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	:	**16-MAY-03**
TIME	:	**10.00**
TIME ALLOWED	:	**3 Hours**

TURN OVER

*Answer **FOUR QUESTIONS, AT LEAST ONE FORM 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.

a) A fermentation process is carried out in a chemostat culture using a single growth limiting substrate.

i) Derive an expression for a well-mixed single stage chemostat showing that the specific growth growth rate is equal to the dilution rate at steady state. [8]

ii) Calculate the steady-state growth limiting substrate concentration given that the input rate of medium is 0.8 L h^{-1} and the chemostat has a working volume of 1000 mL. It is assumed that cell growth can be described by the Monod equation and the organism has a substrate affinity constant of 5 mg L^{-1} and a maximum specific growth rate of 1.0 h^{-1}. [5]

iii) Explain what is meant by critical dilution rate with the help of a diagram. [5]

b) Industrial fermentations are often run in fed-batch mode. Briefly describe the various operating strategies of fed-batch fermentations in which feedback control might be used. [7]

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2.

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

b) A fermentation production plant employs a continuous steriliser to supply medium at a rate of 15 $m^3 h^{-1}$ and is operated at 135 °C. The medium contains spores at a concentration of 5×10^6 mL^{-1} and a contamination risk of 1 organism surviving every 50 days of operation is considered acceptable. Calculate for this process:

i) The specific death rate constant given that the activation energy is 283 kJ mol^{-1} and the Arrhenius constant is 1×10^{36} s^{-1}. The ideal gas constant is 8.314 J mol^{-1} K^{-1}. [2]

ii) The total Del factor and the holding pipe residence time. [4]

iii) The length of the holding pipe given that the internal diameter is 100 mm. [4]

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 28 °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.

You have been asked to evaluate a microbial fermentation process for the aerobic growth of yeast on glucose using ammonia as a nitrogen source. Laboratory scale fermentation data indicates that a final biomass concentration of 20 g_{DCW} L^{-1} can be achieved while analysis of the biomass composition indicates a molar C : H : O : N ratio of 1.0 : 1.7 : 0.5 : 0.2 and an ash content of 6% w/w.

As a basis for future scale-up calculate (on a mass basis) the yield of biomass on substrate, $Y_{X/S}$, and the yield of biomass on oxygen, $Y_{X/02}$. Clearly state any assumptions made. [25]

4.

a) You have been asked to design a 500 L pilot scale fermenter for the aerobic growth of a recombinant *E. coli*. This is to be fitted with two existing Rushton turbine impellers ($N_p = 5.7$) each having a blade width of 3 cm. Estimate the physical dimensions of the tank and specify the location of each impeller clearly stating any assumptions made. [15]

b) The correlations below are commonly used to estimate the gassed power requirements, P_g, in such stirred-tank fermenters:

$$P_g = 0.72\left[\frac{P_{ug}^2 N d_i^3}{Q^{0.56}}\right]^{0.45} \qquad \frac{P_g}{P_{ug}} = 0.1\left(\frac{Q}{NV}\right)^{-0.25}\left(\frac{N^2 d_i^4}{g W_i V^{2/3}}\right)^{-0.2}$$

where P_{ug}, is the ungassed power, Q is the volumetric gas flow rate, V is the volume of fermentation broth, N is the impeller rotational speed, d_i is the impeller diameter and W_i is the width of the impeller blade.

Using both correlations calculate P_g for the fermenter you designed in Part (a). You may assume that the fermenter is operated at an impeller speed of 500 rpm, an aeration rate of 0.75 vvm and that the density and viscosity of the fermentation broth are 1020 kg m^{-3} and 0.02 Ns m^{-2} respectively. Clearly state any further assumptions made in your calculations. [10]

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5.

a) You are involved in the scale-up of an aerobic microbial culture to a 5 m^3, total volume, stirred-tank production fermenter. Pilot scale data indicates that the culture has a maximum oxygen uptake rate (OUR) of 100 mmol O_2 L^{-1} h^{-1} and previous experience of the production vessel suggests that an overall oxygen mass transfer coefficient of 410 h^{-1} can be achieved. Estimate the minimum dissolved oxygen tension (DOT) of the culture and comment on the feasibility of the process. Clearly state any assumptions made. [17]

Data and equations:

The production fermenter is to be aerated at 0.8 vvm and operated with an overpressure of 0.4 atm.

The oxygen transfer rate is given by

$$OTR = k_L a \left[\frac{(1 - DOT)(C^*_{in} - C^*_{out})}{\ln\left(C^*_{in} / C^*_{out}\right)} \right]$$

where C^* is the saturation concentration of oxygen in the broth. 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).

b) Assuming that growth of the culture in the production fermenter is oxygen limited suggest a number of engineering solutions that might be implemented to overcome the problem. In each case outline the quantitative benefit that could be achieved. [8]

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SECTION B

6.

This question concerns the application of biocatalysis in synthetic organic chemistry.

a) Under what conditions is it favourable to use biocatalysis in industrial chemistry? [5]

b) What are the key limitations for the implementation of biocatalysis? [5]

c) Define the standard measures used to describe the productivity of a biocatalytic reaction. [5]

d) What numerical target should be the aim for these metrics to enable successful commercialisation of a given process? [5]

e) Describe the key reaction types used by biocatalysis, giving examples as appropriate. Why are these types of conversion favoured for biocatalysis rather than chemocatalysis? [5]

7.

a) Two categories of cells have been used in the manufacture of products in mammalian cell culture.

i) List these two cell types and describe the key characteristics of each. [6]

ii) Which cell type is most suitable for production of proteins at an industrial scale and why? [2]

b) Animal cells require a more complex growth medium than microbial cells.

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

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

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c) Describe the major events of the cell cycle. [3]

d) Draw a process flow diagram for the major steps in the downstream processing of a typical mammalian cell product, describing the role of each step. [5]

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