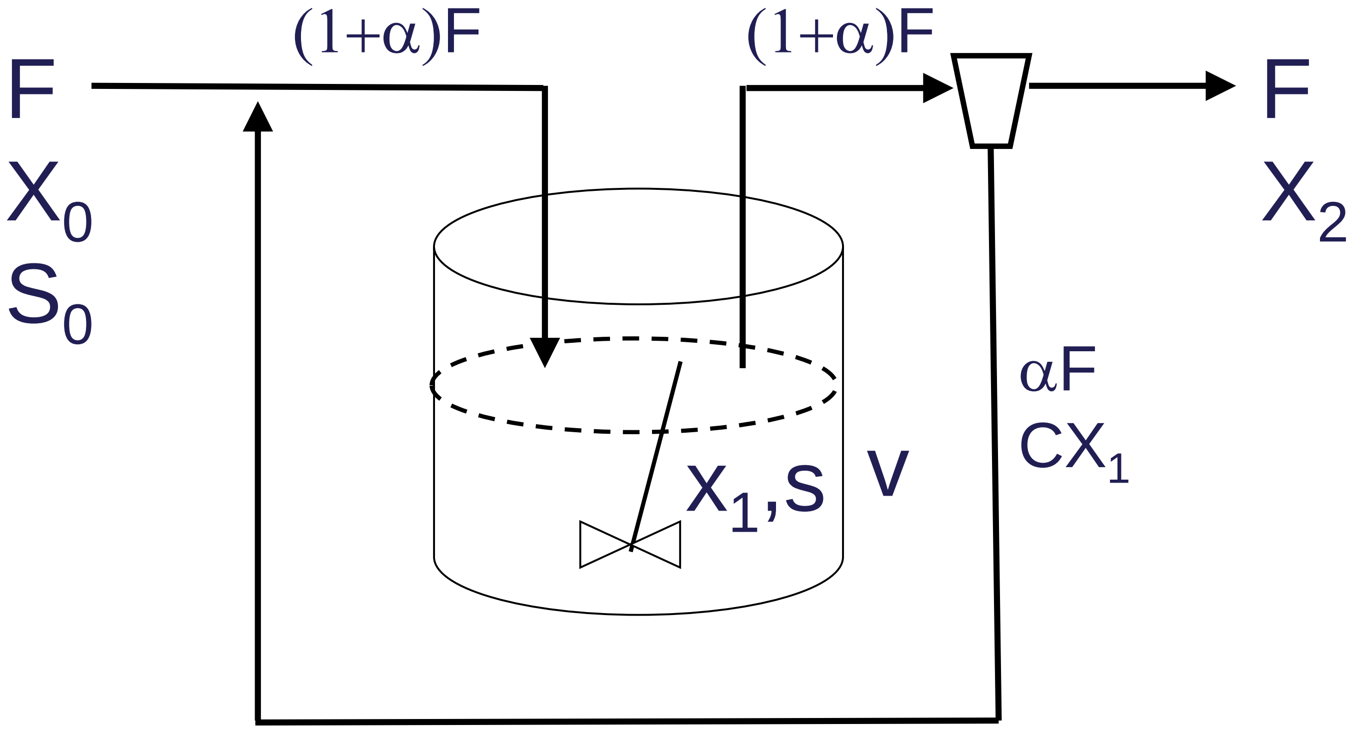
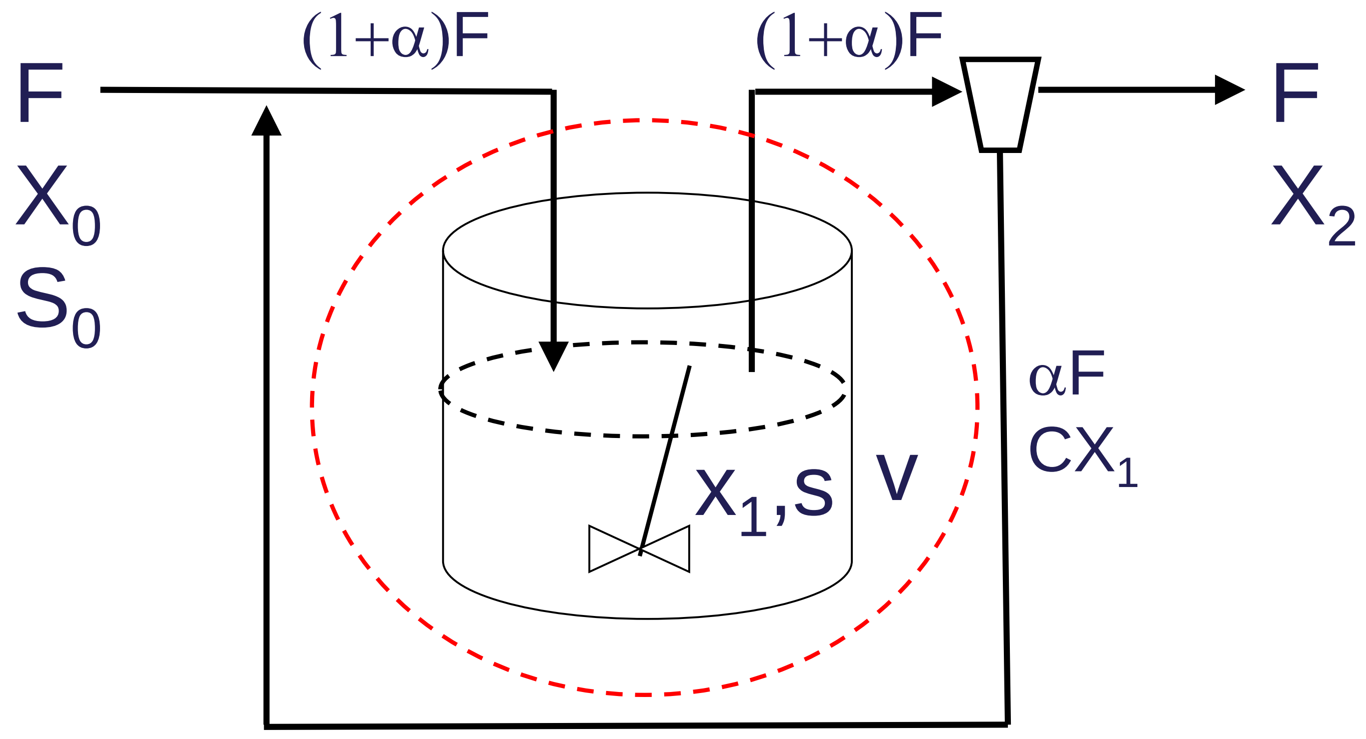
Chemostat with Recycle



Chemostat with Recycle

- Higher cell concentration
- Longer residence time
  - high specific productivity
- Higher stability
  - Ex: waste-water treatment
    - – Minimizing the effects of process perturbation

Chemostat with Recycle



F (L/h) : Flow Rate
X (g/L) : Cell Concentration
S (g/L) : Substrate Concentration

V (L) : Working Volume
α : Recycle Ratio
C : Concentration Factor

Mass Balance

Acc = In – Out + Gen – Con

Accumulation rate = Input rate – Output rate + Generation rate – Consumption rate

$$\frac{d(\quad)}{dt} =$$

Mass Balances

- cell

$$\frac{d\left(X_1 V\right)}{dt} = \alpha F C X_1 - (1+\alpha) F X_1 + \mu X_1 V \ldots(1)$$

At steady state

$$\{\alpha F C - (1+\alpha) F + \mu V\} X_1 = 0\ldots\ldots(2)$$

Mass Balances

At steady state

$$\{\alpha FC-(1+\alpha)F+\mu V\}X_1=0.....(2)$$

/ V

$$\{(\alpha C-1-\alpha)D+\mu\}X_1=0$$

$$\mu=(1+\alpha-\alpha C)D.......(3)$$

At steady-state

$$\mu = (1 + \alpha - \alpha C)D.......(3)$$

C > 1 → α(1-C) < 0 → 1+α(1-C) < 1

$$\mu < D.......(4)$$

A chemostat can be operated at dilution rates higher than the (maximum) specific growth rate when cell cycle is used.

Mass Balances

- substrate

$$\frac{d(SV)}{dt} = S_0F + S\alpha F - S(1+\alpha)F - \frac{\mu X_1 V}{Y} \text{.....(5)}$$

At steady state

$$S_0D + S\alpha D - S(1+\alpha)D = \frac{\mu X_1}{Y}$$

$$(S_0 - S)D = \frac{\mu X_1}{Y} \text{........(6)}$$

(3)

(6)

$$X_1 = \frac{Y(S_0 - S)}{1+\alpha-\alpha C} \text{........(7)}$$

At steady-state

$$X_1 = \frac{Y(S_0 - S)}{1+\alpha-\alpha C} \text{........}(7)$$

Compare with the X in chemostat without cell recycle

$$X = Y\,(S_0\text{-}S)$$

The steady-state cell concentration in a chemostat is increased by a factor of **$(1+\alpha-\alpha C)$** by cell recycle. (Not exactly!)

k

Concentrations at Steady State

$$(1+\alpha-\alpha C)D=\mu$$

(By Monod equation)

$$=\frac{\mu_m S}{K_S+S}$$

$$\boxed{S=\frac{kDK_S}{\mu_m-kD}\text{........}(8)}$$

where k= (1+α-αC)

Concentrations at Steady State

(7) $\longrightarrow$ $$X_1 = \frac{Y(S_0 - S)}{k}$$

(8)

$$\boxed{= \frac{Y}{k}\left(S_0 - \frac{kDK_S}{\mu_m - kD}\right) \ldots\ldots\ldots (9)}$$

where k= (1+α-αC)

Mass Balances

- Cell mass balance around the cell separator

$$(1+\alpha)FX_1 = FX_2 + \alpha FCX_1$$

$$X_2 = (1+\alpha-\alpha C)X_1$$

$$= kX_1 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(10)$$

Productivity

$$Productivity = \frac{X_2(g/L)\times F(L/hr)}{V(L)} = DX_2$$

$$DX_2 \underset{(10)}{=} kDX_1$$

$$\underset{(9)}{=} Y\left(S_0 D - \frac{kD^2 K_S}{\mu_m - kD}\right)$$

$$= Y\left(S_0 D - \frac{D^2 K_S}{\frac{1}{k}\mu_m - D}\right) \text{.......}(11)$$

Productivity

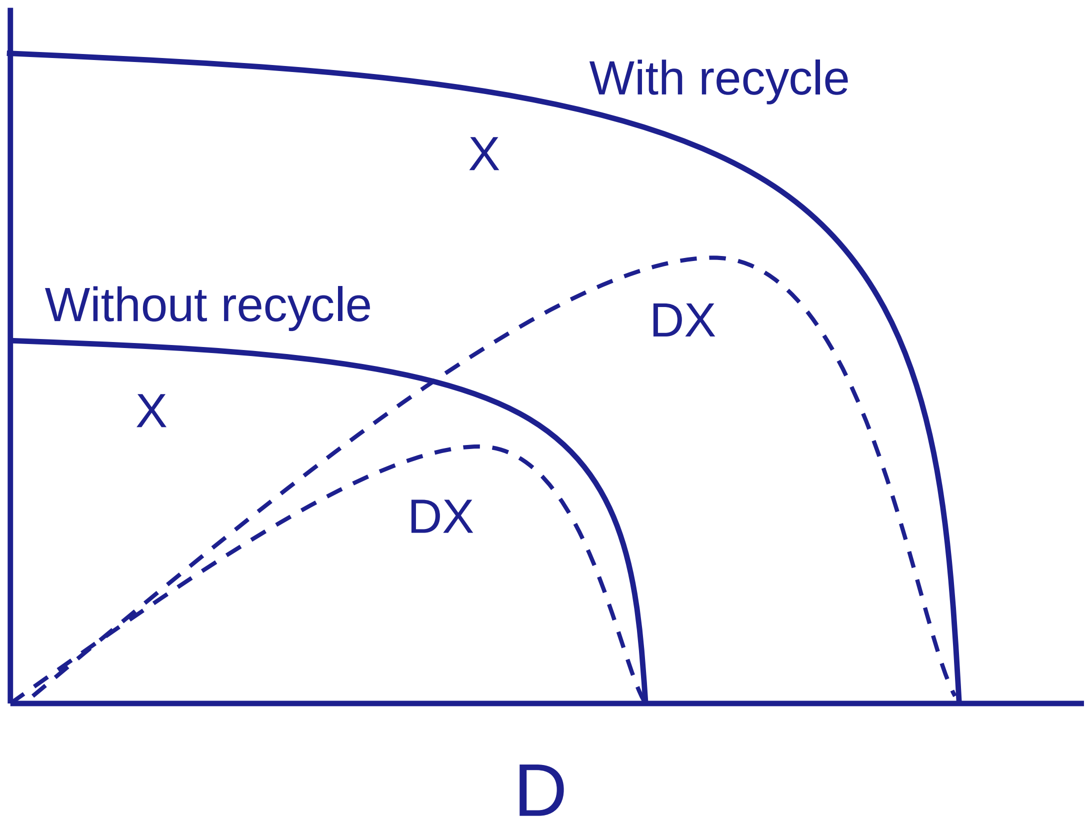
$$DX_2 = Y\left(S_0 D - \frac{D^2 K_S}{\frac{1}{k}\mu_m - D} \right) \text{.......(11)}$$

where k= 1+α(1–C)<1 ← C>1

Compare Eq.(11) with the productivity without cell recycle.

$$DX = Y(S_0 D - \frac{D^2 K_S}{\mu_m - D})$$

Chemostat with Cell Recycle



Cell Recycle System

Cell concentrations and productivities are higher with cell recycle, resulting in higher rates of substrate consumption.

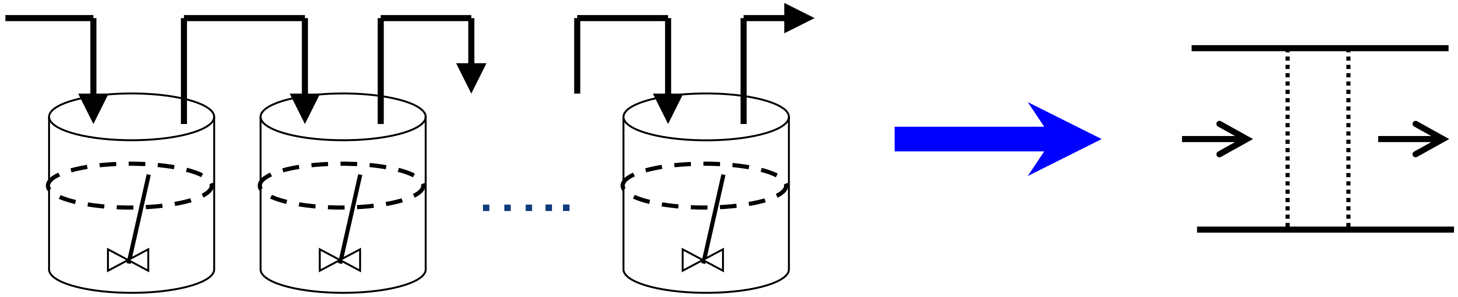
Recycle system --- used extensively in waste treatment

--- increasing use in ethanol production

Multistage Chemostat Systems

The growth and product formation steps need to be separated if optimal conditions for each step are different.

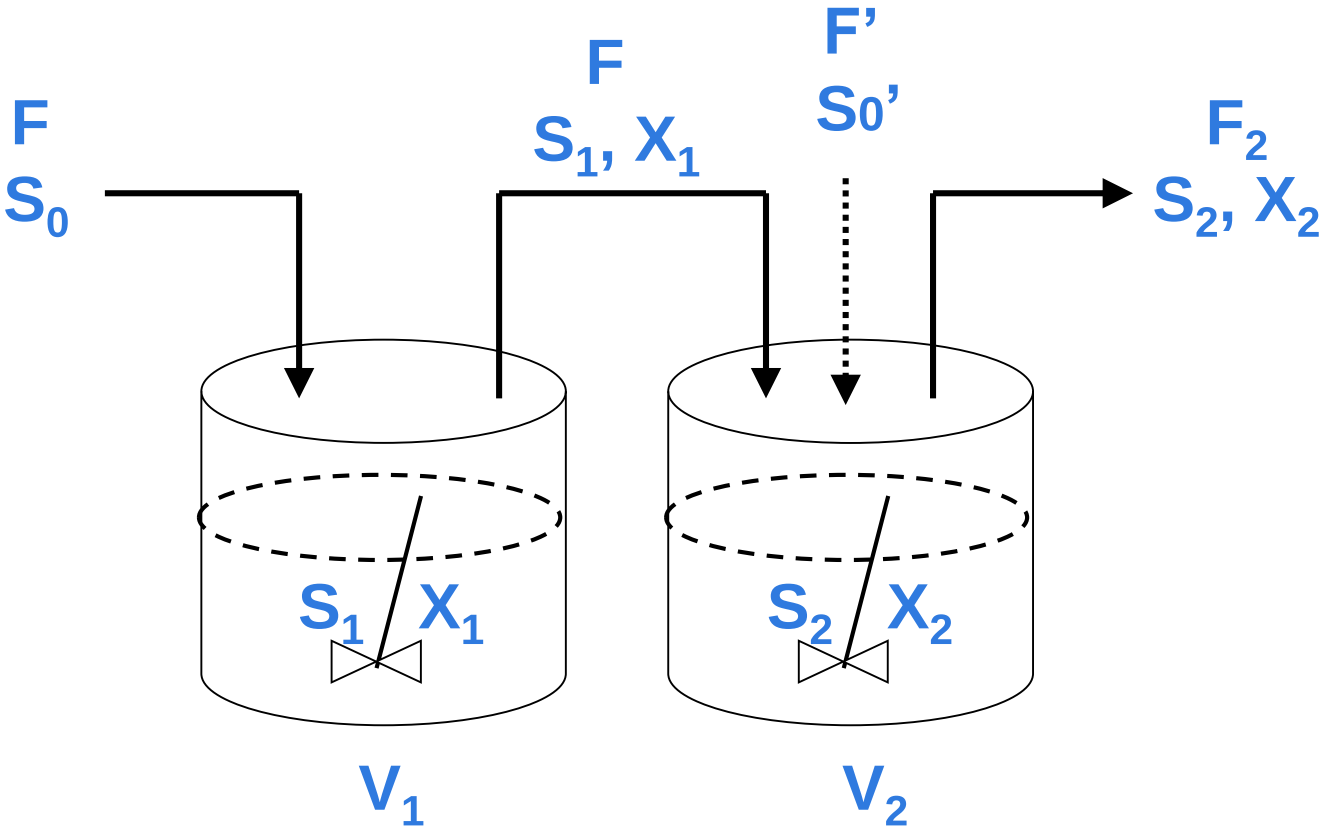
- particularly for secondary metabolite production
- the culture of genetically engineered cells



Multistage CSTR

PFR

Multistage Chemostat Systems



Mass Balance

Acc = In – Out + Gen – Con

Accumulation rate = Input rate – Output rate + Generation rate – Consumption rate

$$\frac{d(\quad)}{dt} =$$

Mass Balances for the First Stage

- cell

$$\frac{d(X_1V_1)}{dt} = 0 - X_1F + \mu_1 X_1 V_1 - 0 \ldots\ldots\ldots(1)$$

- substrate

$$\frac{d(S_1V_1)}{dt} = S_0F - S_1F + 0 - \frac{1}{Y}\mu_1 X_1 V_1 \ldots\ldots.(2)$$

Concentrations at Steady State

At steady state

$$S_1 = \frac{D_1 K_S}{\mu_m - D_1} \quad ---(3)$$

$$X_1 = Y\left(S_0 - \frac{D_1 K_S}{\mu_m - D_1}\right) ---(4)$$

where $D_1 = F / V_1$

Mass Balances for the Second Stage

- cell

$$\frac{d(X_2V_2)}{dt} = X_1F - X_2F + \mu X_2V_2 - 0.........(5)$$

/ V

$$\frac{dX_2}{dt} = (X_1 - X_2)D_2 + \mu_2 X_2$$

At st. st.

$$\mu_2 = D_2\left(1 - \frac{X_1}{X_2}\right)......(6)$$

where $X_1/X_2 < 1$

$\mu_2 < D_2$

Mass Balances for the Second Stage

- substrate

$$\frac{d(S_2V_2)}{dt} = S_1F - S_2F + 0 - \frac{1}{Y}\mu_2 X_2 V_2 \ldots\ldots.(7)$$

/ V

$$\frac{dS_2}{dt} = (S_1 - S_2)D_2 - \frac{1}{Y}\mu_2 X_2$$

At st. st.

$$S_2 = S_1 - \frac{\mu_2 X_2}{D_2 Y} \ldots\ldots(8)$$

Mass Balances for the Second Stage

(6) & Monod Eq. $\longrightarrow$

$$\frac{\mu_m S_2}{K_S + S_2} = D_2\left(1 - \frac{X_1}{X_2}\right)$$

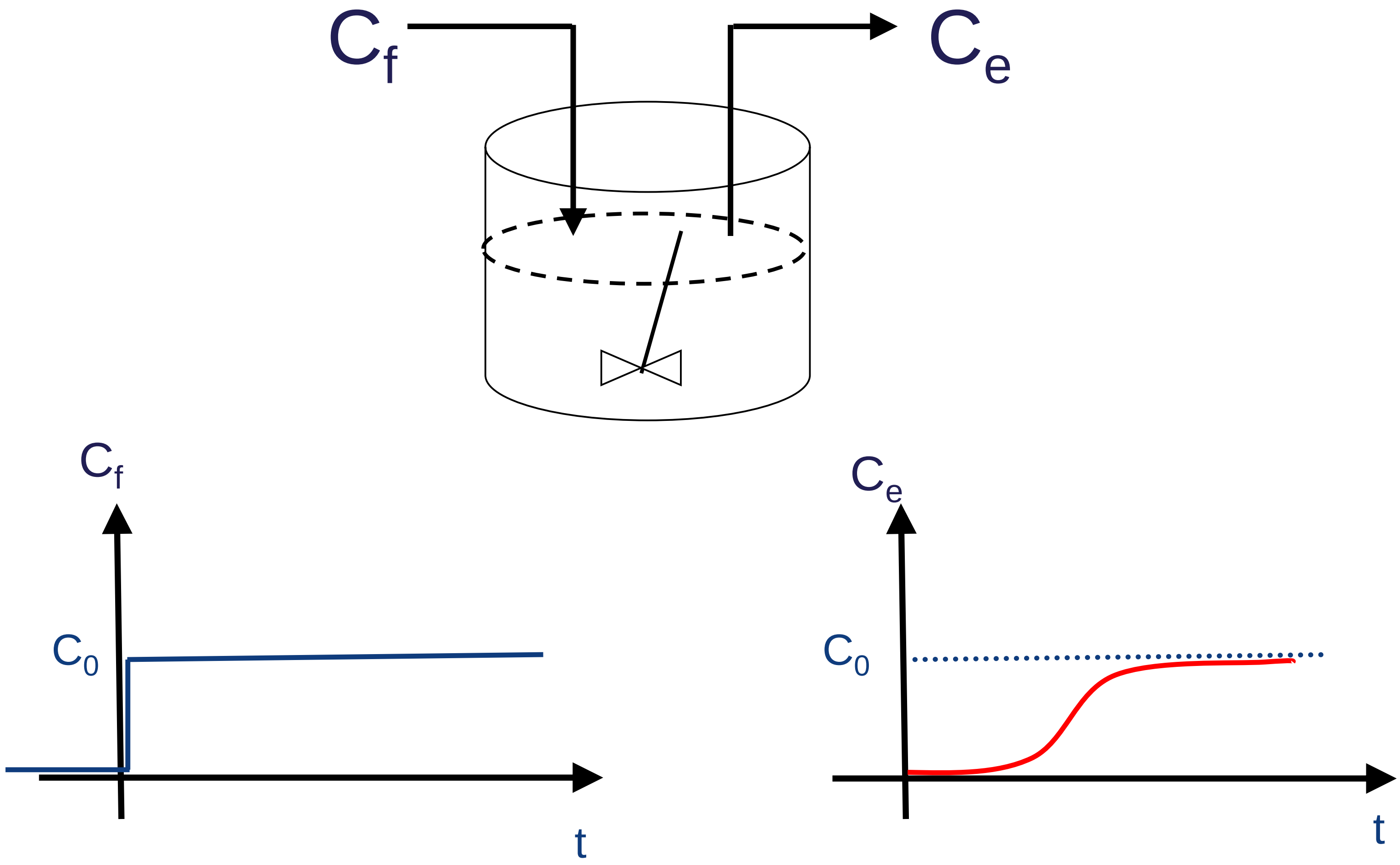
(8) & Monod Eq. $\longrightarrow$

$$S_2 = S_1 - \frac{X_2}{D_2 Y}\frac{\mu_m S_2}{K_s + S_2}$$

X_1 and S_1 are known. (Eq. (3) & (4))

Above equations can be solved simultaneously for X_2 and S_2.

Residence Time Distribution (RTD)



Residence Time Distribution (RTD)

$$C_f = C_0 U(t) \text{.......}(9)$$

Unit-step function

$U(t) = 0$ when $t < 0$

$U(t) = 1$ when $t \geq 0$

Response to unit-step input

$$\mathcal{F} = \frac{C_e(t)}{C_0} \text{...........}(10)$$

Residence Time Distribution (RTD)

$\mathcal{E}(t)$: residence time distribution function

$\mathcal{E}(t)dt$: fraction of fluid in exit function which has the residence time between t and $t+dt$

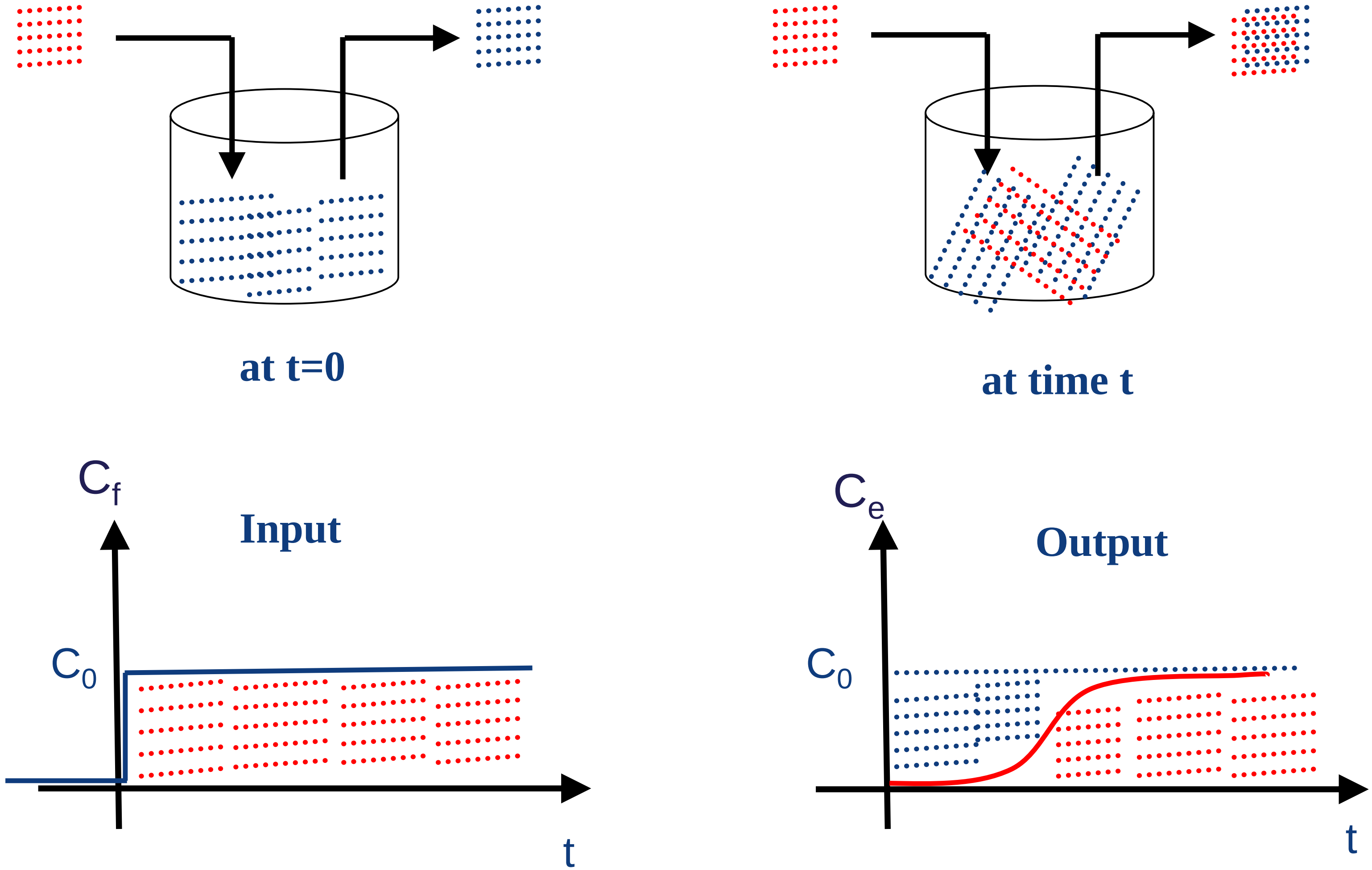
Residence Time Distribution (RTD)

The fraction of the exit stream which has resided in the vessel for times smaller than *t* is

$$\int_0^t \mathcal{E}(t)dt\ldots\ldots\ldots\ldots\ldots(11)$$

$$\int_0^\infty \mathcal{E}(t)dt = 1\ldots\ldots\ldots\ldots\ldots(12)$$

Residence Time Distribution (RTD)



Residence Time Distribution

- At time t, every red particle has the residence time less than t, and every blue particle has the residence time greater than t.

Concentration of red particle

$$C_e(t) = C_0 \int_0^t \mathcal{E}(x)dx + 0\int_t^\infty \mathcal{E}(x)dx \ldots\ldots(13)$$

Residence Time Distribution (RTD)

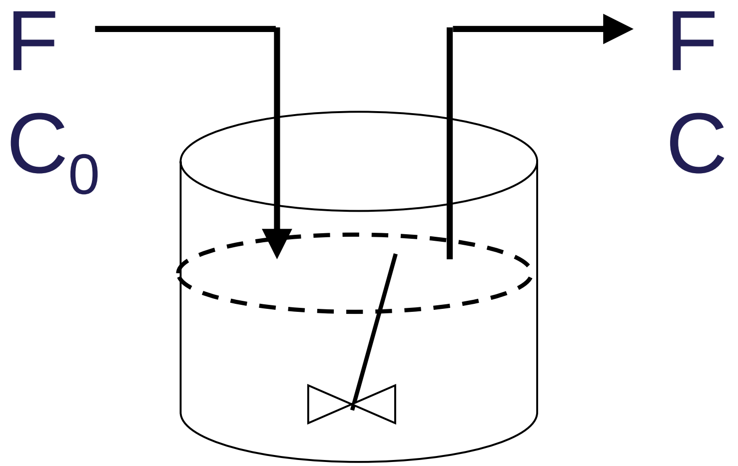
(10) → **(13)**

$$\mathcal{F}(t)=\int_0^t \mathcal{E}(t)dt........(14)$$

$$\therefore \mathcal{E}(t)=\frac{d\mathcal{F}(t)}{dt}..............(15)$$

The residence time distribution function, $\mathcal{E}$(t), can be obtained by differentiating an experimentally determined $\mathcal{F}$ curve.

Mass Balance on Non-reactive Tracer



$$\frac{d(CV)}{dt} = F(C_0 - C)..........(16)$$

I.C. $\quad C(0) = 0$

Mass Balance on Non-reactive Tracer

$$\int_0^C \frac{1}{C_0 - C} dC = \int_0^t \frac{F}{V} dt$$

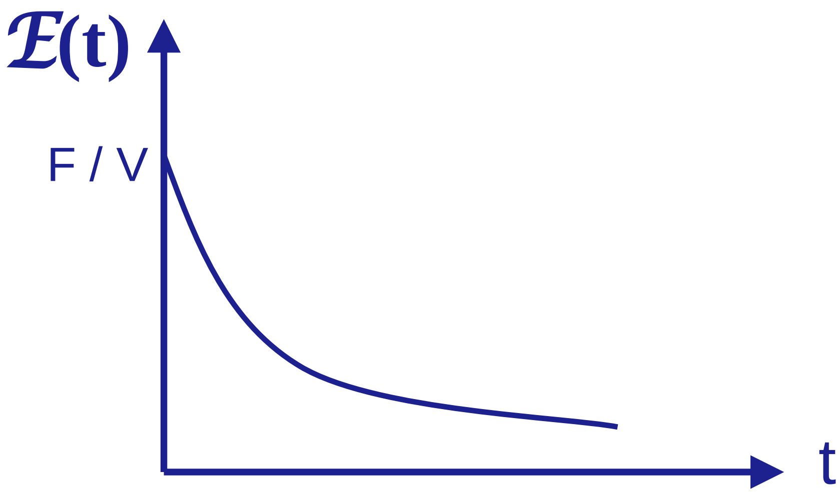
$$-\left[\ln(C_0 - C)\right]_0^C = \frac{F}{V}(t - 0)$$

$$\frac{C}{C_0} = 1 - e^{-\frac{F}{V}t} \quad \text{............}(17)$$

Mass Balance on Non-reactive Tracer

(10) $\longrightarrow$ $$\mathcal{F}(t) = \frac{C(t)}{C_0} = 1 - e^{-\frac{F}{V}t} \text{............}(18)$$

(15) $\longrightarrow$ $$\mathcal{E}(t) = \frac{d\mathcal{F}(t)}{dt} = \frac{F}{V} e^{-\frac{F}{V}t} \text{............}(19)$$



Mean Residence Time (τ_M)

$$\tau_M = \int_0^\infty t\mathcal{E}(t)dt$$

$$= \int_0^\infty t\frac{F}{V}e^{-\frac{F}{V}t}dt$$

$$= \frac{V}{F} \text{.............}(20)$$

$$\mathcal{E}(t) = \frac{1}{\tau_M}e^{-t/\tau_M} \text{.............}(21)$$