Fluidized Bed Processing: Pharmaceutical Bead Coating

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Objectives

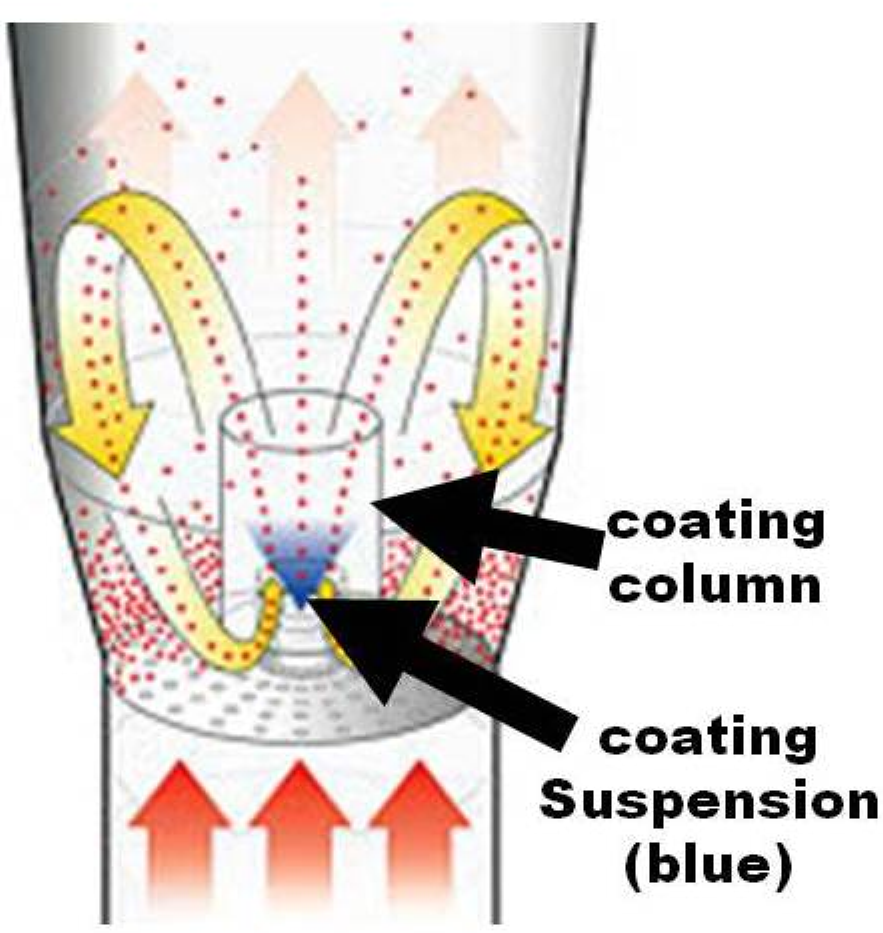
- Theoretically model the pharmaceutical bead coating process in a bottom spray fluid bed dryer
- Create a analytical tool to simulate the process with user defined process parameter inputs
- Design a manufacturing plant and process that utilizes minimum energy, produces minimal discharge, and is economically feasible

Background

- Examples of coated bead products:
  - Cymbalta®, Cingulair®, Prozac®, Nexium®
- What is the benefit of coated beads?
  - Multiple layers: extended formulations, gastric coatings
  - Consistent bioavailability: movement into small intestine for absorption into body regardless of meals
  - Flexibility in dosage form

Coated Pharma Beads
www.glatt.com

Process Description



Hot drying air
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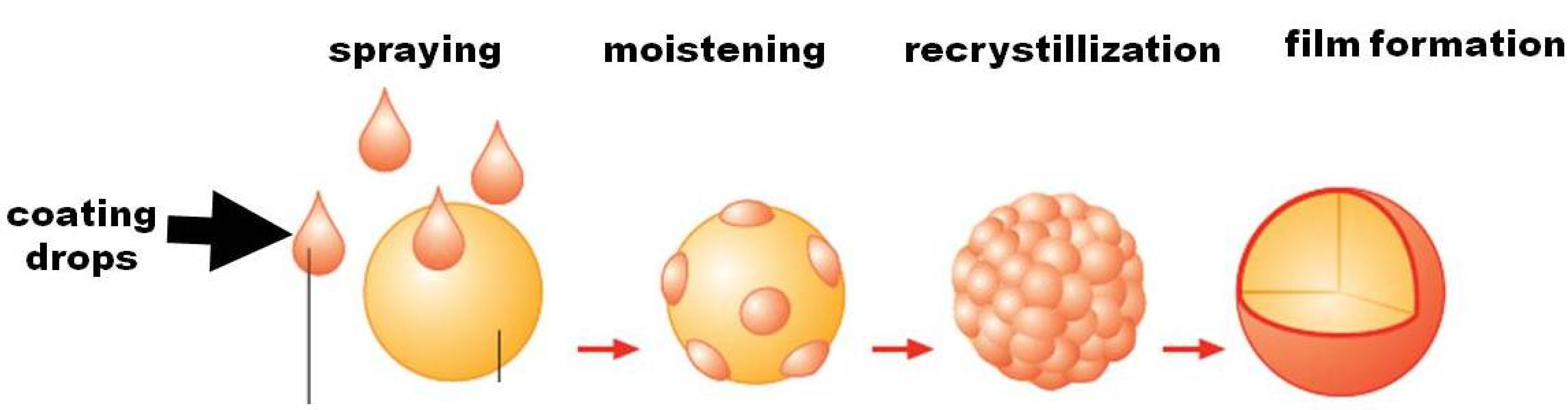
1. Beads are pushed through the coating column by the hot drying air
2. While moving through the coating column, beads are sprayed with coating suspension (shown in blue)
3. As beads circulate through the bed as shown by the yellow arrows, the coating suspension dries and leaves a thin layer of solids on the bead

Stages of Bead Coating



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Design Equations

- **Equation modeling moisture content in beads during drying**

$$Q_0 - Q = \frac{\rho_g}{\rho_s} \frac{C_{pg}(T_{in} - T_{out})}{L} \frac{t}{(1-\varepsilon_m)\frac{H_{bed}}{v_{air}}}$$

Q = moisture content
C_p = heat capacity of bead
ρ = density of bead
T = temperature

L = latent heat of vaporization of water
t = time of drying
ε = void fraction in packed bed of beads
H_{bed} = height of beads in fluid bed
v_{air} = velocity of drying air

- **Equation modeling bead movement in fluid bed during drying**

$$\frac{\partial v_{particle}}{\partial t} - \frac{3\pi\mu_{air} d_{particle}}{m_{particle}} v_{particle} = -g + \frac{3\pi\mu_{air} d_{particle}}{m_{particle}} v_{air}$$

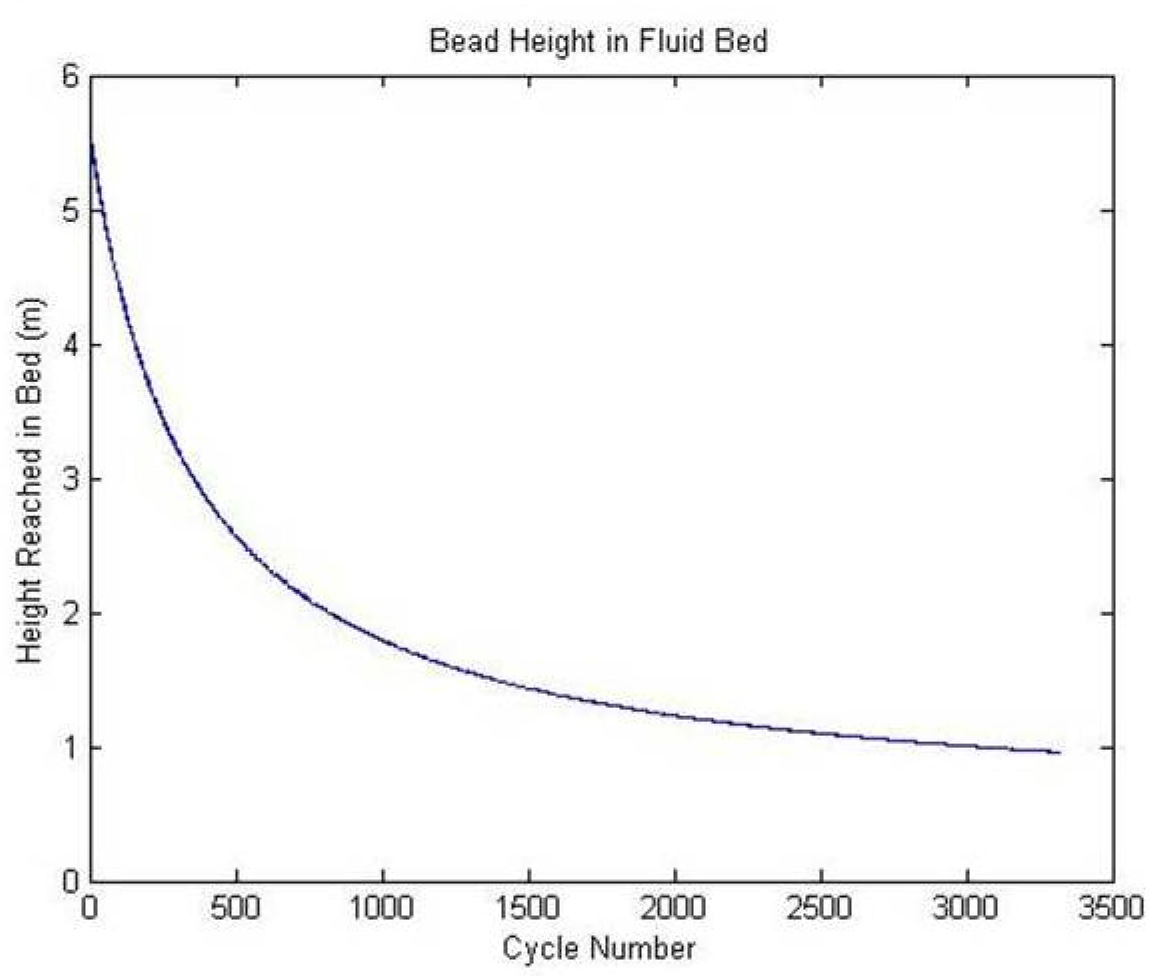
$v_{particle}$ = velocity of bead in fluid bed
v_{air} = velocity of drying air
μ = viscosity of air

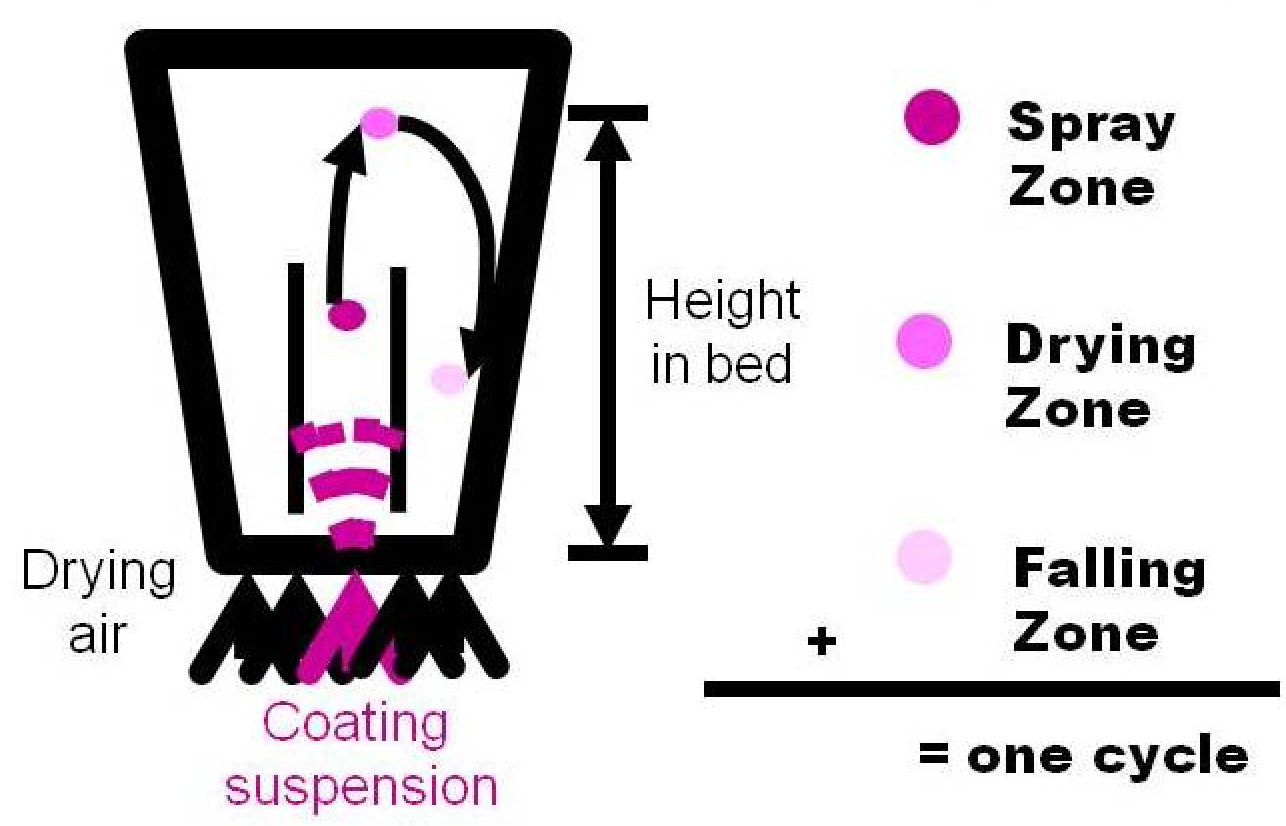
$d_{particle}$ = diameter of bead
$m_{particle}$ = mass of bead
g = gravitational constant

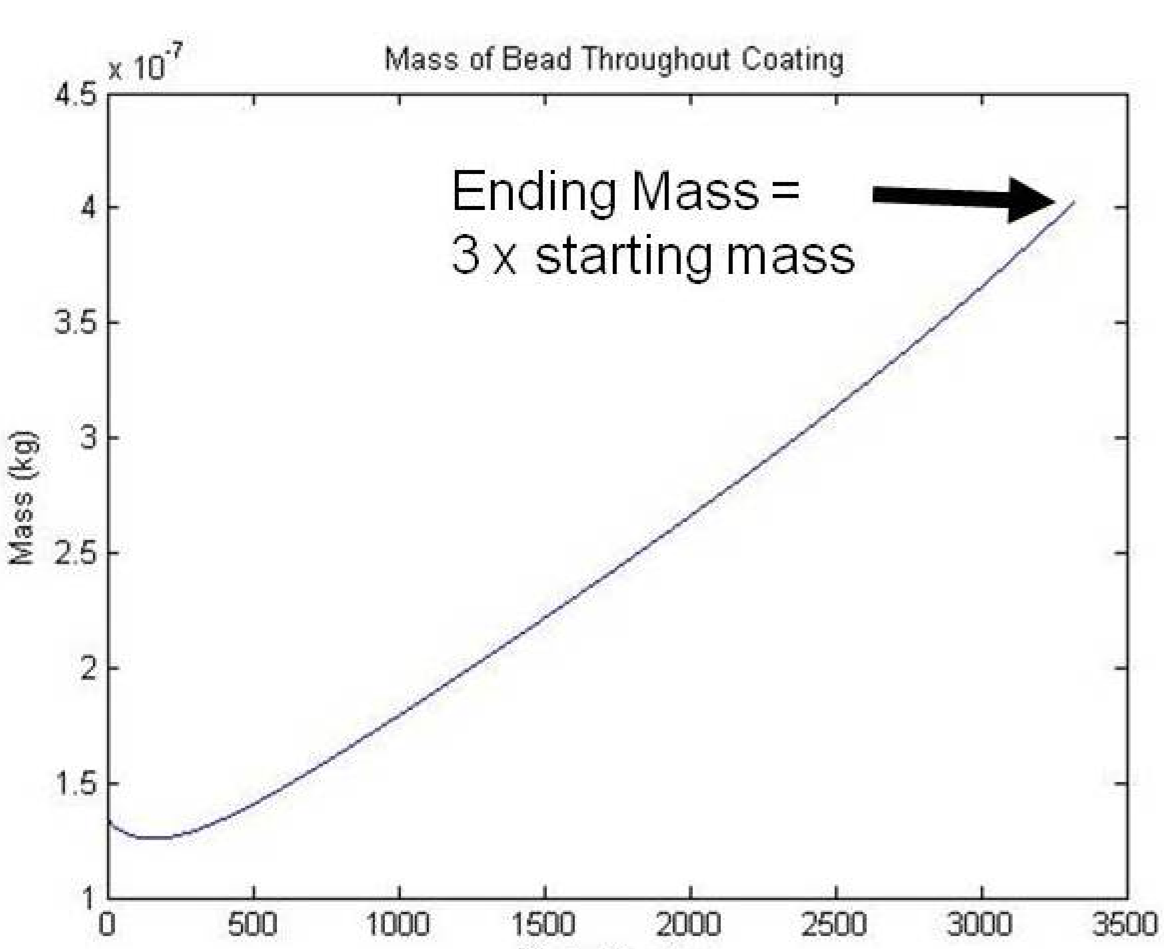
Matlab Simulation Program

Utilizing the design equations above, a matlab simulation program was written. The table below indicates input process values that were obtained from pilot scale lab experience and industry references.

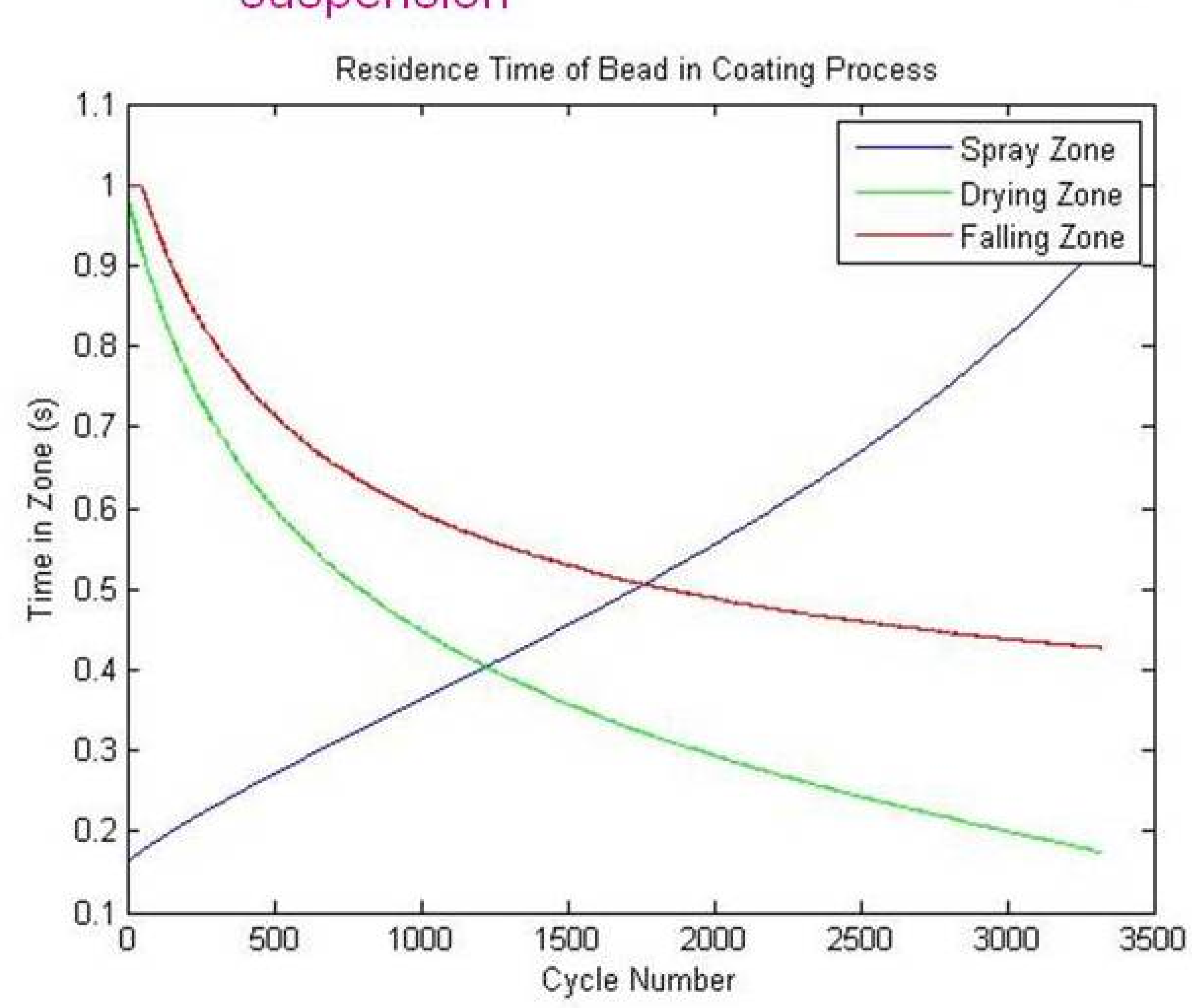
Process Parameter	Value
Inlet Air Velocity (m/s)	100
Fluid Bed Diameter (m)	3.5
Batch Size (kg)	500
ΔT (inlet to outlet air)	5
Air Viscosity (Pa s)	2.1 e -5
Solids in Coating Suspension (%)	20
Mass of non-pariel (μg)	134
Diameter of non-pariel (μm)	67.06
Suspension added per bead per pass (ng)	40.2
Change in bead diameter per pass (μm)	0.11
Desired change in bead mass (%)	300







Total Process Time = 15.178 hrs



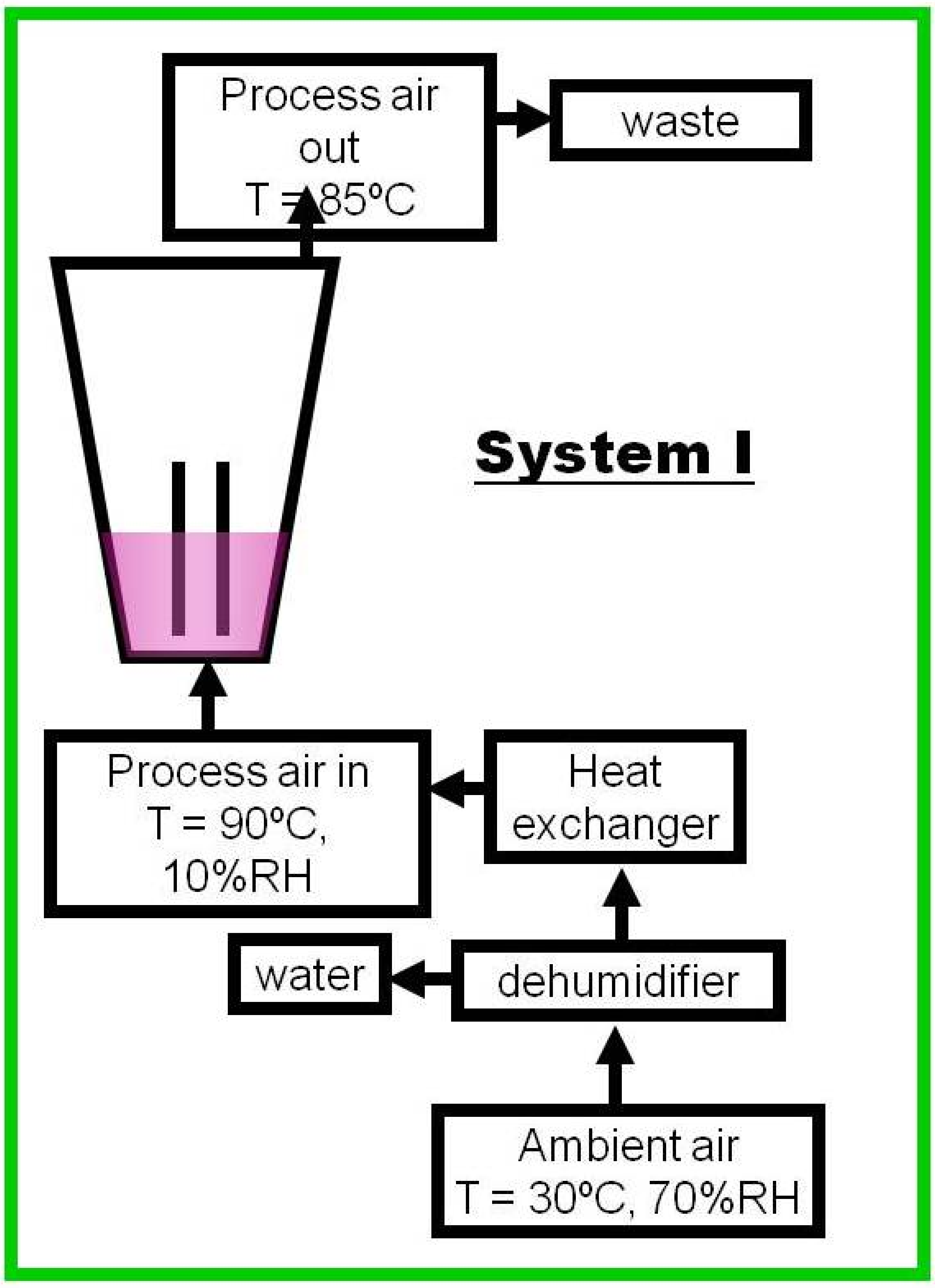
Why Theoretically Model?

In the pharmaceutical industry, creating a DOE and running experiments on full scale equipment to define process parameters is a costly step in the design of a process. The creation of simulation programs may enable significant cost reduction in this step.

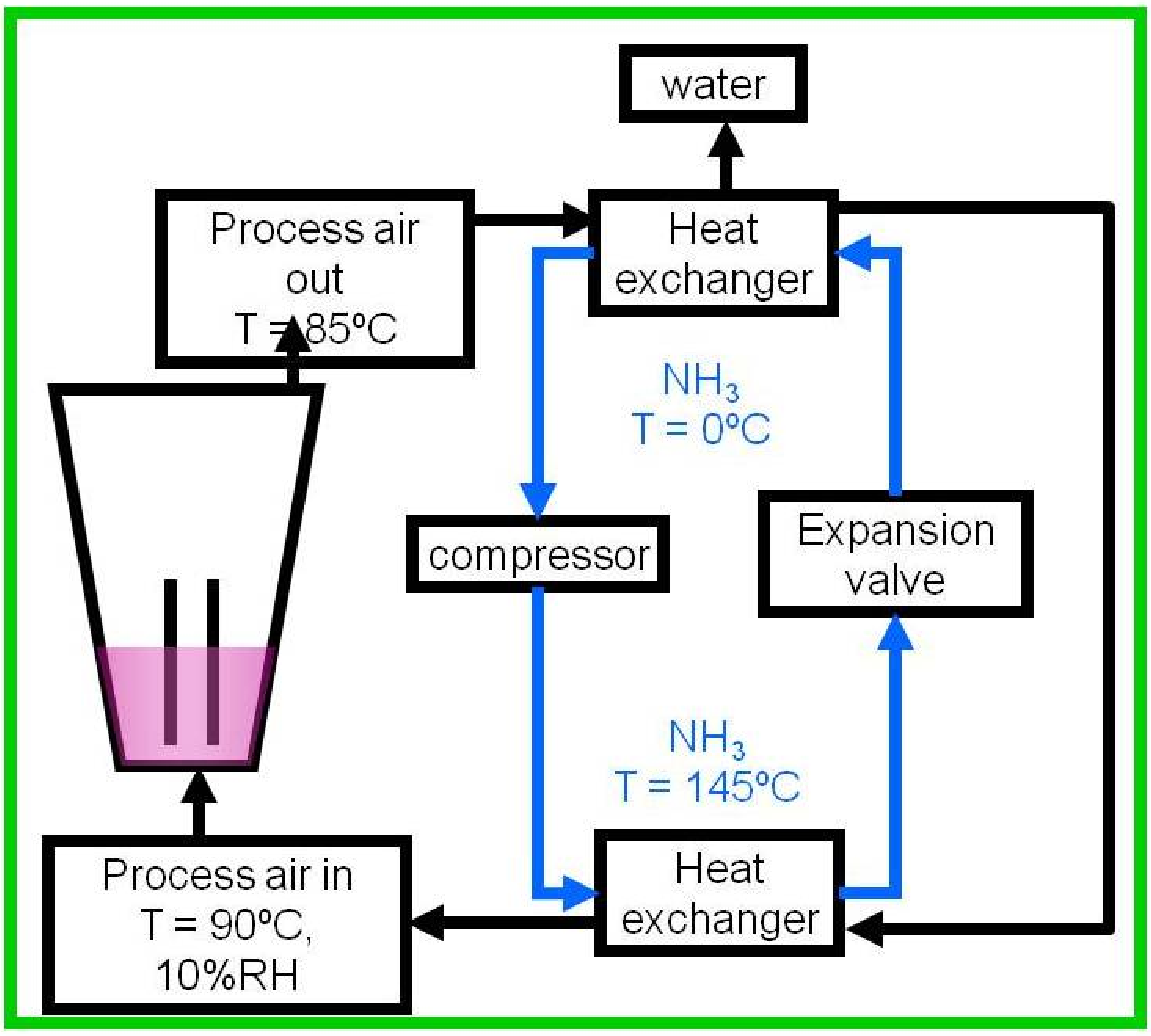
- **Define process parameter ranges**
- **Calculate processing times (aid in process scheduleing)**
- **Determine significant processing parameters**

Economic Process Design

The bead coating process requires that the water in the coating suspension be evaporated once it has coated the surface of the bead. Because of this, hot and dehumidified process air must be used. Two system designs to condition air for processing were analyzed.



System II



<u>System I</u>: A typical system in which ambient air is dehumidified and then heated to processing temperatures. The outlet process air is then sent back into the environment as waste.

<u>System II</u>: This system recycles the processing air by utilizing a heat pump. The hot process air is cooled and dehumidified using ammonia, and then is cycled to another heat exchanger to be heated to processing temperatures. The ammonia is also the heating agent and is heated by the compressor.

<u>Economic Comparison:</u>

System I may require less capital investment because less equipment needs to be purchased but system II recycles air and may be a more efficient process, and also reduces waste. A 15 year annual cost comparison was performed assuming:

- 35% tax rate
- 25% minimum required rate of return
- 5 % inflation
- 10% salvage on equipment

<u>System I</u>

Annual cost = $63,472

<u>System II</u>

Annual cost = $15,755

→ Implementation of an air recycle system saves nearly $50,000 per year and improves taxation on the environment by utilizing less energy and discharging less waste into the ambient air.