UNIVERSITY COLLEGE LONDON

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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	:	**20-MAY-02**
TIME	:	**14.30**
TIME ALLOWED	:	**3 hours**

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UNIVERSITY OF LONDON

Biochemical Engineering

E141

Answer ***FOUR QUESTIONS***
ALL *questions carry a total of* ***25 MARKS*** *each, distributed as shown* [ ]

1. a) In process scale-down, regime analysis is often used. Describe the purpose of the regime analysis and the four steps in its application to scale-down. [5]

b) A regime analysis of a batch process that produces a viscous compound was performed. The viscous product changes a variety of characteristic times as shown in the table below. Comment on the rate limiting regime(s) at the various time intervals shown and whether or not gradients will be established in the reactor. [15]

Batch time (h)	Mixing time = t_m (s)	Oxygen consumption time = t_{OC} (s)	Oxygen transfer time = t_{OT} (s)
0	10	380	1
20	10	340	3.0
40	18	260	6.5
60	26	114	11
80	65	60	22
100	100	15	68

c) Explain the use of a two-compartment model system in scale-down experiments and describe the set-up with the help of a diagram. [5]

2. a) A fermentation process for an antibiotic is to 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 operating conditions for a 150 m^3 (total volume) production reactor with 80% fill volume using a k_La value of 550 h^{-1} and given that the maximum air flow rate is 0.5 vvm. 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 0.02 Ns m^{-2}. [12]

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

b) A regime analysis for a fermentation process in a given reactor was carried out. The characteristic times for liquid mixing (t_m), oxygen transfer (t_{OT}), oxygen consumption (t_{OC}), circulation time (t_C) are 10 s, 11 s, 50 s, 2.5 s respectively. Is this reactor performance governed by a pure or mixed regime and is oxygen limiting? [5]

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3. a) Explain the mechanism by which extensive mixing in mechanically agitated bioreactors can cause shear damage to microorganisms and describe the types for organisms that are most affected. [10]

b) A 5L-stirred tank reactor (70% working volume) is used for the production of a growth hormone by recombinant CHO cells on microcarrier beads with a diameter of 120 μm. The cell culture is agitated using a paddle impeller with a 6 cm diameter and the stirrer speed is set at 120 rpm. Air and carbon dioxide are supplied by flow through the reactor headspace. The microcarrier suspension has a density of ca. 1010 kg m^{-3} and a viscosity of 1.3 10^{-3} Pa s.

i) Estimate the Reynolds number and comment on the type of flow in the reactor. [3]

ii) Calculate the average energy dissipation in the reactor assuming that the power number is constant and can be approximated to 2. [5]

iii) Estimate the microscale of turbulence in the impeller region of the reactor and comment on the value obtained. Clearly state any assumptions you made. [7]

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4. a) The destruction of microorganisms by steam is described as a first-order chemical reaction. The equation is as follows:

$$N_t/N_0 = e^{-kt}$$

Where N_0 is the number of viable organisms present at the start of the sterilisation, N_t the number of viable organisms present after a treatment period of time, t, k is the reaction rate constant or specific death rate

Derive the following relationship that relates the Del factor (∇) to the Arrhenius constant (A) and the activation energy (E).

$$\nabla = A\, t\, e^{-(E/RT)}$$

where R is the gas constant and T is the absolute temperature. [5]

b) A fermentation process requires 100 m^3 batches of complex medium to be steam sterilised at 120°C. Assuming:

1. the medium before sterilisation contains $5x10^6$ bacterial spores mL^{-1};
2. the rate of sterilisation below 100°C is insignificant;
3. a probability of non-sterility after sterilisation is 1 in 1000;
4. the amount of sterilisation (∇) during heating from 100°C to 120°C is 10;
5. The death rate constant k at 120°C is 1.8 min^{-1};

i) Calculate the holding time at 120 °C if the rate of heating from 100 °C to 120°C is 1.5°C min^{-1} and the rate of cooling from 120°C to 100°C is 2.5°C min^{-1}. [10]

ii) Justify the use of assumptions (2) and (3) in these calculations and the assumption that the temperature rise and fall between 100°C and 120°C is linear. [10]

5. a) Produce a table to list the main differences between microbial and mammalian cells, which affects their capacity for bioprocessing. [5]

b) Describe the types of protein products made by mammalian cell culture systems and the features of these products that mean they can only be made in mammalian cell systems? [3]

c) Compare and contrast systems used for growth of attached cells and suspension cells. [5]

d) 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 remaining in their optimisation. [12]

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6. a) Briefly outline the design and operating characteristics of two types of impellers used in industrial fermentation processes. [6]

b) You have been asked to design a 500 L pilot scale stirred-tank fermenter to be fitted with a mixed impeller system. This comprises of a Rushton turbine impeller (N_P = 5.7) and a Lightnin A315 up-pumping impeller (N_P = 2.5). Specify the dimensions of the vessel and the size and location of each impeller. Clearly state, and justify, any assumptions made. [11]

c) Your vessel is to be used for the cultivation of a filamentous microorganism that attains a maximum broth viscosity of 0.03 Ns m^{-2}. If the maximum impeller speed to be used is 500 rpm specify the size of the motor required. Clearly state any assumptions made. [8]

7. a) This question concerns oxygen transfer in an aerated stirred-tank fermenter. Derive an expression relating the overall oxygen transfer rate to the oxygen mass transfer coefficient, k_La, the dissolved oxygen tension, DOT, and the saturation concentration of oxygen, C^*, at the inlet and outlet of the vessel. Clearly state any assumptions made. [12]

b) A pilot scale penicillin fermentation is to be evaluated in a 5 m^3 vessel (unaerated liquid height = 2.8 m). Previous studies have shown that the culture has a maximum oxygen uptake rate of 60 mmol O_2 L^{-1} h^{-1} and that the maximum k_La of the vessel is 300 h^{-1}. If the concentration of oxygen in the exit gas is 16% v/v estimate the minimum DOT of the culture. Clearly state any assumptions made. [13]

You may assume a value of the Henry's Law constant as 28.9 atm m^3 kg^{-1} (1 atm is equivalent to $1x10^5$ Pa).

END OF PAPER