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BATCHREACTOR APPLICATION EXAMPLE

SOLVENT CHANGE

EXAMPLE PURPOSE
This example illustrates how BatchReactor can be used to simulate a solvent change process by alternating heating and feeding phases to replace an initial solvent mixture by an almost pure solvent. The goal is to facilitate subsequent separation steps while respecting the process constraints, particularly the temperature limit related to the stability of thermosensitive compounds.

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CORRESPONDING BATCHCOLUMN FILES	*BATCHREA_EX_EN-Solvent-change.pbpc*

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Energy

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1. INTRODUCTION

After a chemical reaction, the resulting products are generally found in a reaction medium consisting of solvents and active compounds (API: Active Pharmaceutical Ingredients). To enable downstream separation operations, the solvent composition must be adjusted. This is particularly relevant when a solvent mixture is used, and it becomes necessary to favor a single solvent to facilitate the purification step.

Implementing successive sequences of heating and solvent feeding is an effective strategy to achieve this goal. In particular, the partial removal of a first solvent by evaporation, followed by the controlled addition of a second, allows the composition of the reaction medium to be gradually transformed. The process results in an almost pure solvent, better suited for separation and recovery of the API.

BatchReactor, the batch reactor simulation software from Fives ProSim, allows modeling this type of process. It offers the ability to accurately represent the heating, evaporation, and feeding steps, and to track the evolution of the mixture composition throughout the campaign.

In the example presented here, a tank contains a mixture of ethanol and toluene, as well as a dissolved API. The API is not modeled in the simulation as the chemical reaction is not taken into account. The objective is solely to focus on the solvent change without unnecessarily complicating the modeling. The process involves reducing the ethanol fraction by evaporation while adding toluene, to obtain an almost pure toluene solvent at the end of the operation. This configuration significantly simplifies the subsequent separation of the solvent and the API.

Objectives of the Case Study:

- Change the current solvent (ethanol-toluene mixture) to almost pure toluene,
- **Specification**: achieve an ethanol content in the solvent of less than 1 ppm,
- **Constraint**: maintain the reactor temperature below the API degradation temperature, set at 70°C.

Here is the scenario:

Step 1 – Heating Phase 1

The process begins with a heating phase under controlled pressure. The goal is to remove part of the ethanol in the solvent by evaporation, reducing the liquid load in the reactor.

Step 2 – Feeding Phase 1

Once the target volume is reached, a first feeding of toluene is carried out. This step is performed under constant pressure and is accompanied by a nitrogen supply. Nitrogen has a dual role: to inert the reactor and to compensate for the pressure drop caused by reactor cooling.

Step 3 – Heating Phase 2

A second heating phase is then initiated under similar conditions to the first. It allows the continued removal of residual ethanol and brings the reactor volume back to its defined minimum value.

Step 4 – Feeding Phase 2

Finally, a second feeding of toluene is carried out. As with the first step, it is performed under constant pressure and accompanied by nitrogen feeding. This step adjusts the final solvent composition and ensures a residual ethanol content in line with the specification.

2. COMPOUNDS

The compounds considered in the simulation are the following ones:

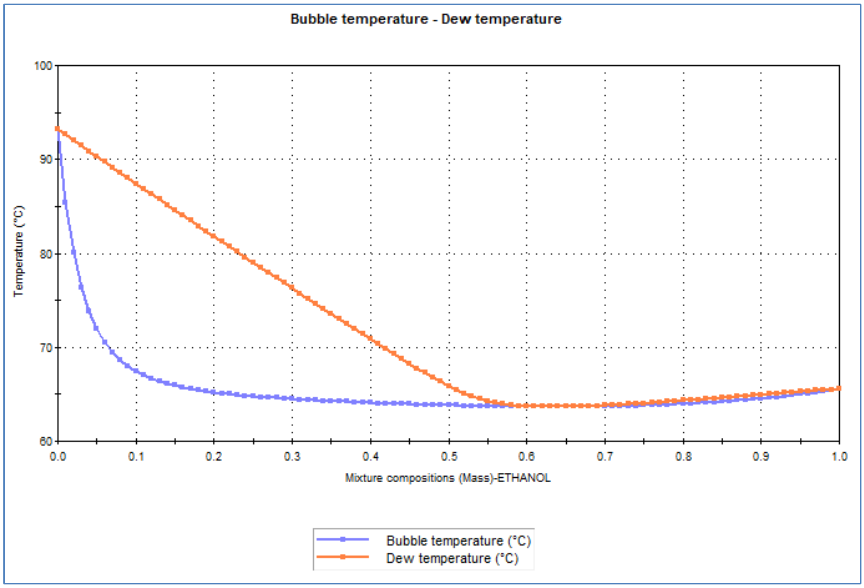
Name	Formula	CAS number[1]
Ethanol	C_2H_6O	64-17-5
Toluene	C_7H_8	108-88-3
Nitrogen	N_2	7727-37-9

The compounds come from the standard database of Simulis Thermodynamics, the calculation server of physico-chemical properties and phase equilibria used in BatchReactor. The physico-chemical properties stored in this database are taken from the DIPPR database [ROW24].

3. THERMODYNAMIC MODEL

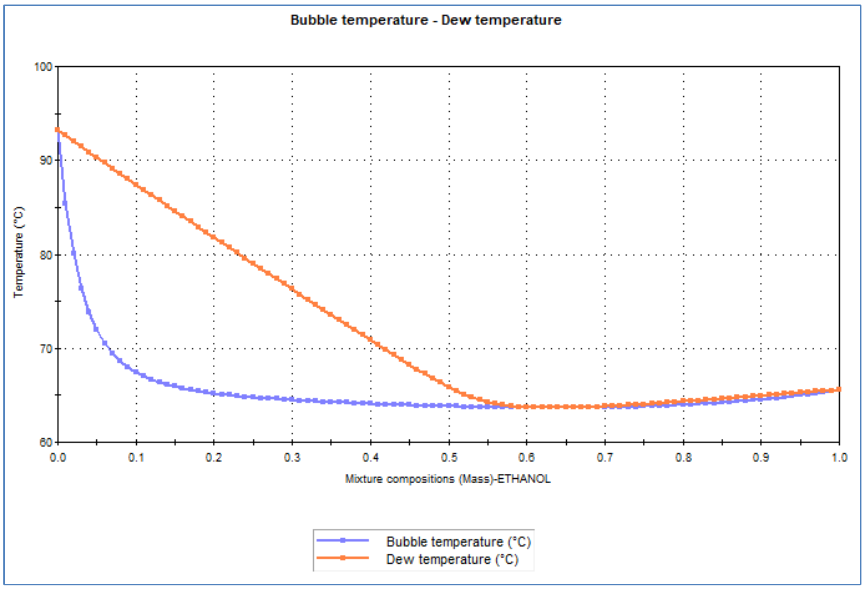
Due to the pressure level in this process (lower than atmospheric pressure) and the polar nature of the compounds, the *UNIFAC modified Larsen* profile is chosen. This model is based on an heterogeneous approach and allows a rigorous representation of the non-ideal thermodynamic behavior (leading to the formation of azeotropes) of the solvent mixture. As an illustration, the vapor-liquid equilibrium curves of the "ethanol-toluene" binary are presented in the graphs below.

For a pressure of 0.6 bar:



[1] *CAS Registry Numbers® are the intellectual property of the American Chemical Society and are used by Fives ProSim SAS with the express permission of ACS. CAS Registry Numbers® have not been verified by ACS and may be inaccurate.*

For a pressure of 0.25 bar:



4. SIMULATION

4.1. Process Description

4.1.1. Reactor

The reactor model is very simple, as the objective is simply to establish material and energy balances and to develop a relevant scenario. Therefore, the dimensions of the equipment are not necessary.

The initial conditions are detailed below:

- ✓ Temperature : 20°C
- ✓ Pressure : 0.6 bar
- ✓ Total mass : 100 kg
- ✓ Initial mass composition
  - Ethanol : 40%
  - Toluene : 60%
- ✓ Head space composition: nitrogen

The reactor global volume is 150 l.

The alarms are set as follows:

- ✓ Temperature
  - Minimum : 0°C
  - Maximum : 200°C
- ✓ Volume
  - Minimum : 1 l
  - Maximum : 150 l

4.1.2. Feeds

There are 2 feeds involved:

- ✓ **Inert**:
  - Temperature : 20°C
  - Pressure : 1 atm
  - Composition : Pure nitrogen
  - Flowrate : 150 l/h

- ✓ **Toluene**:
  - Temperature : 20°C
  - Pressure : 1 atm
  - Composition : Pure toluene
  - Flowrate : 70 kg/h

These feeds are activated according to the steps specified in the following paragraph.

4.2. Operating mode

The operating mode consists of 4 steps that are divided into 2 phases “Heating & Feeding of new solvent”. The steps are all the "Specified heat duty" type (step without thermal device). The operating parameters are indicated below:

Heating 1

The objective of this step is to heat in order to evaporate the ethanol and reduce the charge volume to a limit of 60 l.

- ✓ Heat duty : 4 kW
- ✓ Operating pressure : 0.6 bar
- ✓ Feeds
  - Toluene : Not activated
  - Inert : Activated
- ✓ End event : Total load inside the reactor = 60 l

Feed 1

The objective of this step is to inject pure toluene into the reactor to replace the previously extracted ethanol.

- ✓ Heat duty : 0 kW (adiabatic)
- ✓ Operating pressure : 0.6 bar
- ✓ Feeds
  - Toluene : Activated
  - Inert : Activated
- ✓ End event : Total load inside the reactor = 140 l

Heating 2

The objective of this step is to heat to evaporate the ethanol and reduce the charge volume to a limit of 60 l.

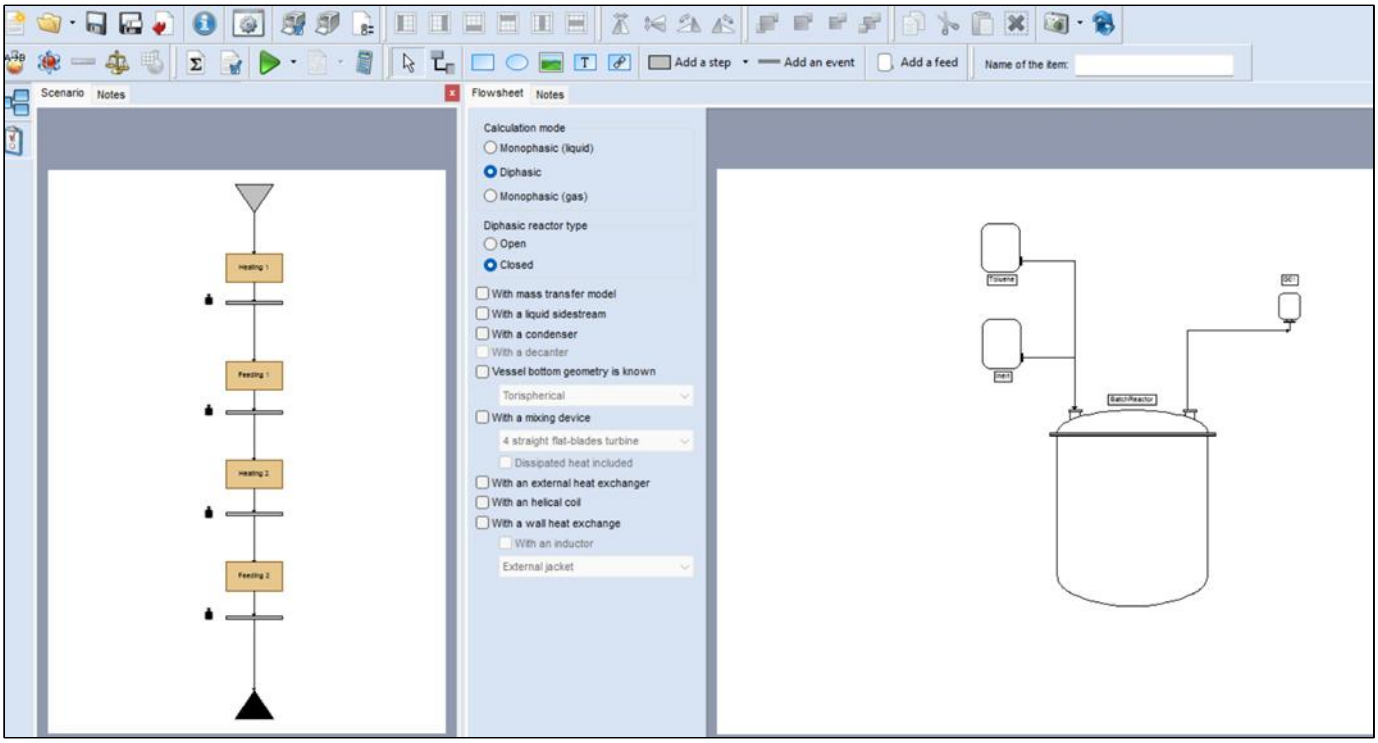
- ✓ Heat duty : 4 kW
- ✓ Operating pressure : 0.6 bar
- ✓ Feeds
  - Toluene : Not activated
  - Inert : Activated
- ✓ End event : Total load inside the reactor = 60 l

Feed 2

The objective of this step is to inject pure toluene into the reactor to replace the previously extracted ethanol.

- ✓ Heat duty : 0 kW (adiabatic)
- ✓ Operating pressure : 0.6 bar
- ✓ Feeds
  - Toluene : Activated
  - Inert : Activated
- ✓ End event : Total load inside the reactor = 100 l

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



5. RESULTS

5.1. Verification of specifications and constraints

Here is a summary of the key results obtained at the end of the simulation:

Quantity	Value
Maximum temperature reached	92.7°C
Total operating time	7h 49m 23s
Ethanol mass fraction at the end of operation	0.89 ppm

- Specification on the ethanol content ✓ Verified
- Constraint on the maximum temperature (70°C) ⚠ Not verified

5.2. Update of the operating mode

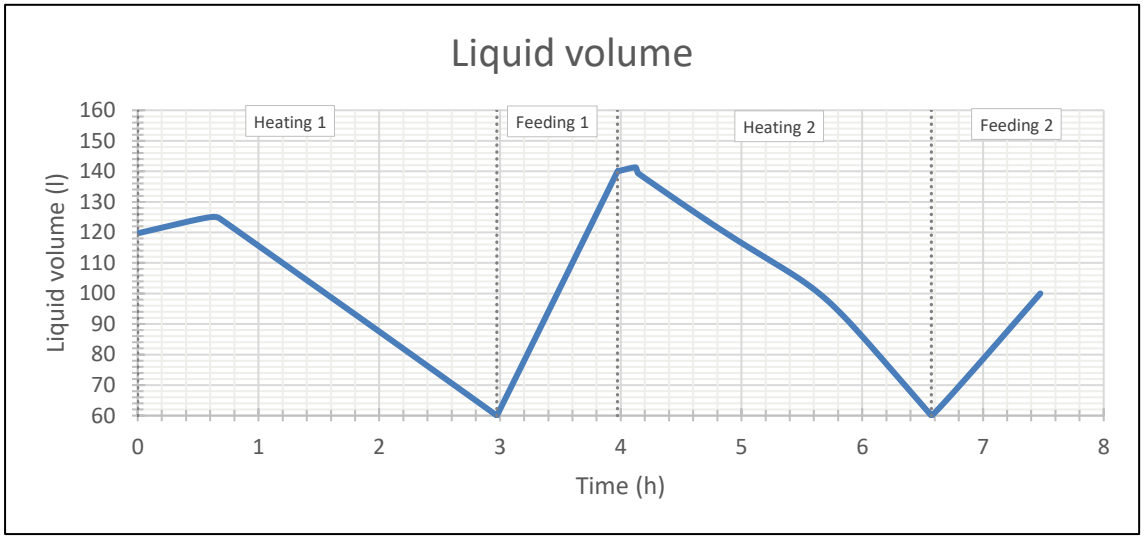
The maximum allowable temperature (70°C) is reached during the second “Heating & Feeding” phase. This temperature is directly related to the composition in the reactor and the operating pressure. To limit the temperature increase, the solution is to reduce the pressure. The pressure is therefore reduced from 0.6 bar to 0.25 bar in 10 minutes during the heating step. It is then maintained at a value of 0.25 bar during the following feeding step. The key results obtained are as follows:

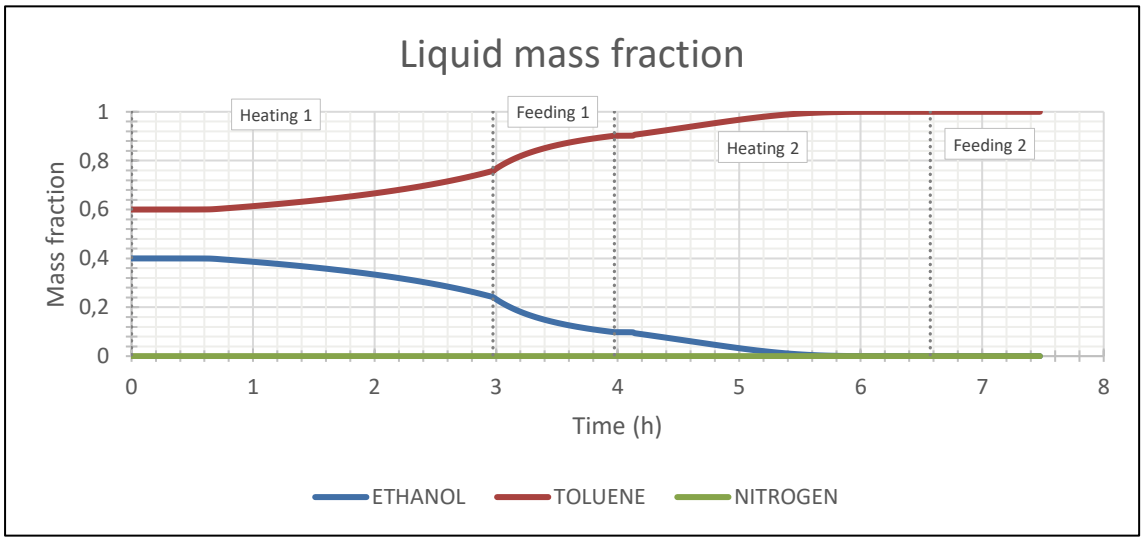
Quantity	Value
Maximum temperature reached	67.4°C
Total operating time	7h 28m 29s
Ethanol mass fraction at the end of operation	0.09 ppm

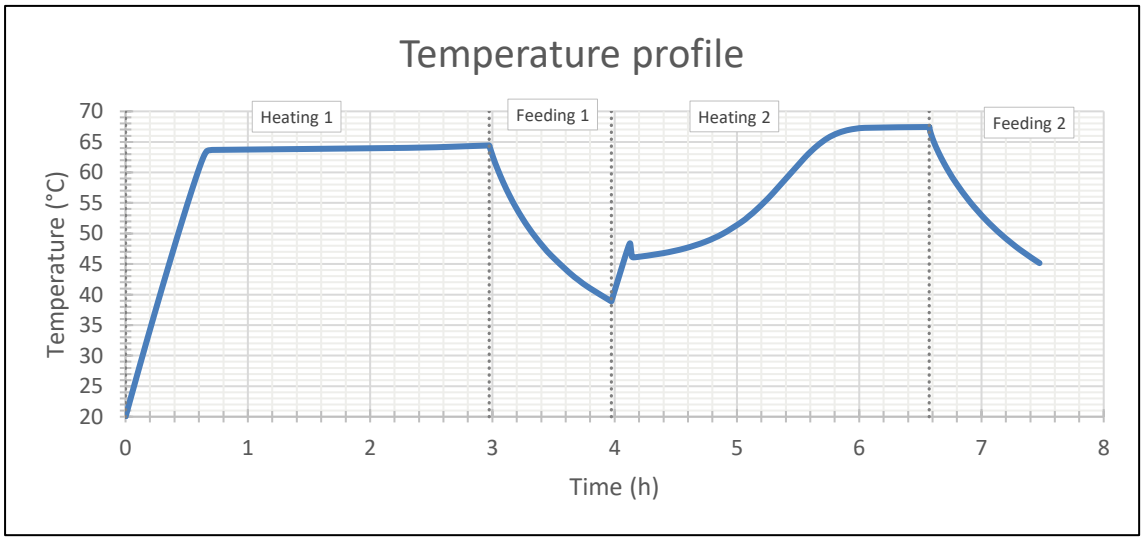
- Specification on the ethanol content ✓ Verified
- Constraint on the maximum temperature (70°C) ✓ Verified

5.3. Profiles

Several profiles are available at the end of the simulation (temperature, pressure, compositions, volume, etc.). The following figures illustrate the evolution of key quantities over time and throughout the steps.







5.4. Tabulated results

The Word report generated at the end of the simulation contains summary tables, including the tables below that represent the material balances at the end of the campaign:

Characteristics of the overall load extracted from the reactor:

Compound	Load	
	(kg)	Mass fraction
ETHANOL	39.9509	0.325199
TOLUENE	81.5804	0.664062
NITROGEN	1.31934	1.07393E-002
Total	**122.851**	**1.0**

Characteristics of the final charge in the reactor:

Compound	Liquid phase (kg)	Vapor phase (kg)
ETHANOL	8.05000E-006	4.01605E-008
TOLUENE	84.5209	1.73054E-002
NITROGEN	1.33873E-004	7.96913E-003
Total	**84.5210**	**2.52746E-002**

6. REFERENCE

[ROW24] 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 (2023)