UNIVERSITY COLLEGE LONDON

University of London

EXAMINATION FOR INTERNAL STUDENTS

For The Following Qualification:-

M.Sc.

Bioprocessing G2: Fermentation

COURSE CODE	:	**BENGEG02**
DATE	:	**15-MAY-06**
TIME	:	**10.00**
TIME ALLOWED	:	**3 Hours**

TURN OVER

Answer 4 questions, at least one from each section. Any extra answers will not be marked. Marks distributed as shown [ ]

SECTION A

1.

This question concerns the design of a facility for the industrial production of the antibiotic oxytetracycline by *Streptomyces rimosus*.

(a) Discuss the factors influencing the total installed fermentation capacity and in particular the trade-off between single and multiple vessels. [8]

(b) If the cultures are to be performed in stirred-tank bioreactors discuss the factors influencing the choice of vessel aspect ratio. [7]

(c) Each bioreactor is to have a total volume of $20m^3$. The cultures are to be operated in a fed-batch mode that results in a 50% v/v increase in initial broth volume. Specify the design of the tank including its dimensions and the number, type and locations of impellers. Clearly state, and justify, any assumptions made. [10]

2.

(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) Describe the influence of aeration on the gassed power requirement, P_g, and how the ratio of P_g/P_{ug} varies as a function of Aeration number. [7]

(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 of 0.2 m and the typical agitation rate for the vessel is 500 rpm. If the broth is aerated at a rate of 0.75 vvm estimate the gassed power requirement, P_g, clearly stating any assumptions made. [11]

PLEASE TURN OVER

3.

(a) Outline the stages involved in the transport of oxygen from a gas bubble to the site of utilisation within the cell and how the cellular requirements for oxygen vary during the time course of an aerobic batch fermentation process. [12]

(b) The culture of an aerobic microorganism is to be performed in a $6m^3$, total volume, stirred-tank bioreactor. Under typical operating conditions the vessel has an overall oxygen mass transfer coefficient of 450 h^{-1} when aerated at 0.9 vvm. If the maximum oxygen uptake rate of the culture is 65 mmol O_2 L^{-1} h^{-1} estimate the minimum dissolved oxygen tension (DOT). Clearly state, and justify, any assumptions made.

The value of the Henry's Law constant under the conditions of operation may be taken as 28.9 atm m^3 kg^{-1} (1 atm is equivalent to $1x10^5$ Pa). [13]

4.

You are involved in the scale-up of a fermentation process from 20L to 2 m^3 using a filamentous fungus to produce a recombinant protein. Both bioreactors have an aspect ratio of 3:1 and are equipped with 3 Rushton turbines with a tank to impeller diameter ratio of 3:1. The stirrer speed in the 20L reactor is set at 500 rpm and the air flow rate is 0.8 vvm. The culture broth has an average density of 1050 kg m^{-3} and a viscosity of 0.003 Pa s.

(a) Calculate the microscale of turbulence in the impeller region of the 20L stirred tank reactor operated with 70% working volume. The gassed power can be assumed to be ca. 50% of the ungassed power input. [10]

(b) Estimate the effect of scale-up on cellular damage if tip speed is used as scale-up criterion and comment on the results obtained. [15]

Clearly state any assumptions made and comment on their validity.

CONTINUED

5.

A scale-down approach is being used to optimise a continuous production process. In order to do this you have conducted a regime analysis of the production scale process.

(a) Describe the purpose of the regime analysis and the four steps in its application to scale-down. [5]

(b) Given the data below determine what mechanism of the process is rate limiting and suggest what experiments might be conducted on the laboratory scale. [15]

K_La	0.04 s^{-1}
r_{O2}^{max}	0.1% of C_{O2}^{*} s^{-1} (r_{O2}^{max} = max. O_2 uptake rate)
C_{O2}	10% of C_{O2}^{*} (C_{O2}^{*} = saturation conc. of O_2)
K_{O2}	0.01% of C_{O2}^{*} (K_{O2} = O_2 saturation constant of the organism being used)
$C_{s,0}$	1 mol m^{-3} ($C_{s,0}$ = input substrate conc.)
K_s	10 mmol m^{-3} (K_s = substrate saturation constant)
r_s^{max}	0.001 mol m^{-3} s^{-1} (r_s^{max} = max. substrate consumption rate)
D	1 h^{-1} (D = dilution rate)

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

SECTION B

6.

This question concerns the different forms in which a biocatalyst can be applied in industrial processes.

(a) Describe each of the different forms in which a biocatalyst can be used to carry out industrial chemistry / pharmaceutical manufacture. [10]

(b) Outline the considerations required to implement and scale-up a whole cell based process for industrial chemistry/pharmaceutical manufacture. [15]

PLEASE TURN OVER

7.

(a) Mammalian cells require a complex growth medium.

i) What are the functions of the growth medium for cell cultivation? [2]

ii) Describe the function of animal serum in the growth medium and discuss its advantages and disadvantages. [7]

(b) Describe the types of products made by mammalian cells taking into account the features of these products that mean they can only be made in mammalian cell systems. [4]

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

END OF PAPER