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 : **16-MAY-03**

TIME : **10.00**

TIME ALLOWED : **3 Hours**

03-C0108-3-80

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) 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. [20]

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 1×10^5 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. [5]

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2.

a) Define the various characteristic times used to describe liquid phase mixing in a batch stirred-tank fermenter. Outline an experimental procedure by which each might be determined. [13]

b) The correlations below are commonly used to estimate the gassed power requirements, P_g, in 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 speed, d_i is the impeller diameter and W_i is the width of the impeller blade.

Using both correlations calculate P_g for a 0.5 m^3 fermenter of standard geometry fitted with two Rushton turbine impellers (N_p = 5.7 if Re >$1x10^4$, W_i = 30mm). 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. [12]

3.

In a 7 litre bioreactor (75% working volume) a filamentous organism is grown aerobically at a stirrer speed of 1000 rpm. The vessel has an aspect ratio of 3:1 and is equipped with 3 Rushton turbines. The tank to impeller diameter ratio is 3:1. The density of the broth is 1015 kg m^{-3} and the viscosity is 0.001 Ns m^{-2}.

a) Estimate the overall energy dissipation in the bioreactor given that the power number is constant and can be approximated to 5.7 and that the gassed power is ca. 50% that of ungassed power. [8]

b) Explain why the use of a constant value for the power number might or might not be justified. [3]

c) Calculate the microscale of turbulence in the impeller region and bulk of the reactor and comment on the impact on the cells grown. [9]

d) Discuss briefly the implications of scale-up using constant tip speed on cell growth and oxygen transfer. [5]

Clearly state any assumptions made.

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4.

a) What are the three main methods of achieving sterilisation and briefly describe how each 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 15 $m^3 h^{-1}$ and is operated at 135 °C. The medium contains spores at a concentration of $5x10^6$ per mL 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 $1x10^{36}$ s^{-1}. The ideal gas constant is 8.314 J mol^{-1} K^{-1}. [3]

ii) The total Del factor and the holding pipe residence time. [5]

iii) The length of the holding pipe given that the internal diameter is 100mm. [5]

Clearly state any assumptions made.

c) Describe the design of a continuous steriliser with indirect heating with the help of a diagram. [6]

5. Optical biosensors can be used for measuring the concentration of antibodies.

a) List the key components of this instrument. [5]

b) Discuss briefly if the instrument can it be used on-line. [5]

c) Discuss the benefit and the potential problems of using an optical biosensor. [5]

d) Consider if the instrument can be used for monitoring and control the antibody production of a mammalian cell culture where the antibody is secreted from the cells. [5]

e) A first order filter has been used for data processing,

$$y_{filt}(t) = (1-\alpha)y(t) + \alpha y_{filt}(t-\Delta t),$$

where t is the sampling instant, Δt is the sampling interval, and $0 < \alpha < 1$. What is the implication of using a different value of α in the formula? [5]

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6.

Consider a biotransformation reactor in which the temperature has to be controlled at 20°C. A proportional controller is suggested for this system. Its transfer function is given as:

$$G(S) = \frac{1}{TS+1}$$

where T is the time constant at 10 minutes.

a) Draw a block diagram to show the closed-loop control system. [4]

b) Calculate the smallest controller gain K_p in order to achieve an accuracy of $\pm$ 0.5°C . [8]

c) Calculate the transient response to see if 2 minutes are enough for the temperature to reach the required accuracy of $\pm$ 0.5°C. [8]

d) Discuss the consequence if K_p is 50. [5]

Note:

$$L^{-1}[\frac{1}{s+a}] = e^{-at}$$

where L^{-1} is the inverse of the Laplace transformation.

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 type. [8]

ii) Which cell type is most suitable for production of proteins at an industrial scale and why? [3]

b) Animal cells require a complex growth medium.

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]

c) Describe the major events of the cell cycle. [5]

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