UNIVERSITY COLLEGE LONDON

University of London

EXAMINATION FOR INTERNAL STUDENTS

For The Following Qualification:-

M.Sc.

Biochem Eng G22: Advanced Bioreactor Engineering

COURSE CODE	:	**BENGEG22**
DATE	:	**09-MAY-05**
TIME	:	**10.00**
TIME ALLOWED	:	**3 Hours**

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

SECTION A

1.

An anaerobic batch fermentation of *Thermoanaerobacter ethanolicus* has been carried out under a controlled pH of 7.0. The following data for biomass (X), glucose (G) and lactate (LA) were obtained during the course of the fermentation.

Time [h]	**Biomass [g L^{-1}]**	**Glucose [g L^{-1}]**	**Lactate [g L^{-1}]**
0	0.01	19.50	0.45
13	0.41	16.88	3.88
14	0.54	14.85	4.94
16	0.92	13.11	6.98
18	0.99	10.40	8.98
19	1.05	8.91	10.30
20	1.15	7.75	10.83
22	1.30	5.18	12.57
24	1.35	3.64	14.58
37	0.69	0.25	16.03

(a) Using appropriate graphs calculate the maximum specific growth rate as well as the growth yield of biomass on glucose ($Y_{X/G}$) and the product yield of lactate on glucose ($Y_{LA/G}$). [15]

(b) Estimate approximate values for the specific uptake rate of glucose and the specific lactate production rate. [7]

(c) Briefly describe the product formation kinetics of lactate. [3]

Three sheets of graph paper are supplied.

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2.

(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 is the number of viable organisms present after a period of time, t, and k is the reaction rate constant or specific death rate constant. 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 ideal gas constant and T is the absolute temperature. [5]

(b) A fermentation process requires 50 m^3 batches of complex medium to be steam sterilised at 121°C. Assuming:

(1) the medium before sterilisation contains $8x10^6$ bacterial spores mL^{-1}
(2) the rate of sterilisation below 100°C is insignificant
(3) the probability of contamination is 1 in 1000
(4) the Del factor for 121°C is 12.55
(5) the death rate constant at 121°C is 2.54 min^{-1}

Calculate the holding time if the rate of heating from 100°C to 121°C is 1.5°C min^{-1} and the rate of cooling from 121°C to 100°C is 3°C min^{-1}. [8]

(c) Justify the use of assumptions (2) and (3) in the above calculations. [5]

(d) Discuss the advantages and disadvantages of a continuous sterilisation process as compared to batch sterilisation. [7]

3.

(a) Outline the various techniques used for the quantification of liquid phase mixing phenomena in stirred-tank fermenters and how mixing times are influenced by fermenter geometry and operation. [13]

(b) By reference to specific examples demonstrate how poor liquid mixing can lead to reduced volumetric productivities in industrial fermentation processes. [12]

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4.

(a) In large scale fermenters the driving force for oxygen transfer will vary as a function of height. Derive an expression showing how the overall oxygen transfer rate of a vessel is related to the oxygen mass transfer coefficient, k_La, the local dissolved oxygen tension, DOT, and the saturation concentration of oxygen in the broth, C^*, at the inlet and outlet of the vessel. Clearly state any assumptions made. [12]

(b) A pilot scale process for the growth of a strictly aerobic *Bacillus sp* is to be operated in a 6 m^3 vessel (unaerated liquid height = 3.2m). Laboratory studies have indicated that the culture has a maximum oxygen uptake rate of 65 mmol O_2 L^{-1} h^{-1} and it is calculated that the maximum k_La of the pilot vessel is 310 h^{-1}. If the concentration of oxygen in the exit gas is 16% v/v estimate the minimum DOT of the culture and comment on the significance of the value obtained. 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).

5.

(a) You have been charged with the design of a 15 m^3 stirred tank fermenter to be used for the production of an intracellular enzyme synthesised in *E. coli*. Clearly stating and justifying any assumptions made calculate:

- the dimensions of the tank
- the number, design and locations of your chosen impellers
- the unaerated and aerated liquid heights
- the number and diameter of any baffles fitted to the tank [14]

(b) Pilot scale fermentations have shown that the *E. coli* broth typically attains a viscosity of 0.015 Ns m^{-2} and a density of 1005 kg m^{-3}. If the maximum impeller speed to be used in the 15 m^3 tank designed in Part (a) is 450 rpm calculate the unaerated and aerated power requirements clearly stating any assumptions made. Specify also the power rating of the motor to be fitted to the fermenter. [11]

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SECTION B

6.

This question concerns the application of biocatalysis to industrial chemistry. Use examples to illustrate your answers and ensure you explain your answers in sufficient depth.

(a) What are the key features of the chemical market served by biocatalysis? [6]

(b) What types of reaction are most commonly assisted by biocatalysis? [6]

(c) What new reaction types might biocatalysis be used for in the future and what are the driving forces behind this? [6]

(d) What new techniques will enable the implementation of these new reaction types? [7]

7.

Write short notes on each of the following.

(a) The importance of cell banking in the context of mammalian cell culture for recombinant product synthesis. [5]

(b) Key features of stable expression of recombinant proteins from mammalian cells. [5]

(c) Key features of transient expression of recombinant proteins from mammalian cells. [5]

(d) Strategies to maximise throughput for antibody producing processes. [10]

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