UNIVERSITI SAINS MALAYSIA

Second Semester Examination
2012/2013 Academic Session

June 2013

EKC 574 – Downstream Processing of Biochemical and Pharmaceutical Products

Duration : 3 hours

Please ensure that this examination paper contains FOUR printed pages and THREE printed pages of Appendix before you begin the examination.

Instruction: Answer **ALL** questions.

Answer ALL questions.

1. Under Good Manufacturing Practice, Facilities Conceptual Design is concerning the segregation of process and building utilities to avoid contamination. Figure Q.1. is the facility layout of a bioprocessing industry.

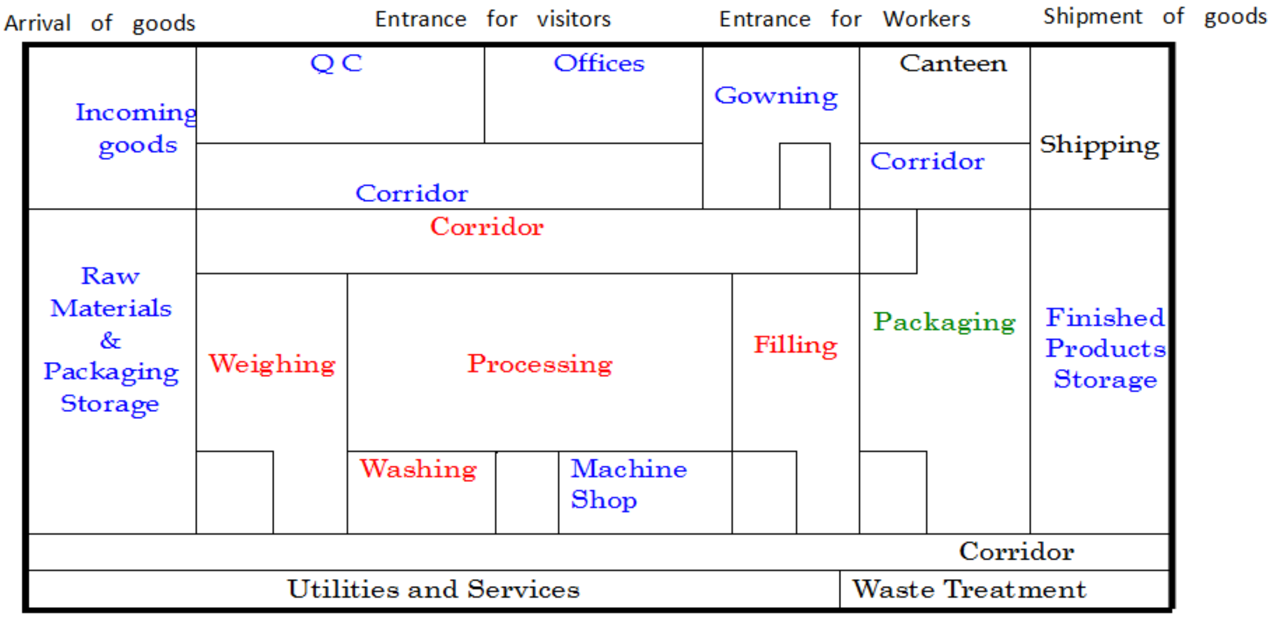


Figure Q.1.

[a] Proposed the material and personnel traffic (show directly on the sketch sheet)
[5 marks]

[b] Suggest on how to prevent contamination between the corridor and the work zone.
[2 marks]

[c] Water for Injection (WFI) is water purified to remove chemicals and microorganisms. List out three unit operations involved in the production of WFI.
[3 marks]

2. Benzylpenicillin is an antibiotic effective against anthrax disease. As part of a purification process, 200 mg of benzylpenicillin is mixed with 25 mL of n-octanol and 25 mL of water. After equilibrium is established, there is a water rich phase that contains essentially no n-octanol and an octanol-rich phase that contains 74 mol% n-octanol and 26 mol% water.

[a] Assuming infinite dilution, determine the concentrations of benzylpenicillin in each of these phases.
[10 marks]

[b] For the real solution, if the ratio of $\frac{\gamma_{BP}^{W}}{\gamma_{BP}^{O}}$ is <1, comment on the concentration changes of benzylpenicillin in the octanol phase.
[3 marks]

[c] What is the major disadvantage of solvent extraction for biological product?

[2 marks]

Data: The molecular weight of benzylpenicillin is 334.5, that of n-octanol is 130.23, the liquid density of n-octanol is 0.826 g/cm^3, and partition coefficient of benzylpenicillin in n-octanol/water is 65.5.

3. A 400 L solution of a protein at 0.05 g/L needs to be concentrated to 1.5 g/L using an ultrafiltration membrane of surface area 500 cm^2 at a flux of 12 x 10^{-5} cm/s. The protein has a diffusion coefficient of 1.8 x 10^{-6} cm^2/s at 15°C.

[a] Determine whether concentration polarization is an important external factor affecting the membrane's performance. Assume that the boundary layer thickness is 0.015 cm.

[3 marks]

[b] Propose a method to reduce the concentration polarization based on the expression of $Sh = f(\mathrm{Re}, Sc)$.

[3 marks]

[c] What is the concentration of protein on the surface of the ultrafiltration membrane for the bulk concentration of 1.5 g/L.

[4 marks]

[d] Calculate the time needed to complete the filtration and achieved the desired final concentrations.

[5 marks]

4. [a] Discuss the significance of *G* value and Σ factor in the scaling up of centrifuges.

[8 marks]

[b] A suspension of yeast cells is to be filtered at a constant filtration rate of 50 L/min. The suspension has a solid content of 70 kg/m^3 of suspension and the yeast cells have a bulk density of 800 kg/m^3. Laboratory tests indicate that the specific cake resistance is 40 m/kg and the viscosity of the filtrate is 2.9 x 10^{-3} kg/m.s. The filter has an area of 0.1 m^2 and the medium offers negligible resistance. How long can the filtration rate be maintained before the pressure drop exceeds 1 $kg/m \cdot s^2$? What volume of cake and filtrate are collected during this time? Note that ρ_0 is expressed in mass of solids per volume of filtrate, and NOT total volume of suspension. [HINT: volume of suspension = volume of filtrate + volume of cake].

[17 marks]

5. [a] Paclitaxel is an anticancer drug that can be produced by plant cell cultures of *Taxus baccata*. However, most of the product is entrapped in the cells and require cell disruption to release the product into the medium. Suggest <u>two</u> techniques that can be used to disrupt the cells.

[8 marks]

[b] Cell-free fermentation liquor contains 8 x 10^{-5} mol/L immunoglobin G. It is proposed to recover at least 90% of this antibody by adsorption on synthetic, non-polar resin. Experimental equilibrium data are correlated as follows:

$$q = 5.5 \text{ x } 10^{-5} y^{0.35}$$

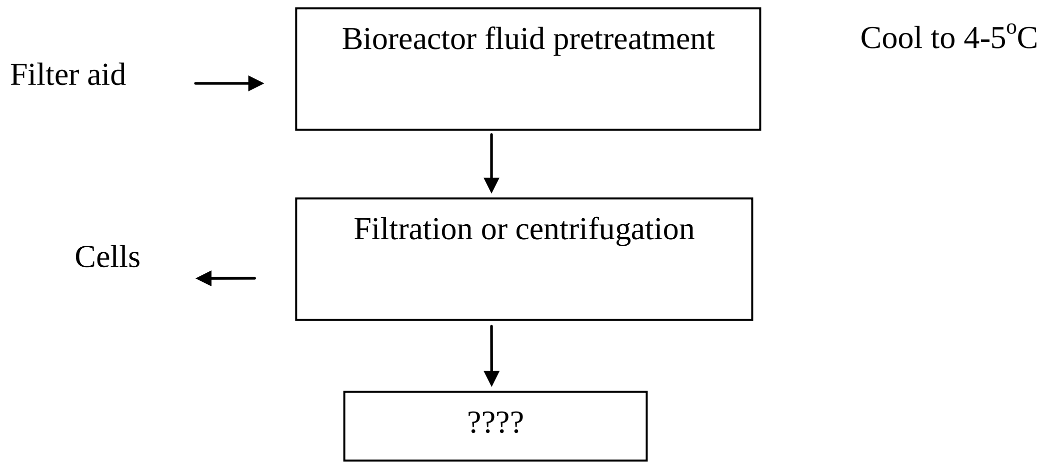
where q is mol solute adsorbed per cm^3 adsorbent and y is liquid-phase solute concentration in mol/L. What minimum quantity of resin is required to treat 2 m^3 fermentation liquor in a single-mixed tank? Show the detail flow chart of the process.

[12 marks]

[c] Describe a vacuum-shelf dryer and its application in industry.

[5 marks]

6. Protease, an enzyme that can degrade proteins, is used in products such as laundry detergent. Because it applications do not involve food products or injectable therapeutics, it need not be produced in a highly purified form. Protease can be produced in solid form. Develop and briefly explain the following steps that would improve the purity of the final product.



[10 marks]

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Appendix

$$J(x) = \frac{D}{\delta(x)} \ln \frac{C_w}{C_b}$$

$$\left(\frac{C_{final}}{C_o}\right) = \left(\frac{V_o}{V_f}\right)^R$$

$$\frac{At}{V} = \frac{\mu\alpha\rho_0}{2\Delta P}\left(\frac{V}{A}\right) + \frac{\mu R_M}{\Delta P}$$

$$R_C = \alpha\rho_0\left(\frac{V}{A}\right)$$

$$\alpha = \alpha'(\Delta P)^s$$

$$\upsilon_g = \frac{\rho_p - \rho_f}{18\mu} D_p{}^2 g$$

$$\upsilon_c = \frac{\rho_p - \rho_f}{18\mu} D_p{}^2 \omega^2 r$$

$$Q = \upsilon_g \left[\frac{2\pi l R^2 \omega^2}{g}\right]$$

$$Q = \upsilon_g \left[\frac{2\pi n \omega^2}{3g}\left(R_0^3 - R_1^3\right)\cot\theta\right]$$

$$Q = \upsilon_g \left[\frac{\pi l (R_0^2 - R_1^2)\omega^2}{g \ln(R_0 / R_1)}\right]$$

g = 980 cm/s^2

$$t_E = \frac{1}{\upsilon\varepsilon}(K + \varepsilon - K\varepsilon)$$

$$\upsilon y_F t^* = L\rho_b q_{sat}$$

$$\theta = 1 - \left(\frac{t_E - t_B}{2t_B}\right)$$

$$q = Ky \qquad q = Ky^n \qquad q = \frac{q_0 y}{K + y}$$

$$B = \frac{dN}{dt} = k_n (c - c^*)^n$$

$$\frac{dM}{dt} = kA(c - c^*)^n$$

$$G \equiv \frac{dL}{dt} = k_g (c - c^*)^n$$

Common Engineering Conversion Factors

Length	**Volume**
1 ft = 12 in = 0.3048 m, 1 yard = 3 ft 1 mi = 5280 ft = 1609.344 m 1 nautical mile (nmi) = 6076 ft	1 ft^3 = 0.028317 m^3 = 7.481 gal , 1 bbl = 42 U.S. gal 1 U.S. gal = 231 in^3 = 3.7853 L = 4qt = 0.833 lmp.gal. 1 L = 0.001 m^3 = 0.035315 ft^3 = 0.2642 U.S. gal
Mass	**Density**
1 slug = 32.174 lb_m = 14.594 kg 1 lb_m = 0.4536 kg = 7000 grains	1 slug/ft^3 = 515.38 kg/m^3 , 1 g/cm^3 = 1000 kg/m^3 1 lb_m/ft^3 = 16.0185 kg/m^3 , 1 lb_m/in^3 = 27.68 g/cm^3
Acceleration & Area	**Velocity**
1 ft/s^2 = 0.3048 m/s^2 1 ft^2 = 0.092903 m^2	1 ft/s = 0.3048 m/s , 1 knot = 1 min/h = 1.6878 ft/s 1 min/h = 1.4666666 ft/s (fps) = 0.44704 m/s
Mass Flow & Mass Flux	**Volume Flow**
1 slug/s = 14.594 kg/s. 1 lb_m/s = 0.4536 kg/s 1 kg/m^2s = 0.2046 lb_m/ft^2s = 0.00636 slug/ft^2s	1 gal/min = 0.00228 ft^3/s = 0.06309 L/s 1 million gal/day = 1.5472 ft^3/s = 0.04381 m^3/s
Pressure	**Force and Surface Tension**
1 lb_f/ft^3 = 47.88 Pa, 1 torr = 1 mm Hg 1 psi = 144 psf, 1 bar = 10^5 Pa 1 atm = 2116.2 psf = 14696 psi = 101,325 Pa = 29.9 in Hg = 33.9 ft H_2O	1 lb_f = 4.448222 N = 16 oz, 1 dyne = 1 g cm/s^2 = 10^{-5}N 1 kg_f = 2.2046 lb_f = 9.80665 N 1 U.S. (short) ton = 2000 lb_f , 1 N = 0.2248 lb_f 1 N/m = 0.0685 lb_f/ft
Power	**Energy and Specific Energy**
1 hp = 550 (ft.lb_f)/s = 745.7 W 1 (ft.lb_f)/s = 1.3558 W 1 Watt = 3.4123 Btu/h = 0.00134 hp	1 ft lb_f = 1.35582 J, 1 hp·h = 2544.5 Btu 1 Btu = 252 cal = 1055.056 J = 778.17 ft lb_f 1 cal = 4.1855 J, 1 ft.lb_f/lb_m = 2.9890 J/kg
Specific Weight	**Heat Flux**
1 lb_f/ft^3 = 157.09 N/m^3	1 W/m^2 = 0.3171 Btu/(h ft^2)
Viscosity	**Kinematic Viscosity**
1 slug/(ft.s) = 47.88 kg/(m.s) = 478.8 poise (p) 1 p=1 g/(cm.s) 0.1 kg/(m.s) = 0.002088 slug/(ft s)	1 ft^2/h = 2.506 .10^{-5} m^2/s, 1 ft^2/s = 0.092903 m^2/s 1 stoke (st) = 1 cm^2/s = 0.0001 m^2/s = 0.001076 ft^2/s
Temperature Scale Readings	
^oF = (9/5)^oC + 32 ^oC = (5/9) (^oF – 32)	^oR = ^oF + 459.69 ^oK = ^oC + 273.16
Thermal Conductivity*	**Gas Constant***
1 cal/(s.cm.^oC) = 242 Btu/(h.ft.^oR) 1 Btu/(h.ft.^oR) = 1.7307 W/(m.K)	R = 82.057 atm.cm^3/(gmol.K) = 62.361 mm Hg.L/(gmol.K) = 1.134 atm.ft^3/(lbmol.K) = 0.083144 bar.L/(gmol.K) = 10.73 psi. ft^3/(lbmol. ^oR) = 555.0 mm Hg.ft^3/(lbmol. ^oR)

- Note that the intervals in absolute (Kelvin) and ^oC are equal. Also, 1 ^oR = 1 ^oF.

Latent heat: 1 J/kg = 4.2995 × 10^{-4} Btu/lb_m = 10.76 lb_f.ft/slug = 0.3345 lb_f.ft/lb_m , 1 Btu/lb_m = 2325.9 J/kg

Heat transfer coefficient: 1 Btu/(h.ft^2.^oF) = 5.6782 W/(m^2.^oC).

Heat generation rate: 1 W/m^3 = 0.09665 Btu/(h ft^3)

Heat transfer per unit length: 1 W/m = 1.0403 Btu/(h ft)

Mass transfer coefficient: 1 m/s = 11.811 ft/h, 1 lb_{mol}/(h.ft^2) = 0.013562 kgmol/(s.m^2)

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Sketch Sheet

Sketch the material and personnel flow onto this sketch sheet. Detach it from the question paper and submit together with your answer booklets