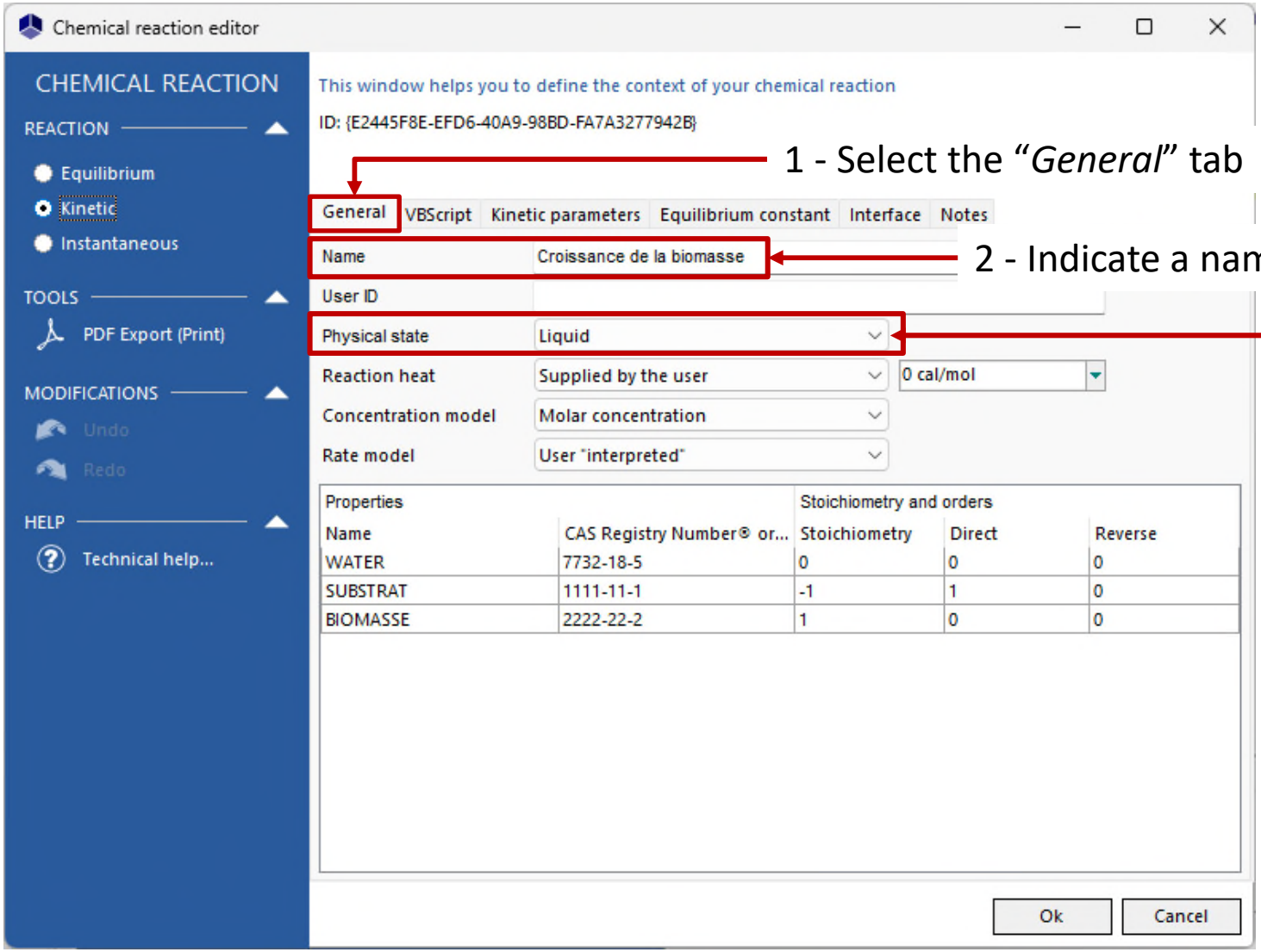
Step 2: Configuration of the bioreaction model

1 - Select "*Add a reaction*"



3 - Double click on the new reaction to configure it

Step 2: Configuration of the bioreaction model

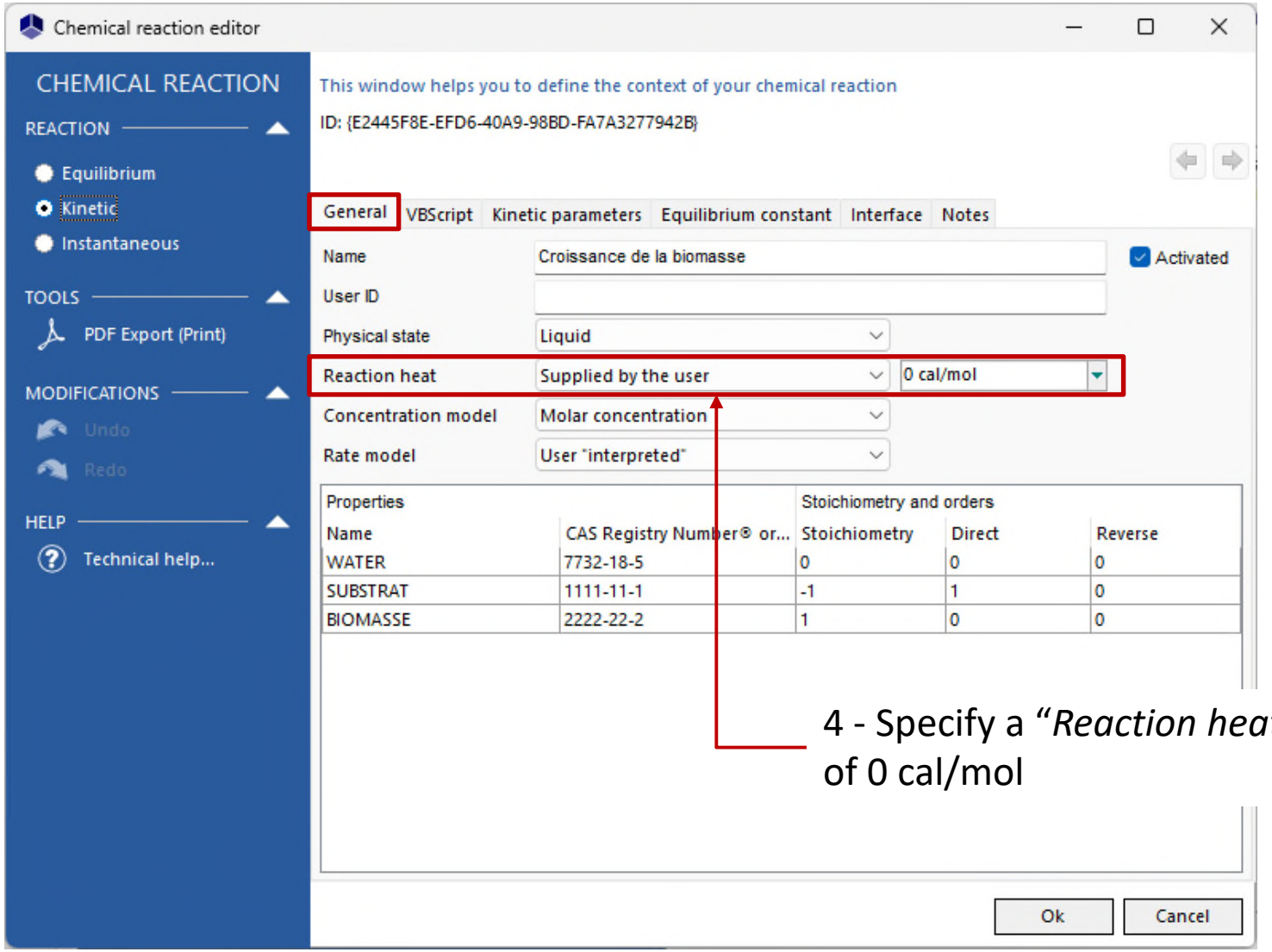


1 - Select the "*General*" tab

2 - Indicate a name (optional)

3 - Indicate the reaction phase

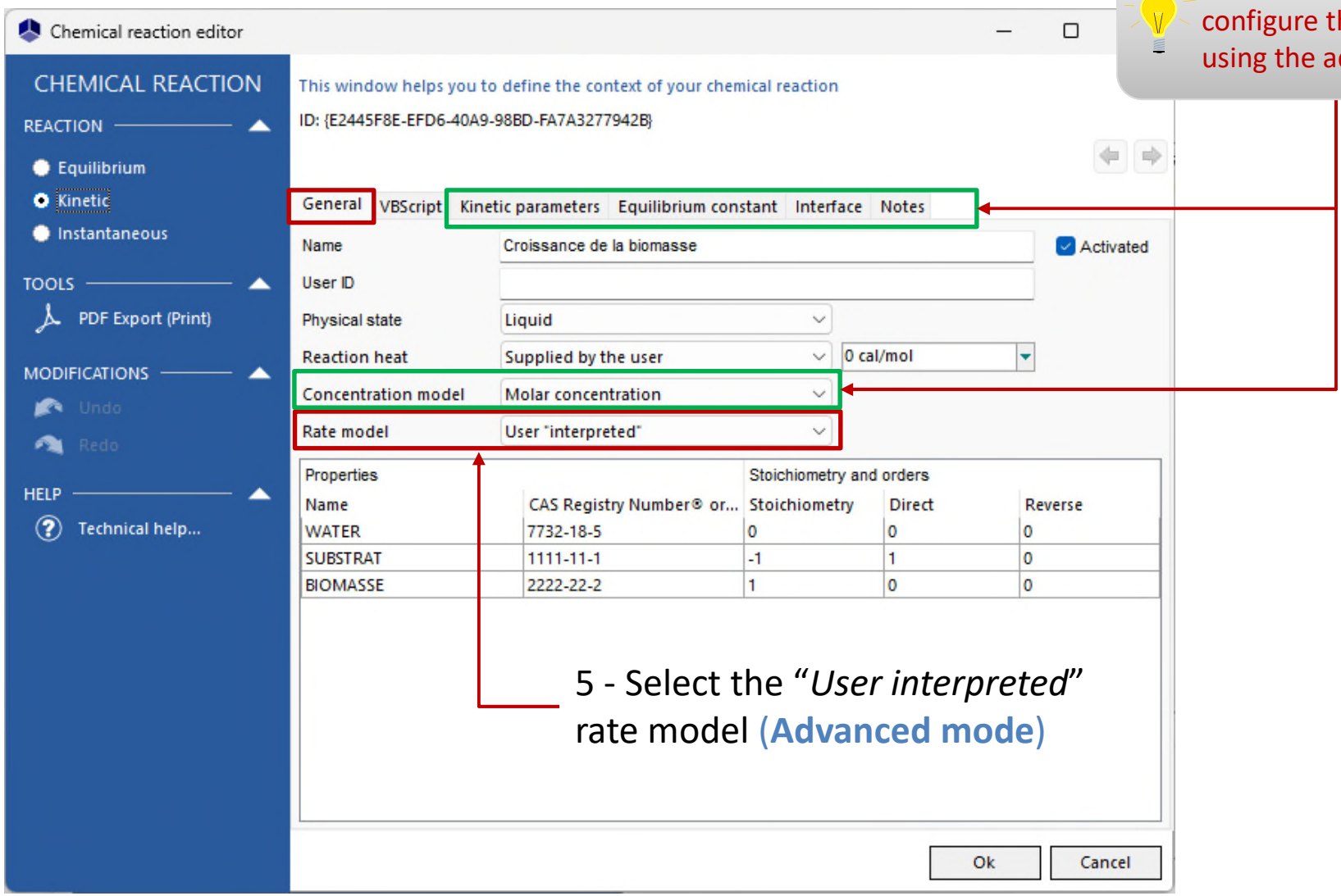
Step 2: Configuration of the bioreaction model



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

Step 2: Configuration of the bioreaction model

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

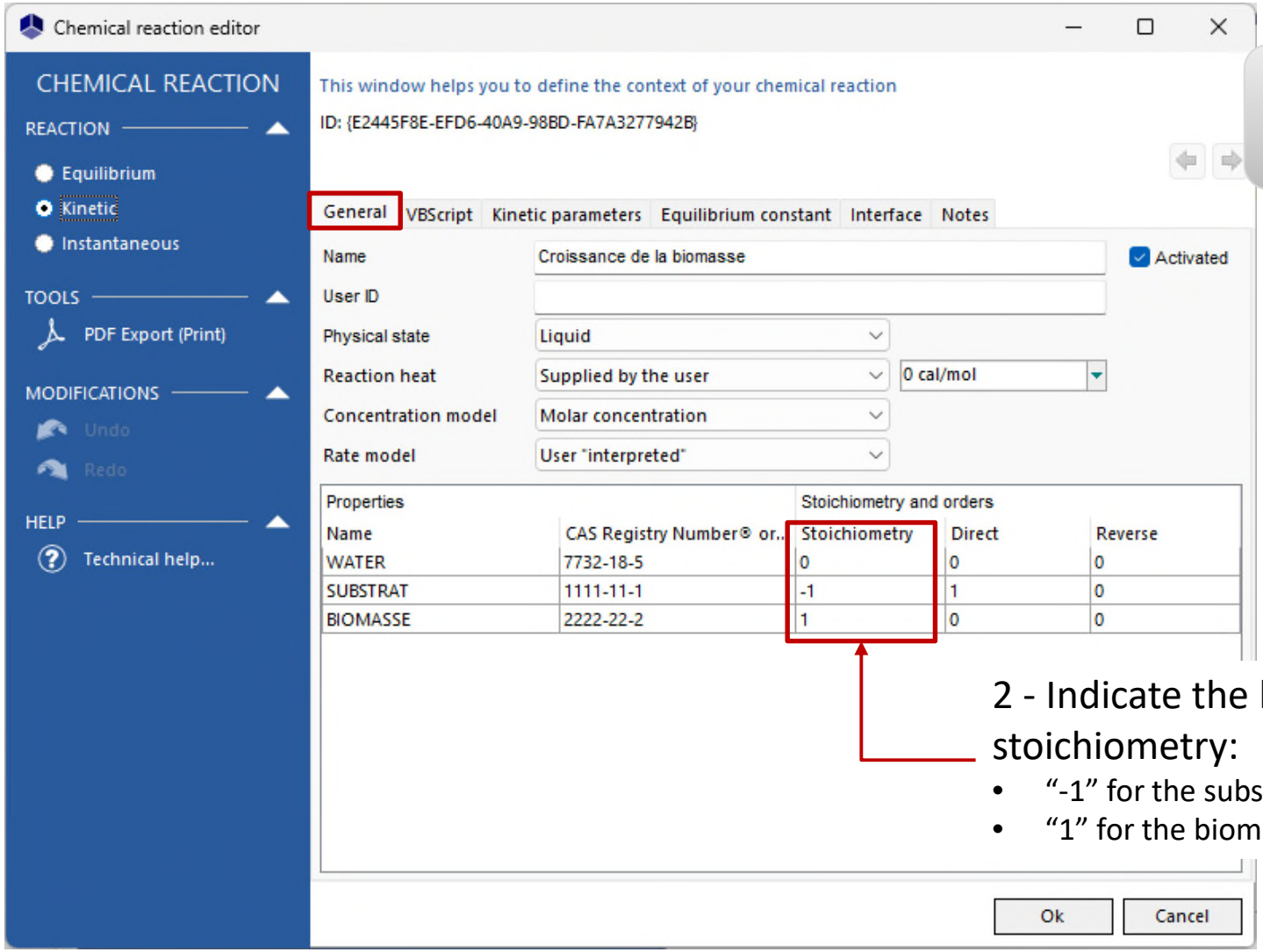


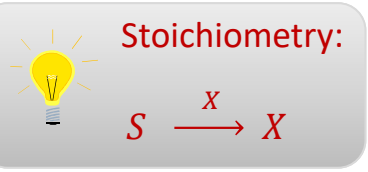
It is not necessary to configure these tabs when using the advanced mode

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

Step 2: Configuration of the bioreaction model

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



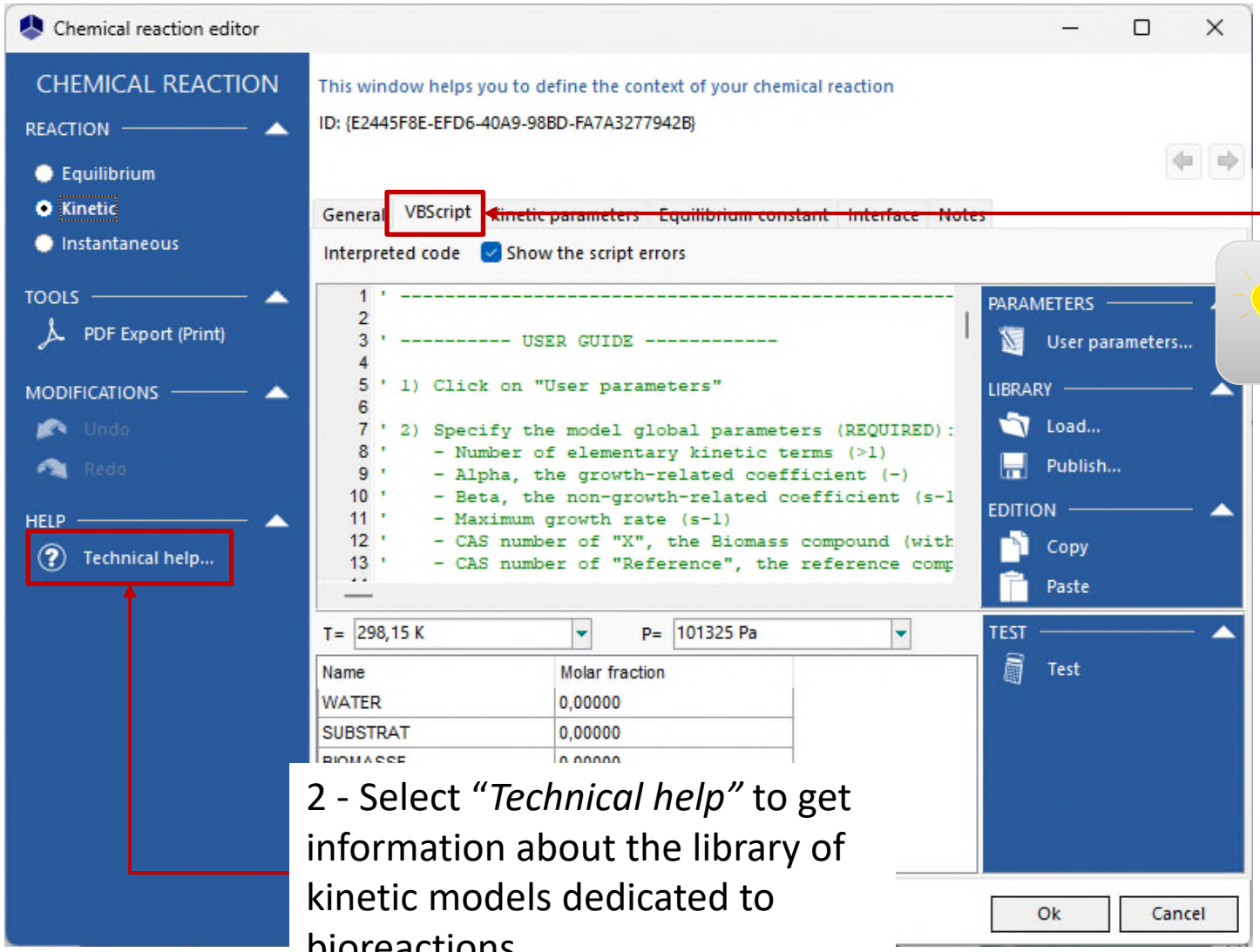


2 - Indicate the bioreaction stoichiometry:

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

Step 2: Configuration of the bioreaction model

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



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 model

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

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

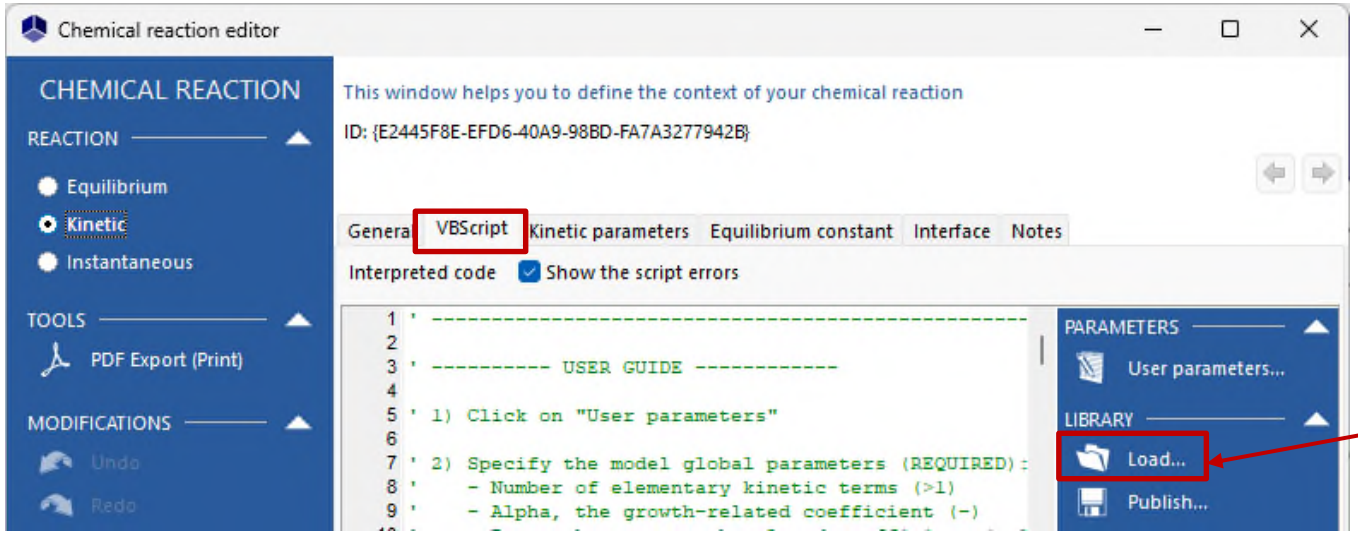
Selection of the elementary kinetic model $r(C_{Si})$

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 model

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

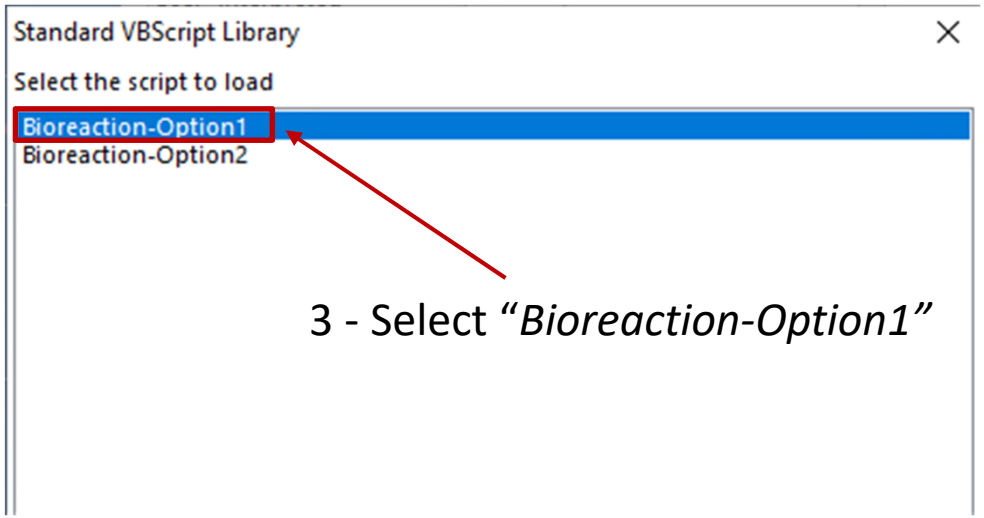


Bioreaction rate:

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

1 - Click on "*Load*"

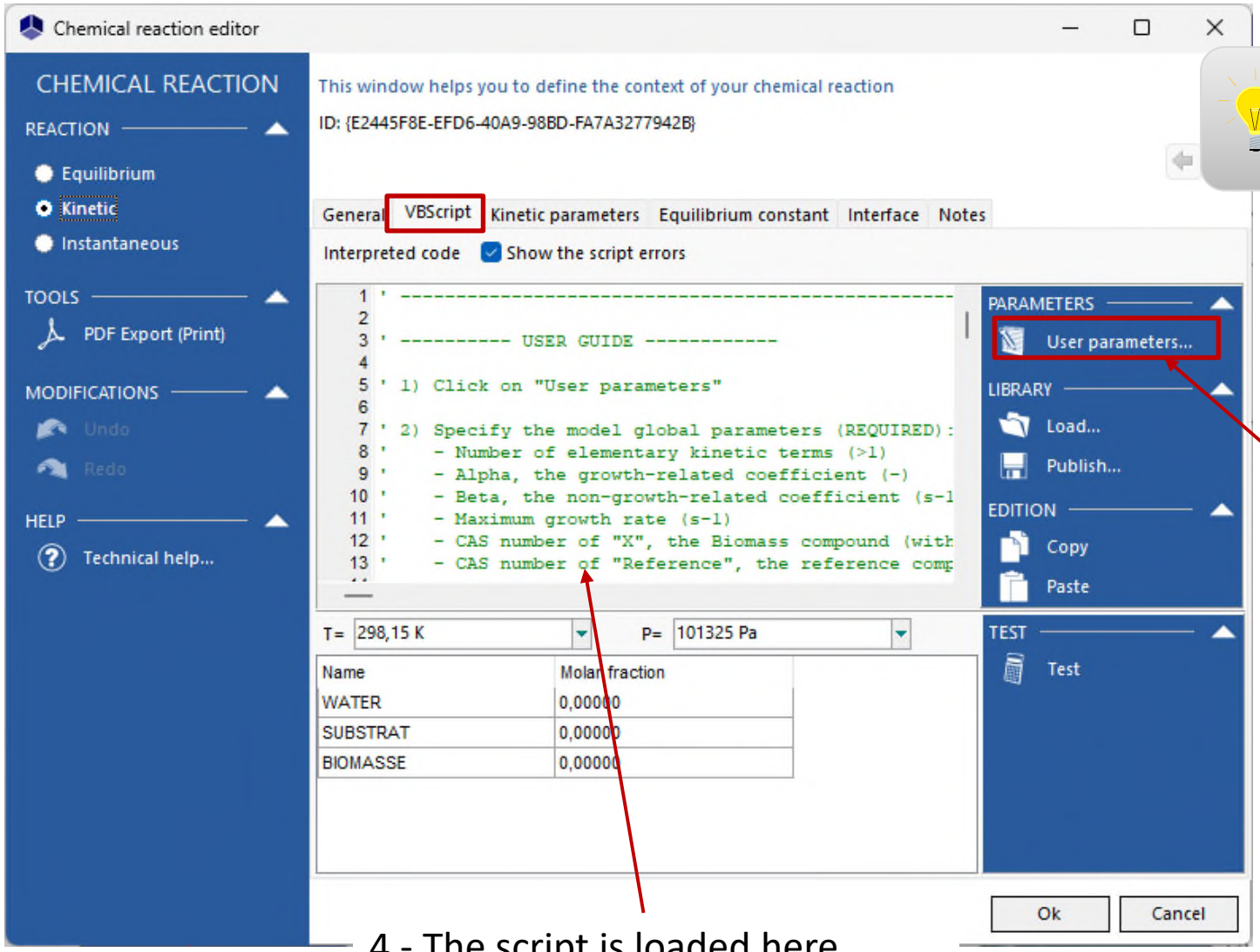
2 - The library of available scripts is displayed here



3 - Select "*Bioreaction-Option1*"

Step 2: Configuration of the bioreaction model

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



Bioreaction rate:

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

5 - Click on *"User parameters"*

4 - The script is loaded here

Step 2: Configuration of the bioreaction model

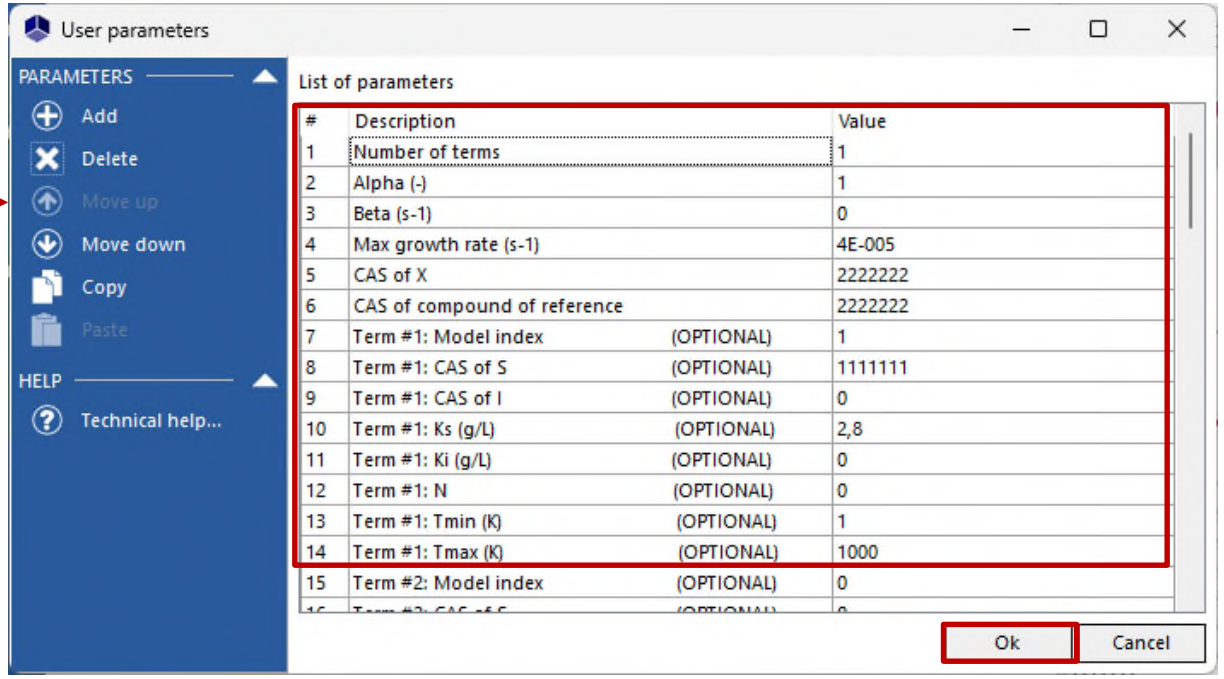
Access the **Advanced mode** to provide a custom kinetic model for the bioreaction

1 - Specify the model input parameters:

- 1 elementary kinetic term, corresponding to the model index #1 (Monod)
- α = 1
- β = 0
- μ_{max} = 4.10^{-5} s^{-1}
- K_S = 2.8 g/L
- CAS number(*) of the biomass (X) and the compound of reference: 2222222
- CAS number(*) of the substrate (S): 1111111

Bioreaction rate:

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



2 - Click on "*Ok*" to confirm... The bioreaction is now correctly configured!

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