Scenario 1

A new small molecule API, designated simply C, is being produced in a batch reactor in a pilot plant. Two liquid raw materials A and B are added to the reactor and the reaction $A+B \xrightarrow{K1} C$ takes place. Unfortunately, C also reacts with B to decrease the yield of C and produce an impurity D by the reaction: $B+C \xrightarrow{K2} D$. This impurity must be removed from the reaction mixture when the reaction reaches completion at time t_f.

The goal of the project is to design and operate a full scale plant which will maximize the production of C at the end of the reaction $C(t_f)$ while minimizing the production of $D(t_f)$ using information gathered in the pilot plant. It is expected that $A(t_f)$ and $B(t_f)$ can be separated from the reaction mixture and may be reused although $D(t_f)$ must be separated and discarded.

The response variables measured in the pilot plant are the amounts of A(t), B(t) , C(t) and D(t) consumed or produced as a function of time t after starting the reaction at $t=t_o$.

The factors which affect the response variables are:

(1) A/B feed ratio
(2) Amount of liquid catalyst, Z (ppm)
(3) Amount of Anti-foaming Agent at time t_o. AF (ppm,)
(4) Temperature profile, T(t) (deg K)
(5) Agitation rate, M(t) (RPM)
(6) Termination time t_f (min)

Figure 1 shows the batch reactor system for Scenario 1

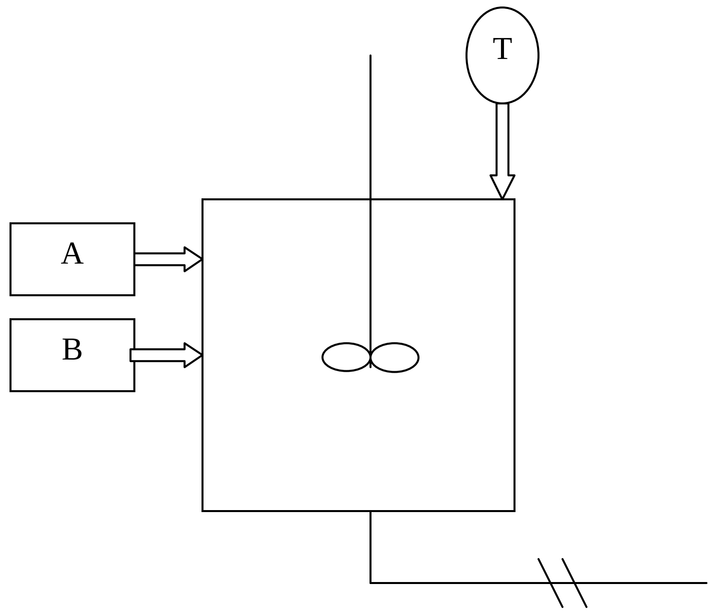

Figure 1: Batch reactor system for Scenario 1

Scenario 2

The test bed shown in the Figure 2 below was constructed to study the feasibility of continuous operation on tablet production with an API and excipients added in powder form to a screw feeder:

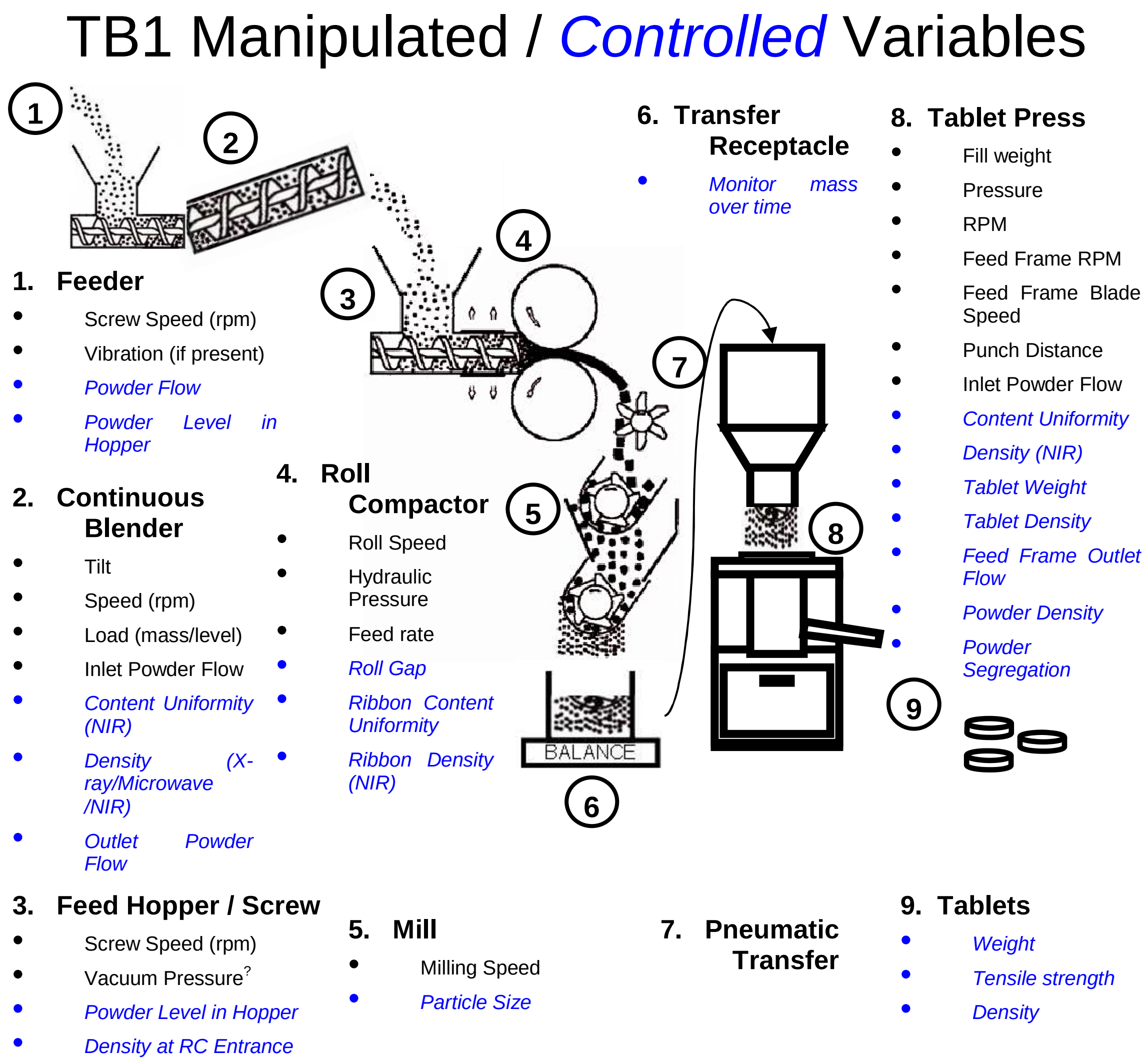

Figure 2: Proposed Continuous Operation for Tableting Process

Sample problems will be taken from the individual process steps.

The response variables for the various units operations as well as the factors are tabulated in Tables 1 and Table 2 respectively.

Unit	Response Variable
Feeder	Powder Flow (kg/hr)
	Powder level in tropper (in)
Continuous Blender	Uniformity (σ/μ)
	Density (g/cm^3)
	Outlet Powder Flow (kg/hr)
Feed Hopper /Screw	Powder level in Hopper (in)
	Density at RC Entrance
Roll Compactor	Roll Gap (mm)
	Ribbon Uniformity (σ/μ)
	Ribbon Density (g/cm^3)
Mill	Particle Size Distribution
Tablet Press	Uniformity (σ/μ)
	Density (g/cm^3)
	Tablet Weight (g)
	Tablet Density (g/cm^3)
	Powder Density (g/cm^3)
Tablets	Weight (g)
	Tensle Strength
	Density (g/cm^3)
	Friability (%)
	Dissolution (%)

Table 1: Response Variables for the various unit operations for the tabletting process

Unit	Factors
Feeder	Screw Speed (rpm)
	Vibration (Frequency)
Continuous Blender	Tilt (degree)
	Speed (rpm)
	Load (Mass/Inch)
	Inlet Powder Flow (Kg/hr)
Feed Hopper /Screw	Screw Speed(rpm)
	Vacuum Press (rpm/lg)
Roll Compactor	Roll Speed (rpm)
	Hydrolic Pressure (ton)
	Feed Rate (Kg/hr)
Mill	Speed (rpm)
Tablet Press	Fill Weight (Kg)
	Pressure (ton)
	Feed from Blade Speed (rpm)
	Punch Distance (mm)
	Inlet Powder Flow (Kg/hr)

Tables 2: Factors for the various unit operations for Tableting Process

Scenario 3

A macromolecule C is being produced in two large 80,000 liter fermenter vessels. The yield of the process is only .5% after seven days and patent protection is only short lived. The R&D department has discovered a set of conditions which have been able to triple the yield of product from .5% to 1% in three days. However, these results have only been achieved in shaker flasks and highly instrumented 20 liter minifermentors. The problem is to try and translate these results to the production vessels to reduce the cost for the coming generic challenge.

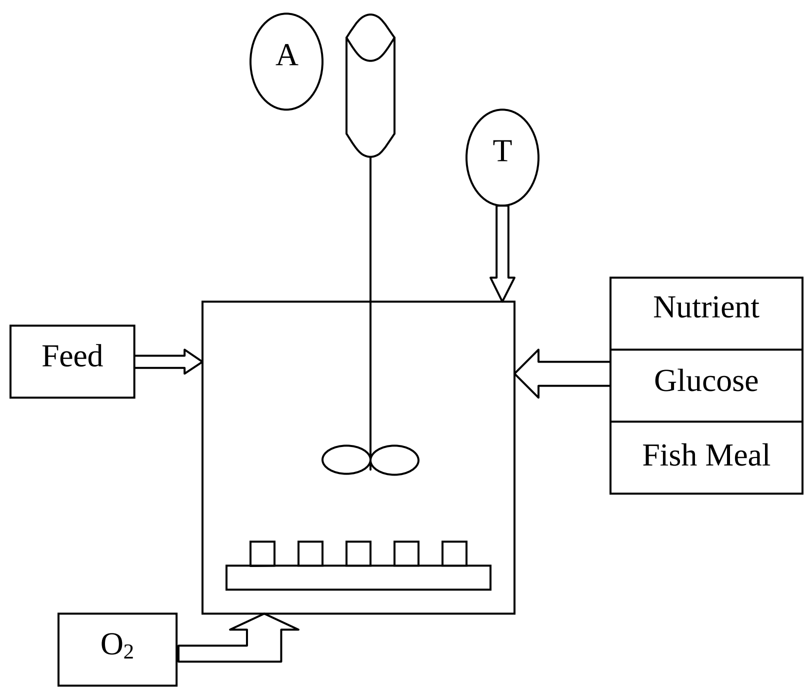

Figure 3: Configuration of large scale fermenter

The response variables for the both the production and small scale fermentors are an online measurement dissolved Oxygen measurement, $O_2(t)$ and the titer $C(t_i)$ for a samples taken at time t_i (hours) after starting the fermentation.

The major factors which influence the results in the production fermentor are shown in Table 3 below:

Factors	Lower Bound	
Agitation A	1000 rpm	1500 rpm
Temperature	50 deg C	70 deg C
Rate of Air		
Addition O_2	10 l/min	50 l/min
Fish Meal FM	2%	4%
Glucose Addition GA	20g/h	70g/h
Nutrient Addition	5g/h	8 g/h

Table 3: Factors influencing production of C in fermenter