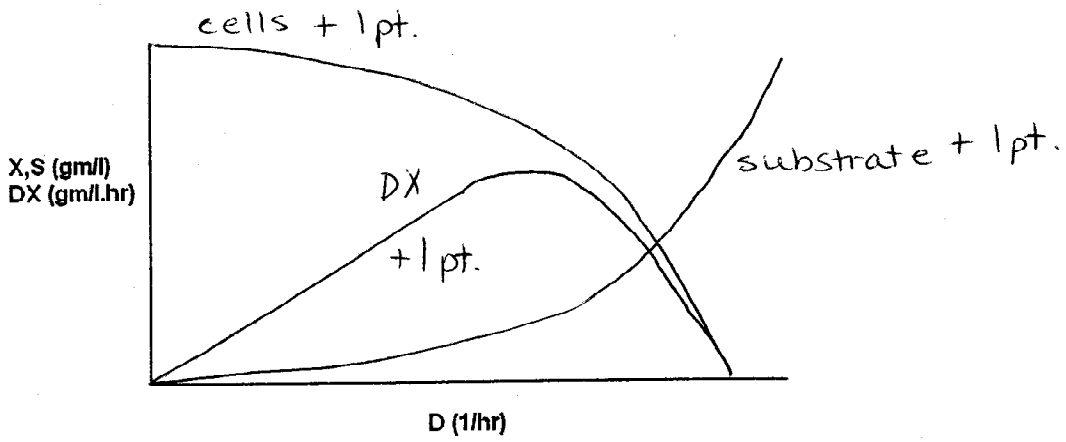
Name: Key

Chemical Engineering 170A November 9, 2007

Midterm Exam II (100 pts)
Closed Book and Closed Notes
Two 8.5 x 11 in. pages of notes (front and back) allowed

1. Sketch the steady state biomass and substrate concentration (X, S in gm/l) and productivity (DX in gm/l·hr) in a chemostat as a function of dilution rate (D in hr^{-1}) on the plot below. Make sure to label each curve. (3 pts)



2. Show that $\mu = D$ for a chemostat at steady state with a sterile feed (4 pts).

2 pts writing mass balance

mass balance biomass

$$V\frac{dX}{dt} = F(X_0 - X) + \mu XV$$

$$\mu X - DX = 0 \; ; \; (\mu - D)X_{ss} = 0 \quad X_{ss} \neq 0 \text{ so } \mu - D = 0 \rightarrow \mu = D$$

@ S.S. $0 = D(X_0 - X) + \mu X$

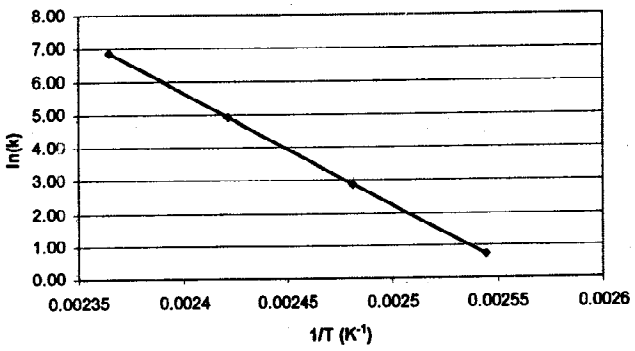
sterile feed $X_0 = 0$ 2 pts. final answer

3. You know the power input (in Watts) to a six-blade pitched-blade impeller (W/D =1/8) used in a continuously stirred tank bioreactor. Assume you know the diameter of the impeller and the impeller speed. The density of the fermentation broth can be taken as that of water. Briefly explain, in words, how you would calculate μ_{app}, the apparent viscosity of the fermentation broth (6 pts). 2pts. power #

Calculate the power # with the diameter D and the speed N of the impeller and ρ the density of the broth. Use chart in Fig 5.20 to find the Re number for the calculated power #. Use Curve 4 for a 6-blade, pitched-blade impeller. From knowing the Re # and D, N, & ρ, you can calculate μ_{app}, the apparent viscosity of the broth. 2pts. for mentioning Re #

2 pts. using chart

4. The following plot relates the rate constant for cell death (k, min^{-1}) of the organism *B. stearothermophilus* to temperature (deg K).



a) What is the activation energy, E_a, for thermal cell death (6 pts)?

slope = $-E_a/R$ $\quad \ln k = \ln k_o - \frac{E_a}{R}\frac{1}{T}$

slope = $\frac{0.80 - 6.90}{0.00254 - 0.00237} = -35882.4\,K$ 3pts. calculation

$-35882.4\,K = -E_a/R$ $\quad E_a = R(35882.4K)$ 3pts. final answer

$E_a = \frac{8.314\ J}{K \cdot mole} \times 35882.4\,K =$ **298.3 kJ/mole**

5. The enzyme urease is immobilized on non-porous polymer beads and is used in a plug flow reactor to convert urea to CO_2 and ammonia. Assume the flow rate is high enough to overcome any external mass transfer effects. If the initial urea concentration is 25 mM, what residence time is needed to convert 80% of the urea to CO_2 and ammonia (6 pts)?

Useful parameters:
Urease V_{max} = 10 mmoles/min·l
K_M = 20 mM

$S_A = 0.80$

$\tau = \frac{C_{A0} S_A}{V_{max}} - \frac{K_M}{V_{max}} \ln(1 - S_A)$ 3pts. equation

$\tau = 25\frac{mmoles}{L} \cdot \frac{min \cdot L}{10 mmoles} \cdot 0.8 - 20\frac{mmoles}{L} \cdot \frac{min \cdot L}{10 mmoles} \cdot \ln(0.2)$

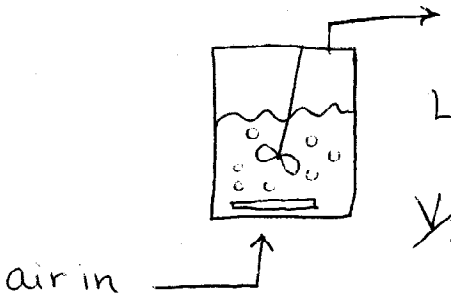
3 pts. calculation and answer

$\tau = 5.22$ mins

6. E. coli have a maximum respiration rate, qO_{2max}, of 240 mg O_2/gdw·hr. It is desired to achieve a cell mass of 20 gdw/l. The k_La is 120 h^{-1} in a 1000 l reactor (800 l liquid volume). A gas stream enriched in oxygen is bubbled through a batch bioreactor to give a value of C_L^* = 28 mg/l. If oxygen becomes growth limiting, growth and respiration are slow and qO_2 can be written as

$$qO_2 = \frac{qO_{2max} C_L}{0.2\frac{mg}{l} + C_L}$$

where C_L is the dissolved oxygen concentration in the fermentor. What is C_L when the cell mass is at 20 g/l (25 pts)?



Liquid Phase O_2 Balance 5 pts. liquid phase mass balance

$$V_L \frac{dC_L}{dt} = k_La(C_L^* - C_L)V_L - qO_2 X V_L$$

In a fed-batch system if oxygen transport is growth limiting then the rate of consumption of oxygen by the cells equals transport of oxygen into the liquid and $\frac{dC_L}{dt} = 0$

$$0 = k_La(C_L^* - C_L) = qO_2 X$$

pseudo steady-state cells aren't growing

5 pts. for equating the two

$$k_La(C_L^* - C_L) = \frac{qO_{2max} C_L}{0.2\frac{mg}{l} + C_L} X$$

$k_La = 120\ h^{-1}$

$C_L^* = 28\ mg/l$

$qO_{2max} = 240 \frac{mg\ O_2}{g \cdot hr}$

$$120(28 - C_L) = \frac{240 C_L (20)}{0.2 + C_L}$$

5 pts. for putting in #'s

$$3360 - 120C_L = \frac{4800 C_L}{0.2 + C_L}; \quad 4800C_L = (0.2 + C_L)(3360 - 120C_L)$$

5 pts. for solving

$$4800C_L = 672 - 24C_L + 3360C_L - 120C_L^2$$

$$120C_L^2 + 1464C_L - 672 = 0 \qquad a = 1 \quad b = 12.2 \quad c = -5.6$$

$$C_L^2 + 12.2C_L - 5.6 = 0 \qquad C_L = \frac{-12.2 \pm \sqrt{(12.2)^2 - 4(1)(-5.6)}}{2(1)}$$

$$C_L = \frac{-12.2 \pm 13.09}{2}$$

$\boxed{C_L = 0.45\ mg/l}$ 5 pts. final answer

other root gives a ⊖ C_L

7. A continuous sterilizer at 120 °C runs at a flow rate such that the flow is turbulent. For fully developed turbulent flow, the modified Peclet number, $(d_t \cdot u_s/D)$ reaches an upper limit of 3.33. The ratio of reactor length to reactor diameter (L/d_t) is 100, and the reactor volume is 5 l. The unsterilized medium contains 10^4 spores/l and the reactor has a residence time of 5 minutes.

a) Calculate the value of the Pe for this reactor. Can you assume the continuous sterilizer behaves as a plug flow reactor? Why or why not? (10 pts)

modified Pe = 3.33 = $\frac{d_t \cdot u_s}{D}$ $\quad Pe = \frac{L \cdot u_s}{D}$ 5 pts. for calculating Pe

$L/d_t = 100$

$d_t = \frac{L}{100}$

$3.33 = \frac{L \cdot u_s}{D \cdot 100}$

$\frac{L \cdot u_s}{D} = 333 = Pe$

5 pts. explanation

The Pe is fairly large which means there is more convection taking place than dispersion so we can assume the continuous reactor is a plug flow reactor.

b) The cell death rate constant k is 2.0 min^{-1} at 120°C. What is the probability of contamination for the medium exiting the reactor after one residence time (10 pts)?

5 pts. for equation $P(t)$ = probability of contamination

$P(t) = (1 - e^{-k\hat{\tau}}) N_0$ $\quad N_0$ = # of spores in 1 residence time

$\hat{\tau} = 5 min$

$k = 2 min^{-1}$

$N_0 = \frac{10^4 spores}{\ell} \times 5\ell = 50{,}000$

$1 - P(t) = 1 - (1 - e^{-2(5)})$ 5 pts. for working out solution & for answer

$= 0.897$ 89.7% probability of contamination

c) What parameters, if any, can you adjust to decrease the probability of contamination (5 pts)?

To decrease probability of contamination you can increase the temperature or increase the residence time (by either increasing the volume of the reactor or decreasing the flow rate).

5 pts. for explanation

(2.5 pts. for temp, 2.5 pts for residence time)

8. You are working for a biotechnology company in the Bay Area that wants to produce an antibody from chinese hamster ovary (CHO) cells in a perfusion bioreactor with a residence time of 2 hours. Data from a batch culture (started from an inoculum of 10^4 cells/ml show that the net specific growth rate at 10 hours of culture is 0.5 hr^{-1} and the growth of CHO cells during the exponential phase can be described by the following:

$$\frac{dX}{dt} = \mu X$$

a) If you plan to operate your perfusion bioreactor at a specific growth rate matching that of the batch system at 10 hours, what is the predicted steady-state value for biomass in the perfusion bioreactor (15 pts)?

5 pts. equation $X^P_{ss} = \frac{F}{V}\int_0^t X^B(t)\,dt$ $\qquad X^B(t) = X_o e^{\mu t} = 10^4 e^{0.5t}$

$F/V = \frac{1}{2\,hrs} = 0.5\ hr^{-1}$

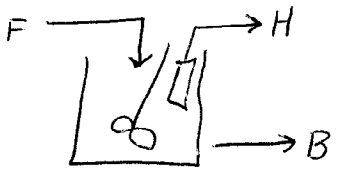
$$X^P_{ss} = \frac{0.5\cdot 10^4\ cells}{h}\ \frac{}{mL} \times \int_0^{10} e^{0.5t}\,dt$$ 5 pts. solving integral

$$X^P_{ss} = 5000\ \frac{cells}{mL\cdot h} \times \frac{h}{0.5} e^{0.5t}\Big]_0^{10} = \frac{5000}{0.5}\left(e^{0.5(10)} - e^0\right)$$

$X^P_{ss} = 10000\,(148.4 - 1) = 1.47 \times 10^6\ cells/mL$

5 pts. final answer

b) The specific antibody production rate in CHO cells is 10 pg/cell·hr, and is growth associated. Calculate the expected steady-state concentration of antibody in the perfusion bioreactor (10 pts).



mass balance on P

5 pts. mass balance @ S.S & equation $\quad V\frac{dP}{dt} = -(H+B)P + \nu X V$

$0 = -\frac{F}{V}P + \nu X \qquad H + B = F$

$\frac{F}{V}P = \nu X \;;\quad P_{ss} = \frac{V}{F}\nu X^P_{ss}$

5 pts. final answer & calculations $\quad P_{ss} = 2\,hr \times \frac{10\,pg}{cell\cdot hr} \times 1.47\times 10^6 \frac{cells}{mL} = 2.94\times 10^7 \frac{pg}{mL}$

$P_{ss} = 29.4\ \mu g/mL$