

The formation of a growth-linked product may be described by the equation-

$$dp/dt = q_p \cdot x \quad \dots\dots\dots(1)$$

Where,

p is the concentration of product and

q_p is the specific rate of product formation (mg product g-l biomass h⁻¹)

- Also, product formation is related to biomass production by the equation:

$$dp/dx = Y_{p/x} \quad \dots\dots\dots(2)$$

- where $Y_{p/x}$ is the yield of product in terms of biomass (g product g-l biomass)

Now equation (2) is multiply by dx/dt , then we have :

$$dx/dt \cdot dp/dx = Y_{p/x} \cdot dx/dt$$

And

$$dp/dt = Y_{p/x} \cdot dx/dt$$

But we know that: $dx/dt = \mu \cdot x$

Therefore we have

$$dp/dt = Y_{p/x} \mu \cdot x$$

$$dp/dt = q_p \cdot x$$

and therefore

$$q_p \cdot x = Y_{p/x} \cdot \mu \cdot x$$

$$q_p = Y_{p/x} \cdot \mu \quad \dots\dots\dots(3)$$

From equation (3) it may be seen that when product formation is growth associated the specific rate of product formation increases with specific growth rate i.e. the specific rate of product formation is directly proportional to specific growth rate i.e. $q_p \propto \mu$

Therefore productivity in batch culture will be greatest at $\mu_{\max}$ and improved product output will be achieved by increasing both μ and biomass concentration.

- The increase in productivity of non-growth linked product in batch culture should be associated with biomass concentration which is maximum at the end of log phase or at the stationary phase.
- However, it is observed that secondary metabolites are produced *only* under certain physiological conditions
- Secondary metabolites are produced mainly under limitation of a particular substrate so that biomass must be in the correct 'physiological state before production can be achieved.
- Therefore, batch process may be used to produce biomass, primary metabolites and secondary metabolites.
- For biomass production, cultural conditions should support the fastest growth rate and maximum cell population
- For primary metabolite production cultural conditions should support to extend the exponential phase accompanied by product excretion and
- For secondary metabolite production, cultural conditions should support a short exponential phase and an extended production phase, or conditions giving a decreased growth rate in the log phase leads to earlier secondary metabolite production.

Kinetics of Product formation in chemostat culture

Chemostat culture

Also called continuous culture

- Exponential growth phase in batch culture may be maintained by
 - the addition of fresh medium to the vessel and removal of cultured medium from vessel at certain time interval.

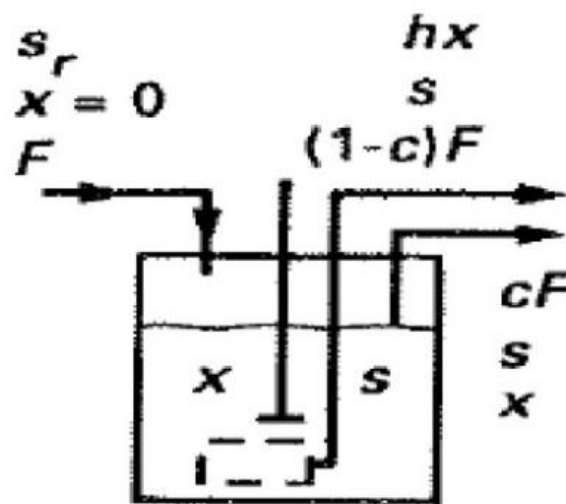


Fig-Diagrammatic representations of chemostats with feedback (Pirt, 1975).

(a) Internal feedback.

F = flow rate of incoming medium ($\text{dm}^3 \text{ h}^{-1}$)

C fraction of the outflow which is not filtered

x = biomass concentration in the vessel and in the unfiltered stream

hx = biomass concentration in the filtered stream

- If medium is fed continuously to such a culture at a suitable rate, a steady state is achieved.
- At steady state,
 - Formation of new biomass by the culture is balanced by the loss of cells from the vessel.

The flow or addition of medium into the vessel is related to the volume of the vessel by the term dilution rate, D , defined as:

$$D = F / V \quad (1)$$

Where

- F is the flow rate ($\text{dm}^3 \text{ h}^{-1}$)
- V is the volume in dm^3

The unit of D is h^{-1}

- The net change in cell concentration over a time a time period is expressed as:

$$dx / dt = \text{growth} - \text{output}$$

$$\text{or } dx / dt = \mu.X - D.x \quad (2)$$

- At steady state condition,
 $dx / dt = 0$

$$\text{or } \mu.X - D.x = 0$$

$$\text{or } \mu.X = D.x$$

$$\text{or } \mu. = D \quad (3)$$

Therefore under steady state conditions the specific growth rate is controlled by the dilution rate, which is an experimental variable. Under batch culture conditions an organism will grow at its maximum specific growth rate and, therefore, it is obvious that a continuous culture may be operated only at dilution rate below the maximum specific growth rate. Therefore within certain limits, the dilution rate may the growth rate of the culture.

The growth of the cells in a continuous culture of this type is controlled by the availability of the growth limiting chemical component of the medium and, therefore, described as a chemostat.

The mechanism of the controlling effect of the dilution rate is described by the following equation by Monod in 1942:

$$\mu = \mu_{\max} s / (K_s + s).$$

At steady state, $\mu = D$, and, therefore,

$$D = \mu_{\max} \bar{s} / (K_s + \bar{s})$$

where $\bar{s}$ is the steady-state concentration of substrate in the chemostat, and

$$\bar{s} = K_s D / (\mu_{\max} - D). \quad \text{—————} \quad 4$$

Equation 4 predicts that the substrate concentration is determined by the dilution rate. In effect, this occurs by growth of the cells depleting the substrate to a concentration that supports the growth rate equal to the dilution rate. If substrate is depleted below the level that supports the growth rate dictated by the dilution rate the following sequence of events takes

- (i) The growth rate of the cells will be less than the dilution rate and they will be washed out of the vessel at a rate greater than they are being produced, resulting in a decrease in biomass concentration.
- (ii) The substrate concentration in the vessel will rise because fewer cells are left in the vessel to consume it.

- (iii) The increased substrate concentration in the vessel will result in the cells growing at a rate greater than the dilution rate and biomass concentration will increase.
- (iv) The steady state will be re-established.

Therefore, a chemostat or continuous process is defined as a nutrient-limited self-balancing culture system which may be maintained in a steady state over a wide range of sub-maximum specific growth rates.

The concentration of cells in the chemostat at steady state is described by the equation:

$$\bar{x} = Y(S_R - \bar{s}) \quad \text{5}$$

where $\bar{x}$ is the steady-state cell concentration in the chemostat.

Now by combining equations (4) and (5), we have

$$\bar{x} = Y[S_R - \{K_s D / (\mu_{\max} - D)\}]. \quad \text{6}$$

Thus, the biomass concentration at steady state is determined by the operational variables, S_R and D . If S_R is increased, $\bar{x}$ will increase but $\bar{s}$, the residual substrate concentration in the chemostat, will remain the same. If D is increased, μ will increase ($\mu = D$) and the residual substrate at the new steady state would have increased to support the elevated growth rate; thus, less substrate will be available to be converted into biomass, resulting in a lower steady state value.

The product formation in chemostat culture is described as

Change/rate in product formation = Production – output

$$dp / dt = q_p x - DP \quad (4)$$

At steady state,

$$dp / dt = 0$$

$$q_p x = DP$$

$$\text{Or} \quad \bar{p} = q_p \cdot x / D \quad (5)$$

where $\bar{p}$ is the steady-state product concentration.

where $\bar{p}$ is the steady-state product concentration.

If q_p is strictly related to μ , then as D increases so will q_p ; thus, the steady-state product concentration ($\bar{p}$) and product output (DP) will behave in the same way as x and Dx , as shown in Fig. 2.10a. If q_p is independent of μ then it will be unaffected by D and thus concentration will decline with increasing D but output will remain constant, as shown in Fig. 2.10b. If product formation occurs only within a certain range of growth rates (dilution rates) then a more complex relationship is produced.

