TECHNOLOGICAL UNIVERSITY DUBLIN
TALLAGHT CAMPUS

Bachelor of Science (Honours)

Pharmaceutical Science - Nanjing Joint Program

Full Time

Semester Seven : January 2024

Manufacturing Technology

Internal Examiners
Dr Adrienne Fleming
Dr Eugene Hickey

External Examiners
Dr David Page

Day
Date
Time

Instructions to Candidates

Section A: A Fleming: Answer any two out of the three questions.
Section B: E HIckey: Answer any two out of the three questions.

Section A **Answer any two questions**

Question 1 Answer all parts (100 marks)

(a) ***'The pharmaceutical industry produces significant waste per kilo of API manufactured'.***

Provide examples of sustainable waste management practices adopted by pharmaceutical companies. Explore the potential challenges and innovations in achieving effective waste reduction within the industry.

(30 marks)

(b) A batch reactor with a volume of 20 m^3 is equipped with a flat blade turbine agitator, having a diameter of 1.2 m, operating at 80 revolutions per minute.The reactor is utilised for the reaction of 6.58 moles of reactant A with reactant B at room temperature. The reaction mixture, which is homogeneous, possesses a density of 1756 kg m^{-3} and a viscosity of 1.1 Ns m^{-2}, along with a calculated rate constant of 3.12 s^{-1}. Reactant A is introduced in a controlled manner down the vessel walls.

Utilising time constant calculations, determine whether product selectivity is influenced more by micro-mixing or reaction kinetics in this process. The specified value for power number for the turbine agitator (P_0) is 1.1.

(30 marks)

(c) (i) Discuss the fundamental differences between batch and continuous processing, focusing on key aspects such as production methods and product quality control. **(20 marks)**

(ii) ***In the realm of quality control and process monitoring, various testing approaches are employed.***

Discuss the differences between online, inline, at line, and off line testing methodologies. **(20 marks)**

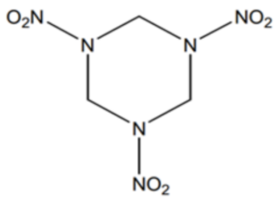
Question 2 Answer all parts (100 marks)

(a) A 0.68 m diameter open straight-blade turbine is employed to agitate reaction mixtures within a 20 m^3 batch reactor equipped with baffles. The reactor has a diameter of 1.2 m, and the introduction of one reagent occurs at the outer walls of the vessel, distanced away from the agitator region.

Given that the agitator speed has been fixed at 160 r.p.m. determine the mixing time (t_{95}) in seconds.
Po = 1.1; ρ= 1490 kg/m^3; μ = 0.015 Ns/m^2

(30 marks)

(b) (i) Explain the role of oxygen balance in ensuring safety within the pharmaceutical industry.
(ii) Assess the following compound as a reagent in a large scale production from a safety perspective?
Explain why, using your knowledge of oxygen balance.



(30 marks)

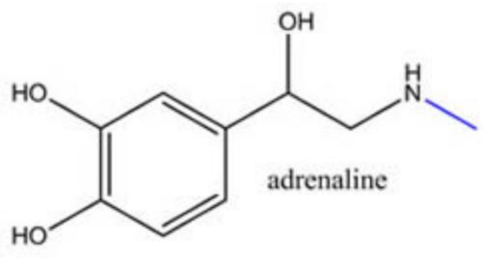
(c) **Imagine you are a member of a team assigned to assess the design of a chemical reactor for full-scale production in a pharmaceutical manufacturing plant.**
Outline the key considerations and steps your team would take in evaluating the reactor design. Provide specific examples of potential challenges that might arise in full-scale production and propose strategies for addressing them.

(40 marks)

Question 3 Answer all parts (100 marks)

(a) In the context of the pharmaceutical industry, discuss the significance and applications of polymorphism.
Provide specific examples and consider the challenges associated with polymorphism in manufacturing **(30 marks)**

(b) Identify the potential structural modifications to the following structure that could be varied to potentially enhance drug potency and activity in the body.



(20 marks)

(c) A new plant is being designed for the production of the API Paracetamol.
Given that the installation cost of a $10m^3$ reactor in 2011 has been calculated to be €125000, predict the cost in 2016, given the following CEI cost index data:
CEI (2011) = 420 and CEI (2016) = 525 **(20 marks)**

(d) A second order condensation reaction (C_A = 66 mol. ; $k = 2.6 \times 10^{-4}\ s^{-1}$) is to be run in a Volume= 2000 L vessel of surface area $A=38\ m^2$ with a heat transfer coefficient of $U=3.4 \times 10^{-2}\ W/m^2/K$ at $T=90^0C$. The following thermodynamic results were obtained from calorimetry experiments:
$\Delta H = -254\ J\ mol^{-1}$; $E_A = 1.34\ J\ mol^{-1}$. $R = 8.314\ J\ K^{-1}\ mol^{-1}$]
(i) Determine whether the reaction below becomes self-heating or not when run on a large scale.
(ii) Decide whether steam needs to be continually fed through the jacket of the vessel to maintain reflux throughout the reaction.
(30 marks)

SECTION B: [Dr. Eugene Hickey]

You are required to answer TWO complete questions

Question 4 (100 marks)

a) A stream has a composition of 14.0% benzene, 37.9% toluene, 48.1% ethylene, all percentages by mass. The toluene flow rate of the stream is 58.8kg/hr. Calculate the benzene flow rate. (20 marks)

b) In the chlorination of ethylene to produce DCE, the conversion of ethylene is 93%. If 73mol of DCE is produced from 100mol of ethylene supplied, calculate the selectivity and yield. (20 marks)

c) CO_2 at a rate of 3.5kg/hr is added to an air stream. After mixing the stream has 0.23% v/v CO_2. Normal air has 0.03% CO2 by mol. Calculate the flow rate of the air stream. Take the average molar mass of air (both before and after mixing) to be 28.9g/mol. (20 marks)

c) An FCC crystal has a unit cell volume of 8.95nm³. What is the atomic radius in nm? (15 marks)

d) What is meant by the *Packing Fraction* of crystals? (15 marks)

e) A unit cell has parameters a=b=4.18nm, and c=2.25nm. It has angles $\alpha = 90^0$, $\beta = 90^0$, and $\gamma = 90^0$. What is the shape of the unit cell? (10 marks)

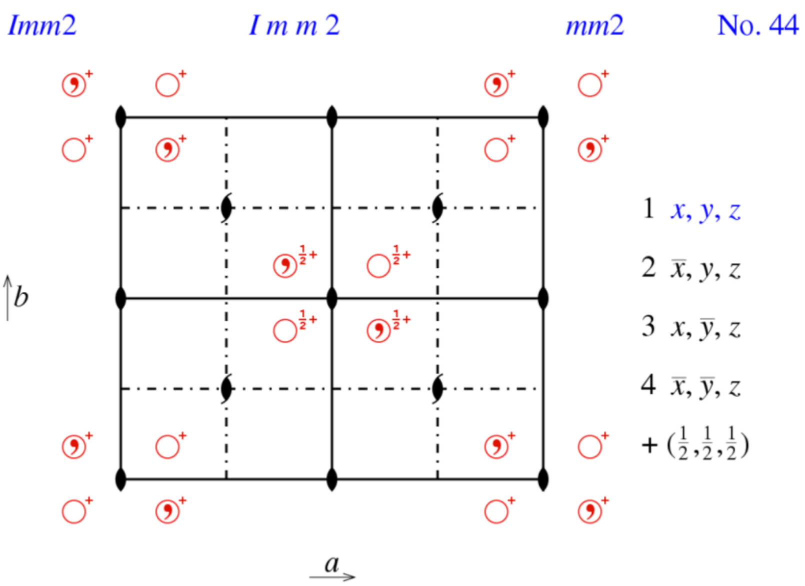
Question 5　　　　　　　　　　　　　　　　　　　　　　　　　(100 marks)

a)　Draw a rough sketch of a 1-2 Shell and Tube heat exchanger.
(10 marks)

b)　A parallel flow heat exchanger has a hot stream entering at 95°C and leaving at 81°C. The cold stream enters at 37°C and leaves at 64°C. The flow rate of the hot stream is 4.52kg/s. Both streams are water (shc=4180J/kg/°C) in liquid phase.

(i) Show that the flow rate of the cold stream is 2.34kg/s　(10 marks)
(ii) Show that the LMTD for this process is 33.4°C.　(10 marks)
(iii) Show that the heat flow between the hot and cold streams is 265kW　(10 marks)
(iv) Calculate the UA value of the heat exchanger.　(10 marks)

c)　The diagram below shows the orthorhombic space group, Imm2



(i)　What does orthorhombic mean in terms of the length of the three sides, a, b, c, and the angles between them, α, ß, and γ?
(10 marks)
(ii)　Is this space group Primitive, Face Centred, Body Centred, or Base Centred?　(5 marks)
(iii)　What does **mm2** mean in the space group title?　(10 marks)
(iv)　Is there a centre of symmetry in the cell? Justify your answer.
(5 marks)
(v)　What is the multiplicity of the general position, (x, y, z), for the space group?　(10 marks)

(vi)　What kind of symmetry is denoted by the symbol in the diagram above?　(5 marks)
(vii)　What kind of symmetry is denoted by the symbol in the diagram above?　(5 marks)

Question 6 (100 marks)

a) Draw a labelled diagram of a distillation column showing the following features:
   (i) the location of the feed stream (3 marks)
   (ii) the position of the reflux drum (3 marks)
   (iii) the location of the reboiler (3 marks)
   (iv) the location of the condenser (3 marks)
   (v) indicate on the diagram the temperature profile up the column (4 marks)
   (vi) indicate on the diagram the pressure profile up the column (4 marks)

b) Three problems that may arise with inappropriately designed distillation columns are:
   (i) flooding
   (ii) weeping
   (iii) entrainment
   Explain what is meant by each of these terms and how each effects distillation column performance (15 marks)

c) The feed stream to a distillation column has a flow rate of 138kmol/hr and a composition of 51% benzene. The top composition is 82% benzene and the bottom composition is 12% benzene. Calculate the flow rate in kmol/hr of the bottom stream. (15 marks)

d) The Bragg Equation gives the conditions for coherent scattering of x-rays from a crystal lattice, It is written as: $n\lambda = 2d \sin \theta$. Explain the different terms in this equation. (5 marks)

e) CuKα radiation ($\lambda = 0.154051$nm) is incident on a powder crystal sample. It produces a first order diffraction peak at $2\Theta = 18.2°$. What is the corresponding interplanar spacing, d? (15 marks)

f) A cubic lattice has a lattice parameter of 3.29nm. What is the interplanar spacing, d, in nm of the (hkl) = (3 2 1) planes? (15 marks)

g) X-ray diffraction on a cubic crystal reveals peaks at (4 2 4), (0 1 5), (5 5 0), and (4 1 1). There are no peaks observed at (4 1 0) or (5 1 1). What type of Bravais lattice is this? (15 marks)

LIST OF FORMULAE

$$t = \frac{-1}{k \ln(1 - x_A)}$$

$\tau_R = 1/kC_{A0}$

$\tau_R = 1 + a/kC_{A0}$ where $a = V_A / V_B$

$$Re = \frac{\rho v D}{\mu}$$

$$Re = \frac{\rho N D^2}{\mu}$$

$P = P_0 N^3 D_A^5 \rho$

$\varepsilon_{mean} = P / V\rho$

$Re_c = 6370 / P_0^{1/3}$

$P_0^{1/3}$ Re Fo = 5.2

$$Fo = \frac{\mu t_{95}}{\rho T^2}$$

The lifetime of an Eddy is τ_K:

$$\tau_K = 12[\upsilon / \varepsilon]^{1/2}$$

where $\upsilon = \mu / \rho$ (kinematic viscosity)

Engulfment Rate E = $\ln 2 / \tau_K$

$\tau_E = 1/E$

$$C_2 = C_2 \left(\frac{S_2}{S_1}\right)^n$$

C_2 = capital cost of project with capacity S_2
C_1 = capital cost of project with capacity S_1

$$D = \frac{C}{10 \ x \ V}$$

D = depreciation in €/kg
C = capital cost in €
V = production volume in kg/year
10 is the plant life

$Q_r = V(-\Delta H_r)k_0 C_A \exp(-E_A/RT)$

$Q_c = UA(T-T_a)$

$MTSR = T_p + \Delta T_{ad}$

$\Delta T_{ad} = \Delta H.n / m.C_p$

$TMR_{ad} = C_p RT^2 / q_0 E_A$

$$\text{Oxygen balance} = \frac{-[1600(2a + b/2 - c)]}{\text{Mol. Wgt.}}$$

$q = mc\Delta T$

$q = UA\ LMTD$

$$LMTD = \frac{\Delta T_L - \Delta T_R}{\log_e(\Delta T_L / \Delta T_R)}$$

Molar mass CO_2 = 44g/mol

Molar Mass Air = 29g/mol

$n\lambda = 2d \sin\theta$

$$d = \frac{a}{\sqrt{h^2 + k^2 + l^2}}$$

$$\frac{1}{d^2} = \frac{h^2}{a^2} + \frac{k^2}{b^2} + \frac{l^2}{c^2}$$

$\lambda_{Cu\,K_\alpha}$ = 0.154051nm

$$\alpha_{AB} = \frac{y_A / x_A}{y_B / x_B}$$

q = liquid fraction

$$slope = \frac{-q}{1-q}$$

q-line goes between (x_F, y_F) and (0,x_F/(1-q))

rectifying line between (x_D, y_D) and (0,x_D/(R+1))

F = D + B

F x_F = Dx_D + B