ProSim

BATCHREACTOR APPLICATION EXAMPLE

WHITE BIOTECHNOLOGY

SIMULATION OF BATCH GLUCONIC ACID PRODUCTION WITH USER DEFINED KINETICS

EXAMPLE PURPOSE
The main interest of this simple example is to show how user can very simply describe his own kinetics models using the advanced mode available in Simulis Reactions, the chemical reactions server used in BatchReactor software. This white biotechnology example deals with the fermentation of glucose to gluconic acid, which involves the oxidation of the aldehyde group of the sugar to a carboxyl group. The mathematical modeling of the reaction mechanisms uses specific equations (Monod type) which are not available in standard chemical reaction libraries such as Simulis Reactions.

ACCESS	☑ Free-Internet	☐ Restricted to ProSim clients	☐ Restricted	☐ Confidential

CORRESPONDING BATCHREACTOR FILE	*BATCHREA_E04_EN - Gluconic acid.pbpr*

TABLE OF CONTENTS

1. INTRODUCTION 3

2. REACTION MECHANISM 4

3. COMPONENTS 5

4. THERMODYNAMIC MODEL 5

5. REACTION MATHEMATICAL MODEL 6

6. REACTION MODEL IMPLEMENTATION USING SIMULIS REACTIONS 7

7. SIMULATION 15

7.1. Process description 15

7.2. Results 17

8. REFERENCES 18

9. NOMENCLATURE 19

1. INTRODUCTION

This example is taken from [COK01] and deals with the fermentation of glucose to gluconic acid, which involves the oxidation of the aldehyde group of the sugar to a carboxyl group. The industrial production of gluconic acid is by strains of *Aspergillus* and *Pseudomonas ovalis*. The enzyme that catalyses the oxidation of glucose is a dehydrogenase, which is capable of transforming glucose to gluconolactone. Gluconic acid is produced by the hydrolysis of the gluconolactone, which can be either enzymatic or non-enzymatic process. The enzyme that is required for the hydrolysis step is gluconolactonase, although the presence of this enzyme in *Apsergillus* and *Pseudomonas* has not been revealed. Rai and Constantinide [RAI73] considered the hydrolysis stage as a non-enzymatic process. The byproduct of the reaction is decomposed to water and oxygen by the enzyme catalase, which is present in the living cells.

Gluconic acid is extensively used in the food, pharmaceutical, and a wide range of products. In the textile industries, gluconic acid, glucono-δ-lactone, and ammonium gluconates are used in acid catalysts. Gluconates are incorporated in antibiotic complexes (e.g., tetracycline) to improve stability, lower the toxicity, and increase antibiotic levels in the blood. Calcium gluconates are employed for treating calcium deficiencies in both humans and animals.

The hydrogen peroxide produced in the glucose oxidase catalyzed reaction contains an antibacterial action. The addition of a catalase converts the hydrogen peroxide to water and oxygen.

2. REACTION MECHANISM

The reaction mechanisms in the fermentation of glucose to gluconic acid are [COK01]:

- Cell growth:

$$Glucose + Cell \rightarrow More\ cells$$

Namely,

$$C_6H_{12}O_6 + Cell \rightarrow More\ cells \quad \text{(R1)}$$

- Glucose oxidation:

$$Glucose + O_2 \rightarrow Gluconolactone + H_2O_2$$

Namely,

$$C_6H_{12}O_6 + O_2 \xrightarrow{Glucoseoxidase} C_6H_{10}O_6 + H_2O_2 \quad \text{(R2)}$$

- Gluconolactone hydrolysis:

$$Gluconolactone + H_2O \rightarrow Gluconic\ acid$$

Namely,

$$C_6H_{10}O_6 + H_2O \rightarrow C_5H_{11}O_5COOH \quad \text{(R3)}$$

- Hydrogen peroxide decomposition:

$$H_2O_2 \rightarrow H_2O + \frac{1}{2}O_2 \quad \text{(R4)}$$

3. COMPONENTS

Components which are taken into account in the simulation are:

Name	CAS number
Water(*)	7732-18-5
Glucose(*)	50-99-7
Gluconolactone	
Gluconic acid	
Oxygen(*)	7782-44-7
Nitrogen(*)	7727-37-9
Hydrogen peroxide(*)	7722-84-1
Cell	

Compounds with an asterisk are taken from the standard database of Simulis Thermodynamics, thermodynamics server used in BatchReactor. The thermophysical parameters stored in this database are the DIPPR recommended values [ROW11]. Oxygen and nitrogen vapor pressures were changed in order to well represent their solubility in water, Henry's law parameters were obtained from [FOG91]. Oxygen and nitrogen liquid specific heat were set equal to their perfect gas specific heat.

Gluconolactone and gluconic acid compounds were created by cloning the glucose compound from the standard database. Only the name, chemical formula, molecular weight and CAS registry number were changed.

Cell compound was created by cloning the water compound from the standard database. Only the name, the chemical formula (arbitrary set to CHON), molar weight, CAS registry number and vapor pressure correlation (set as non volatile) were changed.

For all components, molar volume correlation parameters were changed in order to have the same density as water.

4. THERMODYNAMIC MODEL

Most of the components are non-volatile in the reaction conditions (glucose, gluconolactone, gluconic acid). Reactions occurred at ambient temperature and atmospheric pressure. Liquid phase was thus assimilated to an ideal solution and gas phase was assumed to follow the Perfect Gas law. For enthalpy calculation, the liquid phase at 25°C and 1 atmosphere enthalpy basis is used.

5. REACTION MATHEMATICAL MODEL

Rai and Constantinide [RAI73] developed a mathematical model for the fermentation of the bacterium *Pseudomonas ovalis*, which converts the glucose to gluconic acid. The following equations describe the dynamics of the logarithmic growth phase:

- Rate of cell growth:

$$\frac{dC_{Cell}}{dt} = b_1 C_{Cell}\left(1 - \frac{C_{Cell}}{b_2}\right) \quad \text{(R1)}$$

- Rate of gluconolactone formation:

$$\frac{dC_{Gluconolactone}}{dt} = \frac{b_3 C_{Cell} C_{Glucose}}{b_4 + C_{Glucose}} \quad \text{(R2)}$$

- Rate of gluconic acid formation:

$$\frac{dC_{Gluconicacid}}{dt} = b_5 C_{Gluconolactone} \quad \text{(R1)}$$

- Rate of hydrogen peroxide decomposition:

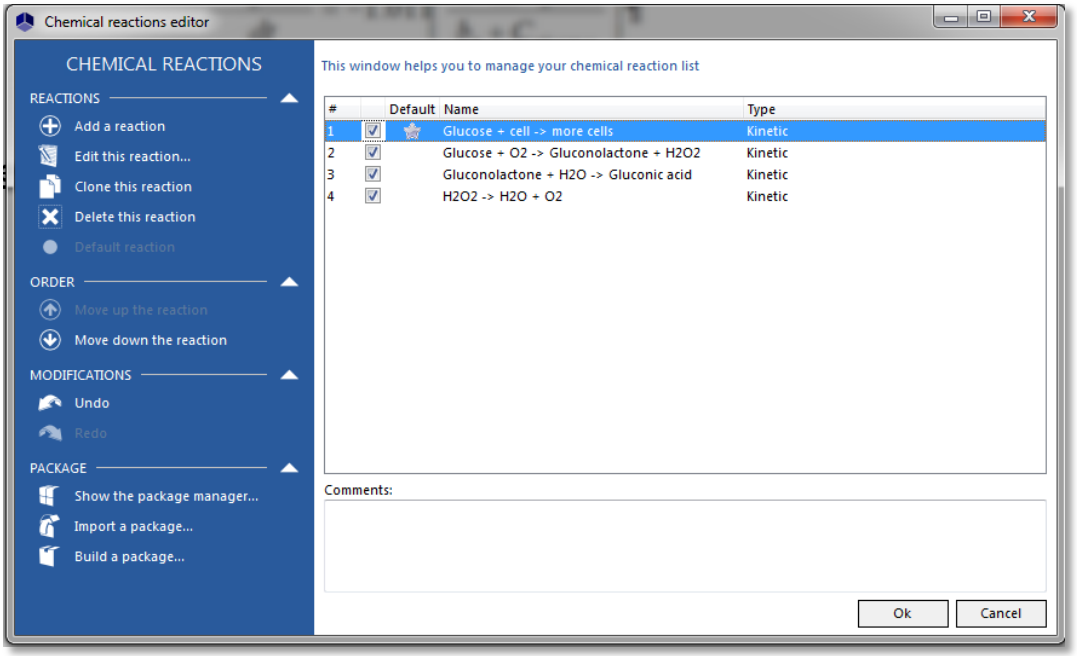
  Hydrogen peroxide decomposition reaction was assumed to be fast reaction following Arrhenius law, with a constant reaction rate of 1.10^6 h^{-1}.

All parameters taken from [COK01] are presented in the following table.

b_1 (h^{-1})	b_2 (g/l)	b_3 (h^{-1})	b_4 (g/l)	b_5 (h^{-1})
0.949	3.439	18.72	37.51	1.169

6. REACTION MODEL IMPLEMENTATION USING SIMULIS REACTIONS

The four reactions (R1), (R2), (R3) and (R4) presented in the paragraphs 2 and 5 were described in Simulis Reactions, as shown in the next screen shot.

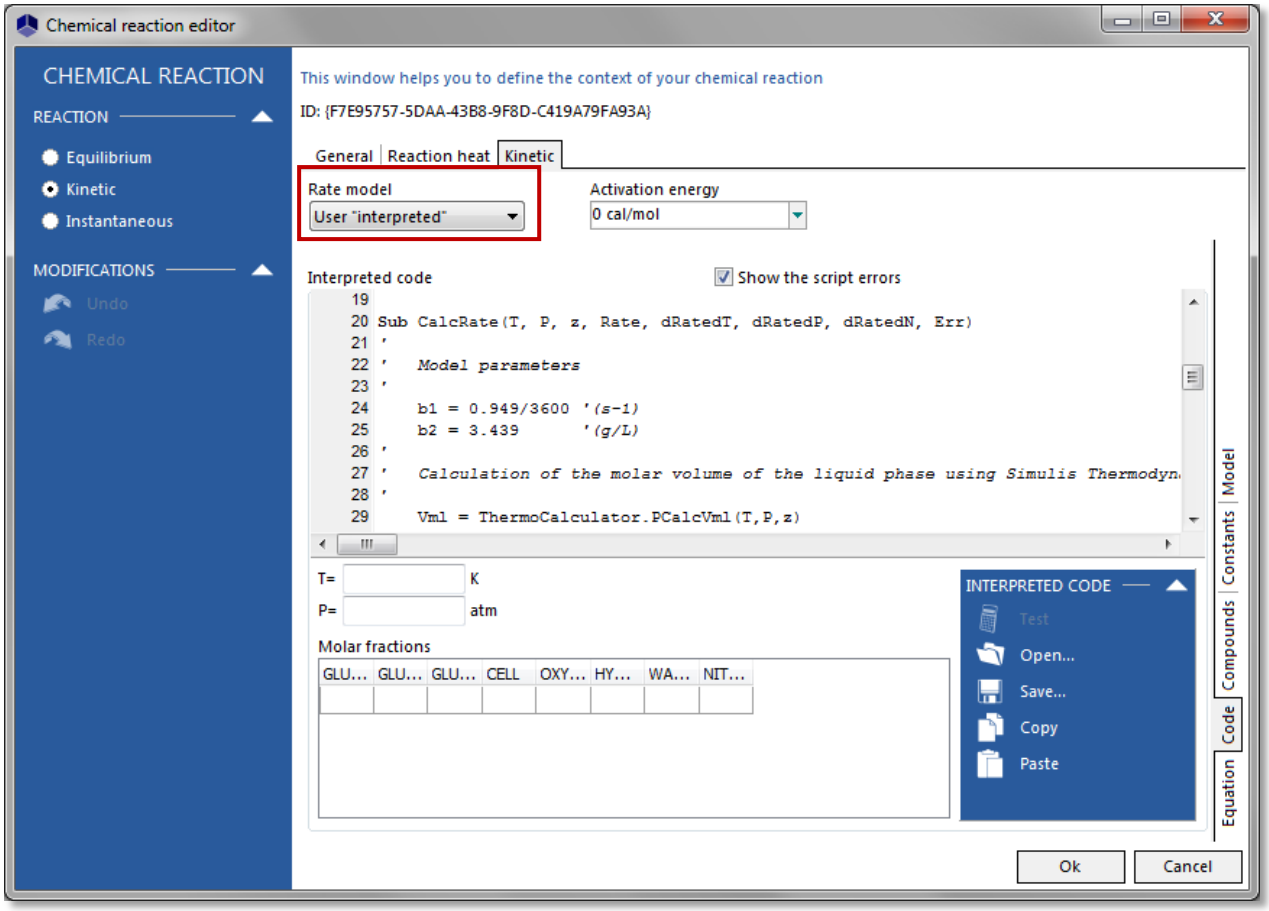


Except for the hydrogen peroxide decomposition, user « interpreted » kinetic rate model was used to implement mathematical models presented by Rai and Constantinide [RAI73], as shown on the next screenshot. Thanks to this functionality of Simulis Reactions, user can write his own code for kinetic model using VBScript (Microsoft Visual Basic Scripting Edition), which is an interpreted language: it doesn't require compilation before being executed and it requires the computer that has to run it has an interpreter (i.e. a program that can understand the whole instructions, e.g. *wscript.exe* in Windows environment). For more information about VBScript language, user can refer to:

http://msdn.microsoft.com/en-us/library/t0aew7h6(v=vs.84).aspx

http://en.wikipedia.org/wiki/VBScript

All reactions take place in the liquid phase. The heat of reaction of each reaction is assumed to be 0.



The VBS code for the (R1) reaction is the following one :

```
' CHECK PROCEDURE

Function CheckRate

  CheckRate = True

End Function




' CALCULATION PROCEDURE

' --- Data ---

' T: Variant - Temperature (K).

' P: Variant - Pressure (atm).

' z: Variant - Molar fractions.

'

' --- Results ---

' Rate: Variant - rate in mol/l/s.

' dRatedT: Variant - rate derivative with the respect to temperature in mol/l/s/K.

' dRatedP: Variant - rate derivative with the respect to pressure in mol/l/s/atm.

' dRatedN: Variant - rate derivative with the respect to number of moles in mol/l/s.

' Err: Variant - Error code.

Sub CalcRate(T, P, z, Rate, dRatedT, dRatedP, dRatedN, Err)
```



```
'
'   Model parameters
'
    b1 = 0.949/3600 '(s-1)
    b2 = 3.439      '(g/l)
'
'   Calculation of the molar volume of the liquid phase using Simulis Thermodynamics Calculator
'
    Vml = ThermoCalculator.PCalcVml(T,P,z)
'
'   Conversion of the molar volume from ProSim unit (cm3/mol) to required unit (l/mol)
'   using Simulis Conversion functions
'
    Set repository = createobject("CverStarDustRepository.StarDust_CVER_Repository")
    Set Qty        = Repository.QuantityByName("Molar volume")
    Vml            = Qty.Convert(Vml, "cm3/mol", "l/mol")
'
    Set MwQty = Repository.QuantityByName("Molar mass")
'
'   Detection of compounds of interest.
'   Pure component properties retrieved from Simulis Thermodynamics Calculator (CAS number, Molecular weight)
'
    CASN_Cell    = "55000-00-5"
    CASN_Glucose = "50-99-7"

    For i = 1 To ThermoCalculator.Compounds.Count
       With ThermoCalculator.Compounds.Items(i-1)
          If (.CasRegistryNumber = CASN_Cell) Then
              ipos_Cell = i - 1
              Mw_Cell   = MwQty.Convert(.Mw.Value, .Mw.UnitName, "g/mol")
              C_Cell    = z(ipos_Cell)/Vml*Mw_Cell
          ElseIf (.CasRegistryNumber = CASN_Glucose) Then
              ipos_Glucose = i - 1
          End If
       End With
    Next
'
'   Calculation of the rate of the reaction
'
'   - Rate expressed as: g of cell / (l s), from Coker et al.
'
```



```
    Rate = b1*C_Cell*(1.-C_Cell/b2)

'

'   - Rate conversion in: mol of cell / (l s)

'

    Rate = Rate/Mw_Cell

'

'   - Rate conversion in:  mol of glucose / (l s)

'

    Rate = Rate*abs(Reaction.StoichiometricCoefficient(ipos_Glucose)/Reaction.StoichiometricCoefficient(ipos_Cell))

End Sub
```


The VBS code for the (R2) reaction is the following one :

```
' CHECK PROCEDURE

Function CheckRate

  CheckRate = True

End Function




' CALCULATION PROCEDURE

' --- Data ---

' T: Variant - Temperature (K).

' P: Variant - Pressure (atm).

' z: Variant - Molar fractions.

'

' --- Results ---

' Rate: Variant - rate in mol/l/s.

' dRatedT: Variant - rate derivative with the respect to temperature in mol/l/s/K.

' dRatedP: Variant - rate derivative with the respect to pressure in mol/l/s/atm.

' dRatedN: Variant - rate derivative with the respect to number of moles in mol/l/s.

' Err: Variant - Error code.


Sub CalcRate(T, P, z, Rate, dRatedT, dRatedP, dRatedN, Err)

'

'   Model parameters

'

    b3 = 18.72/3600 '(s-1)

    b4 = 37.51      ' g/l)

'

'   Calculation of the molar volume of the liquid phase, using Simulis Thermodynamics Calculator

'

    Vml = ThermoCalculator.PCalcVml(T,P,z)

'

'   Conversion of the molar volume from ProSim unit (cm3/mol) to required unit (l/mol)

'   using Simulis Conversion functions

'

    Set repository = createobject("CverStarDustRepository.StarDust_CVER_Repository")

    Set Qty        = Repository.QuantityByName("Molar volume")

    Vml            = Qty.Convert(Vml, "cm3/mol", "l/mol")

'

    Set MwQty = Repository.QuantityByName("Molar mass")

'

'   Detection of compounds of interest.
```



```
'   Pure component properties retrieved from Simulis Thermodynamics Calculator (CAS number, Molecular weight)
'
    CASN_Cell           = "55000-00-5"
    CASN_Glucose        = "50-99-7"
    CASN_Gluconolactone = "90-80-2"

    For i = 1 To ThermoCalculator.Compounds.Count
       With ThermoCalculator.Compounds.Items(i-1)
          If (.CasRegistryNumber = CASN_Cell) Then
              ipos_Cell = i - 1
              Mw_Cell   = MwQty.Convert(.Mw.Value, .Mw.UnitName, "g/mol")
              C_Cell    = z(ipos_Cell)/Vml*Mw_Cell
              CA        = C_Cell
          ElseIf (.CasRegistryNumber = CASN_Glucose) Then
              ipos_Glucose = i - 1
              Mw_Glucose   = MwQty.Convert(.Mw.Value, .Mw.UnitName, "g/mol")
              C_Glucose    = z(ipos_Glucose)/Vml*Mw_Glucose
              CD           = C_Glucose
          ElseIf (.CasRegistryNumber = CASN_Gluconolactone) Then
              ipos_Gluconolactone = i - 1
              Mw_Gluconolactone   = MwQty.Convert(.Mw.Value, .Mw.UnitName, "g/mol")
          End If
       End With
    Next
'
'   Calculation of the rate of the reaction
'
'   - Rate expressed as: g of Gluconolactone / (l s), from Coker et al.
'
    Rate = b3*CA*CD/(b4+CD)
'
'   - Rate conversion in: mol of Gluconolactone / (l s)
'
    Rate = Rate / Mw_Gluconolactone
End Sub
```


The VBS code for the (R3) reaction is the following one :

```
' CHECK PROCEDURE

Function CheckRate

  CheckRate = True

End Function




' CALCULATION PROCEDURE

' --- Data ---

' T: Variant - Temperature (K).

' P: Variant - Pressure (atm).

' z: Variant - Molar fractions.

'

' --- Results ---

' Rate: Variant - rate in mol/l/s.

' dRatedT: Variant - rate derivative with the respect to temperature in mol/l/s/K.

' dRatedP: Variant - rate derivative with the respect to pressure in mol/l/s/atm.

' dRatedN: Variant - rate derivative with the respect to number of moles in mol/l/s.

' Err: Variant - Error code.


Sub CalcRate(T, P, z, Rate, dRatedT, dRatedP, dRatedN, Err)

'

'   Model parameters

'

    b5 = 1.169/3600 '(s-1)

'

'   Calculation of the molar volume of the liquid phase using Simulis Thermodynamics Calculator

'

    Vml = ThermoCalculator.PCalcVml(T,P,z)

'

'   Conversion of the molar volume from ProSim unit (cm3/mol) to required unit (l/mol)

'   using Simulis Conversion functions

'

    Set repository = createobject("CverStarDustRepository.StarDust_CVER_Repository")

    Set Qty        = Repository.QuantityByName("Molar volume")

    Vml            = Qty.Convert(Vml, "cm3/mol", "l/mol")

'

    Set MwQty = Repository.QuantityByName("Molar mass")

'

'   Detection of compounds of interest.

'   Pure component properties retrieved from Simulis Thermodynamics Calculator (CAS number, Molecular weight)
```



```
'
    CASN_Gluconolactone = "90-80-2"
    CASN_GluconicAcid   = "526-95-4"

    For i = 1 To ThermoCalculator.Compounds.Count
       With ThermoCalculator.Compounds.Items(i-1)
          If (.CasRegistryNumber = CASN_Gluconolactone) Then
              ipos_Gluconolactone = i - 1
              Mw_Gluconolactone   = MwQty.Convert(.Mw.Value, .Mw.UnitName, "g/mol")
              C_Gluconolactone    = z(ipos_Gluconolactone)/Vml*Mw_Gluconolactone
              CB = C_Gluconolactone
          ElseIf (.CasRegistryNumber = CASN_GluconicAcid) Then
              ipos_GluconicAcid      = i - 1
              Mw_GluconicAcid        = MwQty.Convert(.Mw.Value, .Mw.UnitName, "g/mol")
          End If
       End With
    Next
'
'   Calculation of the rate of the reaction
'
'   - Rate expressed as: g of gluconic acid / (l s), from Coker et al.
'
    Rate = b5*CB
'
'   - Rate conversion in: mol of gluconic acid / (l s), equivalent to mol of gluconolactone / (l s)
'
    Rate = Rate / Mw_GluconicAcid
End Sub
```


7. SIMULATION

7.1. Process description

The reactor used for the gluconic acid production is described in the table below.

Reactor	
Type	Closed vapor-liquid
Global volume (vapor + liquid)	5.5 m^3
Head space (initial)	Nitrogen

The initial conditions are presented in the following table:

Initial conditions	
Temperature	25°C
Pressure	1 atm
Initial load (kg)	
Glucose	50
Cell	0.5
Oxygen	1.2
Water	950
Nitrogen	3.3
Other compounds	0

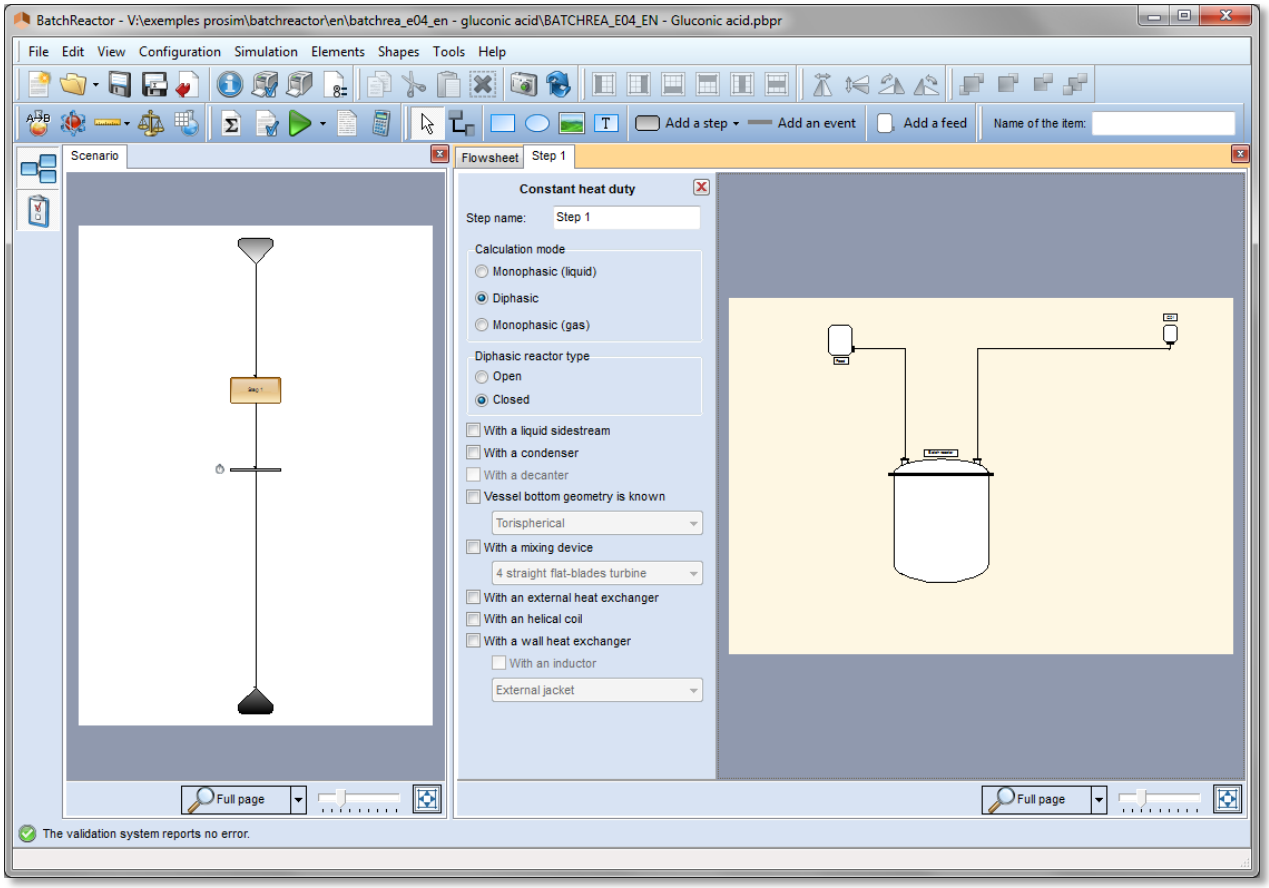
A continuous air stream at ambient condition feeds the reactor in order to carry in the oxygen required for the reactions. The characteristics of this feed are:

Temperature	25°C
Pressure	1 atm
Total flow rate	10 kg/h
Mole fractions	
Oxygen	0.21
Nitrogen	0.79
Other components	0

The recipe consists in one adiabatic step with the following parameters:

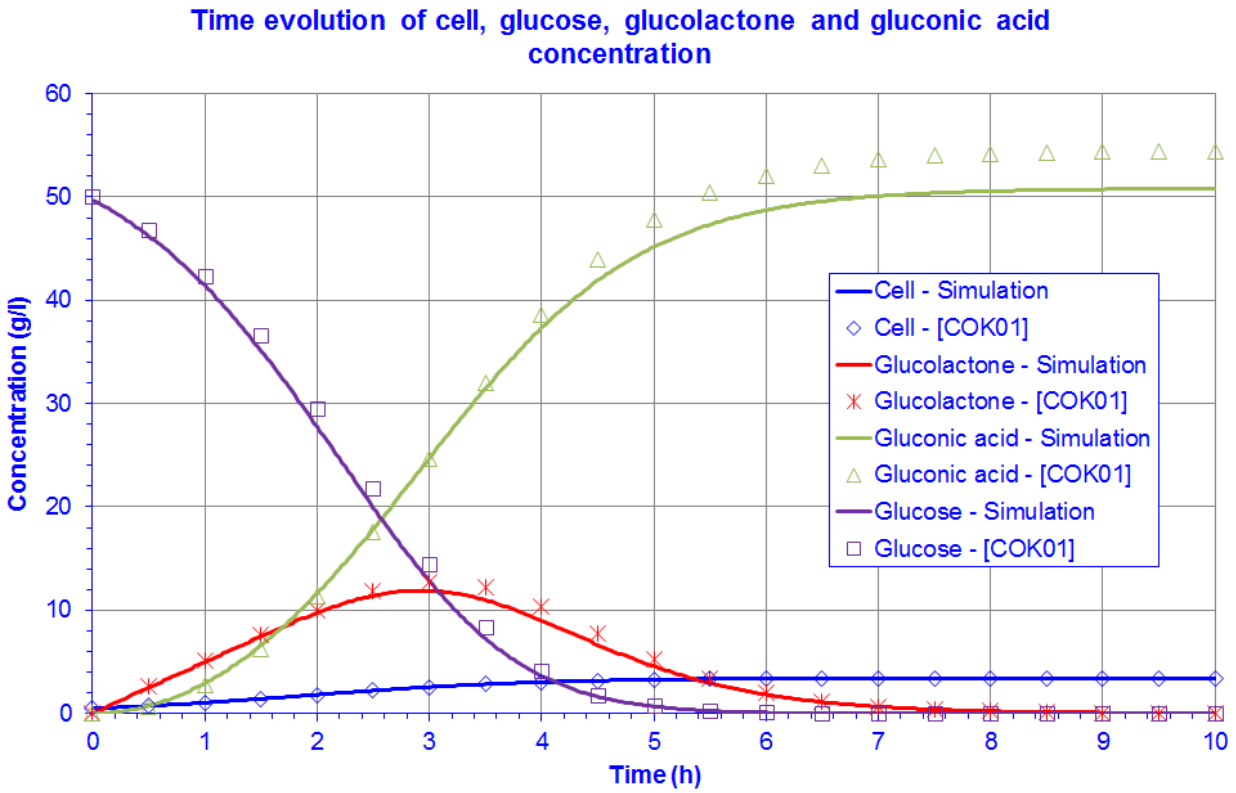
Type	Constant heat duty
Heat duty	0 kcal/h
Pressure	1 atm
Step duration	10 h

The scenario is presented on the left of the following screen shot and the flowsheet on the right part.



7.2. Results

Next graph presents some simulation results obtained with BatchReactor software. The compounds concentrations time curves show a good agreement with data provided by [COK01]. It has to be noticed that using BatchReactor software, all batch parameters can be monitored (liquid volume, gas phase compositions…). Moreover, the detailed modeling of the reactor (heating/cooling system, condenser, vessel geometry…) can be taken into account with BatchReactor.



8. REFERENCES

[COK01] COKER A.K., “Modeling of Chemical Kinetics and Reactor Design”, Gulf Professional Publishing (2001)

[FOG91] FOGG P.G.T., GERRARD W., “Solubility of gases in liquids”, Wiley (1991)

[RAI73] RAI V.R., CONSTANTINIDE A., “Mathematical Modeling and Optimization of the Gluconic Acid Fermentation”, AIChE Symp. Ser., 69(132), 114 (1973)

[ROW11] ROWLEY R.L., WILDING W.V., OSCARSON J.L., GILES N.F., “DIPPR® Data Compilation of Pure Chemical Properties”, Design Institute for Physical Properties, AIChE, New York, NY (2011), http://dippr.byu.edu/

9. NOMENCLATURE

b_1	Kinetic parameter	h^{-1}
b_2	Kinetic parameter	g/l
b_3	Kinetic parameter	h^{-1}
b_4	Kinetic parameter	g/l
b_5	Kinetic parameter	h^{-1}
C_i	Concentration of the compound i	g/l
t	Time	h

