UNIVERSITY COLLEGE LONDON

University of London

EXAMINATION FOR INTERNAL STUDENTS

For The Following Qualifications:-

B.Eng. *B.Sc.* *M.Eng.*

Biochemical Eng E141: Biochemical Reactor Engineering

COURSE CODE	:	**BENGE141**
UNIT VALUE	:	**0.50**
DATE	:	**15-MAY-06**
TIME	:	**10.00**
TIME ALLOWED	:	**3 Hours**

TURN OVER

Answer FOUR QUESTIONS. **Only the first four answers given will be marked.**
ALL questions carry a total of 25 MARKS each, distributed as shown []

1.

a) A fermentation process for a technical enzyme should be transferred from the pilot plant to production using a constant k_La as scale-up criterion.

i) Explain briefly why a constant k_La is often used for scale-up and describe the factors that have an influence on the k_La correlation. [8]

ii) Derive the agitation rate for a 50 m^3 (total volume) production reactor with 80% fill volume using a k_La value of 650 h^{-1} and given that the maximum air flow rate is 0.75 vvm (based on liquid volume). The vessel has an aspect ratio of 3:1 and is equipped with 3 Rushton turbines (Power number/turbine = 5.7). The tank to impeller diameter ratio is 3:1. The broth has a density of 1050 kg m^{-3} and a viscosity of 0.03 Ns m^{-2}. [12]

k_La correlation: $k_La = 0.026 (P_g/V)^{0.4} (v_s)^{0.5}$

iii) If we reduce the superficial gas velocity (v_s) of x m s^{-1} to x/4 m s^{-1} in the production reactor, we find that the k_La value is reduced by 50%. Determine if the medium in the vessel is coalescent or non-coalescent (assume all other parameters remain constant). [5]

2.

a) What are the three main methods of achieving sterilisation and briefly describe how each of those is used to sterilise process equipment and material. [6]

b) A fermentation production plant employs a continuous steriliser to supply medium at a rate of 10 m^3 h^{-1} and is operated at 130°C. Given that the medium contains spores at a concentration of 6×10^6 per mL, the death rate constant k at 130°C is 17.524 min^{-1} and a contamination risk of 1 organism surviving every 50 days of operation is considered acceptable, calculate for this process: [10]

i) The total Del factor
ii) The holding pipe residence time
iii) The length of the holding pipe given that the internal diameter is 80 mm

c) Estimate for the continuous steriliser in part (b) the heating and cooling loads given that a heat recovery system is used to preheat the fresh medium from 20°C to 80°C and the sterilised medium is cooled down by heat exchange with water to an operating temperature of 30°C. The medium has a density of 1030 kg m^{-3} and a heat capacity of 4.2 kJ kg^{-1} K^{-1}. [9]

Clearly state any assumptions made.

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3.

a) Describe the correlation between Power number and Reynolds number for impellers in a stirred-tank bioreactor and how it can be used to estimate the ungassed power requirement, P_{ug}. [7]

b) Briefly comment on how the design of the vessel and the agitation system will influence the ungassed power requirements. [5]

c) A 500L (total volume) stirred-tank bioreactor, fitted with two Rushton turbine impellers, is to be used for the aerobic culture of *E. coli* (broth density and viscosity are 1010 kg m^{-3} and 0.03 Ns m^{-2} respectively). Each impeller has a diameter, d_i, of 0.2 m and the typical agitation rate, N, for the vessel is 500 rpm. The broth is aerated at a rate of 0.75 vvm (based on liquid volume) and it has been shown that the Michael-Miller correlation is suitable for relating the gassed power requirement, P_g, to P_{ug}, the volumetric gas flow rate, Q, and the agitation conditions:

$$P_g = 0.72\left[\frac{P_{ug}^2 N d_i^3}{Q^{0.56}}\right]^{0.45}$$

Using the above information estimate the value of P_g clearly stating any assumptions made. [13]

4.

a) You want to operate a batch fermentation using a recombinant strain of *E. coli* in a 2500 L fermenter (2000 L working volume). The target biomass concentration is 16.5 g (dry cell weight) L^{-1}. Given the information below calculate the minimum quantity of substrate (glucose) required. Clearly state any assumptions made.

Biomass composition	=	$CH_{1.79}O_{0.5}N_{0.2}$
Nitrogen source	=	NH_4OH
Ash content	=	7.2% w/w
Yield of biomass on oxygen	=	1.53 g (O_2) g (dry cell weight)$^{-1}$

[20]

b) Briefly explain how the stoichiometric mass balance would alter if the *E. coli* strain above synthesised a therapeutic protein and this was the target product. [5]

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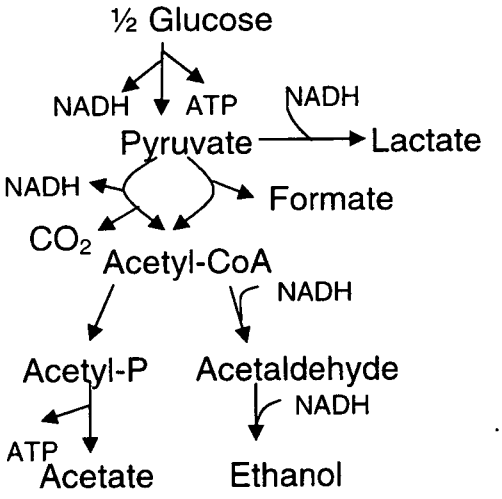
5.

a) Flux balance analysis (FBA) is a method used to aid the engineering of metabolic pathways. Briefly explain the principle and key steps of FBA and discuss the outcomes and limitations of the analysis. [10]

b) The figure below shows the heterofermentative metabolism of lactic acid bacteria. Set up a simple stoichiometric model in matrix notation and derive the balance equations for the reactions of all intracellular metabolites. [15]



6.

a) List 5 key practical requirements of an on-line temperature sensor and briefly discuss its impact on fermentation monitoring and control. [15]

b) Define P control and PI control and briefly discuss their features. [10]

7.

a) An animal cell culture is grown in a 150 L (working volume) bioreactor containing 2 marine impellers. The impeller has a diameter of 20 cm and the stirrer speed is set at 200 rpm. The cell culture broth has a viscosity of 0.001 Pa s and density of 1010 kg m^{-3}. Estimate the microscale of turbulence in the impeller region of the reactor assuming that the power number is constant and can be approximated to 0.5 per impeller and the gassed power is ca. 50% of the ungassed power. Comment on the results obtained and clearly state any assumptions that you made. [13]

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b) Discuss the major features of the design and operation of industrial scale mammalian cell bioreactors. Include in the discussion, the distinguishing features from microbial bioreactors, the two main operational modes used in industry and the challenges concerning their optimisation. [12]

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