054402 Design and Analysis

LECTURE 2: PROCESS CREATION

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Objectives

On completing this part of the course, you should:

1. Understand how to go about assembling design data and creating a preliminary data base.

2. Be able to implement the steps in creating flowsheets involving reactions, separations, and T-P change operations. In so doing, many alternatives are identified that can be assembled into a synthesis tree that contains the most promising alternatives.

3. Know how to select the principal pieces of equipment and to create a detailed process flowsheet, with a material and energy balance and a list of major equipment items.
Schedule - Process Creation

- **Preliminary Database Creation**
  - to assemble data to support the design.
- **Experiments**
  - often necessary to supply missing database items or verify crucial data.
- **Preliminary Process Synthesis**
  - top-down approach.
  - to generate a "synthesis tree" of design alternatives.
  - illustrated by the synthesis of processes for the manufacture of VCM and tPA.
- **Development of Base-case Design**
  - focusing on the most promising alternative(s) from the synthesis tree.

Ref: Seider, Seader and Lewin (2004), Chapter 3

Preliminary Database Creation

- Thermophysical property data
  - physical properties
  - phase equilibria (VLE data)
  - Property prediction methods
- Environmental and safety data
  - toxicity data
  - flammability data
- Chemical Prices
  - e.g. as published in the Chemical Marketing Reporter
- Experiments
  - to check on crucial items above
Preliminary Process Synthesis

Synthesis of chemical processes involves:
- Selection of **processing mode**: continuous or batch
- Fixing the **chemical state** of raw materials, products, and by-products, noting the differences between them.
- Process operations (unit operations) - flowsheet building blocks
- Synthesis steps -
  - Eliminate differences in molecular types
  - Distribute chemicals by matching **sources** and **sinks**
  - Eliminate differences in composition
  - Eliminate differences in temperature, pressure and phase
  - Integrate tasks (combine **tasks** into **unit operations**)

Continuous or batch processing?

| Continuous                                                                 | Fed-batch         | Batch-product removal |
|---                                                                         |                   |                     |
| ![Continuous](image)                                                      | ![Fed-batch](image) | ![Batch-product removal](image) |

Continuous

Batch

Fed-batch

Batch-product removal
The Chemical State

- Decide on the raw material and product specifications (states):
  - Mass (flow rate)
  - Composition (mole or mass fraction of each chemical species having a unique molecular type)
  - Phase (solid, liquid, or gas)
  - Form (e.g., particle-size distribution and particle shape)
  - Temperature
  - Pressure

Process Operations ("Lego")

- Chemical reaction
  - Positioning in the flowsheet involves many considerations (conversion, rates, etc.), related to T and P at which the reaction are carried out.
- Separation of chemicals
  - needed to resolve difference between the desired composition of a product stream and that of its source. Selection of the appropriate method depends on the differences of the physical properties of the chemical species involved.
- Phase separation
- Change of temperature
- Change of pressure
- Change of phase
- Mixing and splitting of streams and branches
### Synthesis Steps

<table>
<thead>
<tr>
<th>Synthesis Step</th>
<th>Process Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Eliminate differences in molecular types</td>
<td>Chemical reaction</td>
</tr>
<tr>
<td>2. Distribute chemicals by matching <em>sources</em> and <em>sinks</em></td>
<td>Mixing</td>
</tr>
<tr>
<td>3. Eliminate differences in composition</td>
<td>Separation</td>
</tr>
<tr>
<td>4. Eliminate differences in temperature, pressure and phase</td>
<td>Temperature, pressure and phase change</td>
</tr>
<tr>
<td>5. Integrate tasks (combine <em>tasks</em> into <em>unit operations</em>)</td>
<td></td>
</tr>
</tbody>
</table>

### Example 1:

*Vinyl Chloride Manufacture*
### Eliminate differences in molecular types

**Chemicals participating in VC Manufacture:**

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Molecular weight</th>
<th>Chemical formula</th>
<th>Chemical structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylene</td>
<td>26.04</td>
<td>C₂H₂</td>
<td>H-C≡C-H</td>
</tr>
<tr>
<td>Chlorine</td>
<td>70.91</td>
<td>Cl₂</td>
<td>Cl-Cl</td>
</tr>
<tr>
<td>1,2-Dichloroethane</td>
<td>98.96</td>
<td>C₂H₄Cl₂</td>
<td>Cl-Cl</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>H-C=CH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>H-H</td>
</tr>
<tr>
<td>Ethylene</td>
<td>28.05</td>
<td>C₂H₄</td>
<td>H-C≡H</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>H-H</td>
</tr>
<tr>
<td>Hydrogen chloride</td>
<td>36.46</td>
<td>HCl</td>
<td>H-Cl</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>62.50</td>
<td>C₂H₅Cl</td>
<td>H-Cl</td>
</tr>
</tbody>
</table>

### Selection of pathway to VCM (1)

**Direct chlorination of ethylene:**

\[ C₂H₄ + Cl₂ \rightarrow C₂H₅Cl + HCl \] \hspace{1cm} (2.1)

**Advantages:**

- Attractive solution to the specific problem denoted as Alternative 2 in analysis of primitive problem.
- Occurs spontaneously at a few hundred °C.

**Disadvantages:**

- Does not give a high yield of VC without simultaneously producing large amounts of by-products such as dichloroethylene.
- Half of the expensive chlorine is consumed to produce HCl by-product, which may not be sold easily.
Hydrochlorination of acetylene:

\[ C_2H_2 + HCl \rightarrow C_2H_3Cl \] (2.2)

**Advantages:**
- This exothermic reaction is a potential solution for the specific problem denoted as Alternative 3. It provides a good conversion (98%) of C₂H₂ VC in the presence of HgCl₂ catalyst impregnated in activated carbon at atmospheric pressure.
- These are fairly moderate reaction conditions, and hence, this reaction deserves further study.

**Disadvantages:**
- Flammability limits of C₂H₂ (2.5 → 100%)

Thermal cracking of C₂H₄Cl₂ from chlorination of C₂H₄:

\[ C_2H_4 + Cl_2 \rightarrow C_2H_4Cl_2 \] (2.3)

\[ C_2H_4Cl_2 \rightarrow C_2H_3Cl + HCl \] (2.4)

\[ C_2H_4 + Cl_2 \rightarrow C_2H_3Cl + HCl \] (2.1)

**Advantages:**
- Conversion of ethylene to 1,2-dichloroethane in exothermic reaction (2.3) is ≈ 98% at 90 °C and 1 atm with a Friedel-Crafts catalyst such as FeCl₃. This intermediate is converted to vinyl chloride by thermal cracking according to the endothermic reaction (2.4), which occurs spontaneously at 500 °C with conversions as high as 65% (Alternative 2).

**Disadvantage:**
- Half of the expensive chlorine is consumed to produce HCl by-product, which may not be sold easily.
**Selection of pathway to VCM (4)**

- **Thermal Cracking of** \( \text{C}_2\text{H}_4\text{Cl}_2 \) **from** **Oxychlorination of** \( \text{C}_2\text{H}_4 \):

  \[
  \text{C}_2\text{H}_4 + 2\text{HCl} + \frac{1}{2}\text{O}_2 \rightarrow \text{C}_2\text{H}_4\text{Cl}_2 + \text{H}_2\text{O} \quad (2.5)
  \]

  \[
  \text{C}_2\text{H}_4\text{Cl}_2 \rightarrow \text{C}_2\text{H}_3\text{Cl} + \text{HCl} \quad (2.4)
  \]

  \[
  \text{C}_2\text{H}_4 + \text{HCl} + \frac{1}{2}\text{O}_2 \rightarrow \text{C}_2\text{H}_3\text{Cl} + \text{H}_2\text{O} \quad (2.6)
  \]

**Advantages:**
- Highly exothermic reaction (2.5) achieves a 95% conversion to \( \text{C}_2\text{H}_4\text{Cl}_2 \) in the presence of \( \text{CuCl}_2 \) catalyst, followed by pyrolysis step (2.4) as Reaction Path 3.
- Excellent candidate when cost of HCl is low
- Solution for specific problem denoted as Alternative 3.

**Disadvantages:**
- Economics dependent on cost of HCl

---

**Selection of pathway to VCM (5)**

- **Balanced Process for Chlorination of Ethylene:**

  \[
  \text{C}_2\text{H}_4 + \text{Cl}_2 \rightarrow \text{C}_2\text{H}_4\text{Cl}_2 \quad (2.3)
  \]

  \[
  \text{C}_2\text{H}_4 + 2\text{HCl} + \frac{1}{2}\text{O}_2 \rightarrow \text{C}_2\text{H}_4\text{Cl}_2 + \text{H}_2\text{O} \quad (2.5)
  \]

  \[
  2\text{C}_2\text{H}_4\text{Cl}_2 \rightarrow 2\text{C}_2\text{H}_3\text{Cl} + 2\text{HCl} \quad (2.4)
  \]

  \[
  2\text{C}_2\text{H}_4 + \text{Cl}_2 + \frac{3}{2}\text{O}_2 \rightarrow 2\text{C}_2\text{H}_3\text{Cl} + \text{H}_2\text{O} \quad (2.7)
  \]

**Advantages:**
- Combination of Reaction Paths 3 and 4 - addresses Alternative 2.
- All \( \text{Cl}_2 \) converted to VC
- No by-products!
Evaluation of Alternative Pathways

1. Reaction Path 1 is eliminated due to its low selectivity.
2. This leaves four alternative paths, to be compared first in terms of Gross Profit.

### Chemical Bulk Prices

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Cost (cents/lb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylene</td>
<td>18</td>
</tr>
<tr>
<td>Acetylene</td>
<td>50</td>
</tr>
<tr>
<td>Chlorine</td>
<td>11</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>22</td>
</tr>
<tr>
<td>Hydrogen chloride</td>
<td>18</td>
</tr>
<tr>
<td>Water</td>
<td>0</td>
</tr>
<tr>
<td>Oxygen (air)</td>
<td>0</td>
</tr>
</tbody>
</table>

### Computing Gross Profit

**Reaction Path**

<table>
<thead>
<tr>
<th>Reaction Path</th>
<th>Overall Reaction</th>
<th>Gross Profit (cents/lb VC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>( \text{C}_2\text{H}_4 + \text{HCl} = \text{C}_2\text{H}_3\text{Cl} )</td>
<td>-9.33</td>
</tr>
<tr>
<td>3</td>
<td>( \text{C}_2\text{H}_4 + \text{Cl}_2 = \text{C}_2\text{H}_3\text{Cl} + \text{HCl} )</td>
<td>11.94</td>
</tr>
<tr>
<td>4</td>
<td>( \text{C}_2\text{H}_4 + \text{HCl} + \frac{1}{2}\text{O}_2 = \text{C}_2\text{H}_3\text{Cl} + \text{H}_2\text{O} )</td>
<td>3.42</td>
</tr>
<tr>
<td>5</td>
<td>( 2\text{C}_2\text{H}_4 + \text{Cl}_2 + \frac{3}{2}\text{O}_2 = 2\text{C}_2\text{H}_3\text{Cl} + \text{H}_2\text{O} )</td>
<td>7.68</td>
</tr>
</tbody>
</table>

**Gross profit** = \( 22(1) + 18(0.583) - 18(0.449) - 11(1.134) = 11.94 \text{ cents/lb VC} \)
**Preliminary Flowsheet for Path**

- Direct Chlorination
- Pyrolysis

- **C₂H₄ + Cl₂ → C₂H₃Cl + HCl**
- **C₂H₄Cl₂ → C₂H₃Cl + HCl**

**800 MM lb/year @ 330 days/y ⇒ 100,000 lb/hr VC**

- On the basis of this principal sink, the HCl sink and reagent sources can be computed (each flow is 1,600 lbmol/h)
- Next step involves distributing the chemicals by matching sources and sinks.

**Distribute the chemicals**

- A conversion of 100% of the C₂H₄ is assumed in the chlorination reaction.
Only 60% of the $C_2H_4Cl_2$ is converted to $C_2H_3Cl$ with a byproduct of HCl, according to Eqn. (2.4).

To satisfy the overall material balance, 158,300 lb/h of $C_2H_4Cl$ must produce 100,000 lb/h of $C_2H_3Cl$ and 58,300 lb/h of HCl.

But a 60% conversion only produces 60,000 lb/h of VC.

The additional $C_2H_4Cl_2$ needed is computed by mass balance to equal:

$$[(1 - 0.6)/0.6] \times 158,300 \text{ or } 105,500 \text{ lb/h}.$$ 

Its source is a recycle stream from the separation of $C_2H_3Cl$ from unreacted $C_2H_4Cl_2$, from a mixing operation, inserted to combine the two sources, to give a total 263,800 lb/h.
Distribute the chemicals

Reactor pressure levels:
- Chlorination reaction: 1.5 atm is recommended, to eliminate the possibility of an air leak into the reactor containing ethylene.
- Pyrolysis reaction: 26 atm is recommended by the B.F. Goodrich patent (1963) without any justification. Since the reaction is irreversible, the elevated pressure does not adversely affect the conversion. Most likely, the patent recommends this pressure to reduce the size of the pyrolysis furnace, although the tube walls must be considerably thicker and many precautions are necessary for operation at elevated pressures.
- The pressure level is also an important consideration in selecting the separation operations, as will be discussed in the next synthesis step.

The product of the chlorination reaction is nearly pure $\text{C}_2\text{H}_4\text{Cl}_2$, and requires no purification.

In contrast, the pyrolysis reactor conversion is only 60%, and one or more separation operations are required to match the required purities in the $\text{C}_2\text{H}_3\text{Cl}$ and HCl sinks.

One possible arrangement is given in the next slide. The data below explains the design decisions made.

<table>
<thead>
<tr>
<th>Chemical</th>
<th>1 atm</th>
<th>4.8 atm</th>
<th>12 atm</th>
<th>26 atm</th>
<th>$T_c$ °C</th>
<th>$P_c$ atm</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCl</td>
<td>-84.8</td>
<td>-51.7</td>
<td>-26.2</td>
<td>0</td>
<td>51.4</td>
<td>82.1</td>
</tr>
<tr>
<td>$\text{C}_2\text{H}_3\text{Cl}$</td>
<td>-13.8</td>
<td>33.1</td>
<td>70.5</td>
<td>110</td>
<td>159</td>
<td>56</td>
</tr>
<tr>
<td>$\text{C}_2\text{H}_4\text{Cl}_2$</td>
<td>83.7</td>
<td>146</td>
<td>193</td>
<td>242</td>
<td>250</td>
<td>50</td>
</tr>
</tbody>
</table>
There may be other, possibly better alternative configurations, as discussed in Lecture 4 (Chapter 7).
Integrate tasks (*tasks \Rightarrow unit operations*)

Algorithmic methods are very effective for the synthesis, analysis and optimization of alternative flowsheets. These will be covered in Section B (Part II)
Develop one or two of the more promising flowsheets from the synthesis tree for more detailed consideration.

Example 2:

Manufacture of Tissue Plasmonigen Activator
tPA is tissue plasminogen activator
A recombinant, therapeutic protein
- comprised of 562 amino acids

Manufacture of tPA

Pharmacology:
- tPA activates plasminogen – to plasmin (an enzyme)
- plasmin dissolves fibrin formations that hold blood clots in place
- blood flow is re-established once the clot blockage dissolves
- important for patients with heart attacks (myocardial infarction) or stroke

Business Strategy:
- has been produced by Genentech (Activase™) since 1986
- sells for $2,000/100 mg dose
- 2003 - Patent protection expires
- Design objective - manufacture generic form of tPA to sell for $200/dose
**Process Synthesis Problem**

Identify Reaction Paths – with help from the Biochemist

1. **Mammalian Cells**

   \[ \text{tPA-DNA sequence + CHO cells} \rightarrow \text{selected high expressing PA-CHO cells} \]

   \( (1-10 \text{ mg from } 10^6 \text{ cells}) \) \( (\text{CHO cells with human melanoma cells}) \) \( \text{tPA-DNA inserted in their genomes} \)

   Selected tPA-CHO cells ("founder cells") amplified to yield about \( 10^6 \text{ cells/mL} \) - during R&D stage. These cells are frozen into 1-mL aliquots at -70°C.
Eliminate differences in molecular types

Prepared in laboratory - stored in 1 mL aliquots at - 70°C

Used as inoculum for the bio-reaction:

\[
\text{tPA-CHO cells + HyQ PF-CHO media + } O_2 \rightarrow \text{Increased cell nos. (2)}
\]

- \(0.39 \times 10^6 \text{ cells/mL-day}\)
- \(50 \text{ pg tPA/cell-day}\)
- \(0.2 \times 10^{-12} \text{ mol } O_2/\text{cell-hr}\)

Rates from Genentech patent (1988)

As tPA-CHO cells reproduce, tPA secretes into liquid media solution.

Companies cost of chemicals produced or sold

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Kg/Kg tPA</th>
<th>Cost, $/Kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPA</td>
<td>1</td>
<td>2,000,000</td>
</tr>
<tr>
<td>HyQ PF CHO powder media</td>
<td>287.2</td>
<td>233</td>
</tr>
<tr>
<td>Water for injection (WFI)</td>
<td>2,228</td>
<td>0.12*</td>
</tr>
<tr>
<td>Air</td>
<td>46.8</td>
<td>1,742</td>
</tr>
<tr>
<td>(CO_2)</td>
<td>3.7</td>
<td>1,447</td>
</tr>
<tr>
<td>tPA-CHO cells</td>
<td></td>
<td>*</td>
</tr>
</tbody>
</table>

* $200/100 mg dose
* $0.45/gal = $450/1,000 gal
* Not included in gross profit estimate - related to cost of research, an operating cost.
Computing Gross Profit

Gross Profit = 2,000,000 - 287.2 × 233 - 2,228 × 0.12
-3.7 × 1,447 - 46.8 × 1,742

= $1,846,000/Kg tPA

Does not include operating costs (cost of research and cost of utilities) and investment cost
- yet, high for a pharmaceutical
- process synthesis proceeds at an accelerated pace
Distribute the chemicals

Cell and tPA production
37%, 10 mL
pH 7.3

- LPA - CHO cells (1 mL aliquot)
- HyQ FCHO media (23,716 Kg/hr)
- H2O (179,250 Kg/hr)
- Air (3,740 Kg/hr)
- CO2 (246 Kg/hr)

- Endotoxins 0.012 Kg/hr
- Cell debris 23.8 Kg/hr
- Waste H2O (178,250 Kg/hr)
- Gas emissions (N2, O2, CO2) 9.6 Kg/hr

Eliminate Differences in Composition

tPA protein must be recovered from other proteins, cell debris, media, water, and gas emissions.

Proteins lose activity (denature) at temperatures above ~ 0°C

Hence - entire separation process designed to operate at 4°C, slightly above freezing point of water.
Eliminate Differences in Composition

Eliminate differences in Temperature
Integrate tasks (tasks \(\Rightarrow\) unit operations)

- Equipment items are selected - often combining operations into a single equipment item
- Key decision - batch or continuous operation
- 80 Kg/yr tPA - batch mode
- Select equipment sizes to produce 1.6 Kg/batch
  \[\Rightarrow\text{i.e., } 80/1.6 = 50 \text{ batch/yr}\]
- To allow for separation losses, produce 2.24 Kg/batch in the cultivators
- Using 5,000 L vessel, 14 day/batch = cycle time
- Hence, run two batch trains in parallel
  \[\Rightarrow\text{ each producing 25 batch/yr}\]
Task Integration – Separation Section

Diagram showing the separation section of a process.

Further details:
- tPA - Synthesis Tree
- Reaction Path
- Distribution of Chemicals
- Separations
- Temperature Changes
- Task Integration

Diagram showing the steps and processes involved in the synthesis of tPA.
Process Creation - Summary

- Preliminary Database Creation
  - needed to provide data to support the design.
- Experiments
  - often necessary to supply missing database items or verify crucial data.
- Preliminary Process Synthesis
  - top-down approach,
  - generates a "synthesis tree" of design alternatives,
  - illustrated by the synthesis of the VCM and tPA processes.
- Development of Base-case Design
  - focusing on the most promising alternative(s) from the synthesis tree.

Next week: Process Design Heuristics