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	:	**09-MAY-05**
TIME	:	**10.00**
TIME ALLOWED	:	**3 Hours**

TURN OVER

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.

You are involved in the scale-up of a microbial filamentous fermentation from 20 L to 2 m^3. Both bioreactors have an aspect ratio of 3:1 and are equipped with 3 Rushton turbines (Power number: 5.7) with a tank to impeller diameter ratio of 3:1.

a) Estimate the microscale of turbulence in the impeller region and bulk of the 20 L reactor (70% working volume) given that the stirrer speed is 800 rpm and the airflow rate is 0.75 vvm. The density of the broth is 1020 kg m^{-3} and the viscosity is 0.003 Ns m^{-2}. [12]

b) Using tip speed as the scale up criterion evaluate the potential shear damage at the 2 m^3 (75% working volume) scale. [8]

c) Comment on the effect of scale up on cellular damage in the impeller region and bulk of the bioreactor. [5]

Clearly state any assumptions made.

2.

a) The inactivation 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, and 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 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 8×10^6 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}

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i) 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}. [10]

ii) Justify the use of assumption (2) and (3) in these calculations and the assumption that the temperature rise and fall between 100°C and 121°C is linear. [10]

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]

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, 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 = 3.2 m). 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).

PLEASE TURN OVER

5.

a) Describe briefly the key components of temperature sensors and the benefits of using these sensors for monitoring bioprocesses. [7]

b) Discuss the general challenges of using on-line biosensors for fermentation control. [8]

c) Describe briefly the features of a first order filter and discuss its advantages and disadvantages. [10]

6.

In order to develop a temperature control system for a 450 L batch fermentation of *E. coli*, a response test to the fermenter heating system is conducted. The results revealed that by changing the heating level, the temperature in the fermenter responds as a first order system with a time constant of 10 minutes. The desirable temperature for the fermentation is 30°C. The proposed control system is utilising a proportional controller with Kp = 15 and its block diagram is shown in Figure 1.

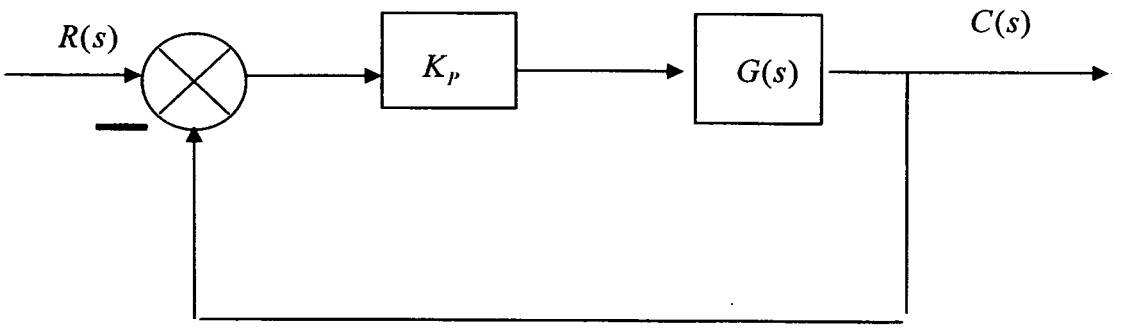

Figure 1. Closed System

a) Derive the transfer function for the closed system above. [5]

b) Derive the steady state error of the closed system. [5]

c) Derive the controller's transient response, u(t) and sketch the diagram. Comments on any issues of the system implementation. [10]

d) If alternatively the proportional controller is placed in the feedback loop as shown in Figure 2, do you think that the accuracy of the system at steady state can be improved? [5]

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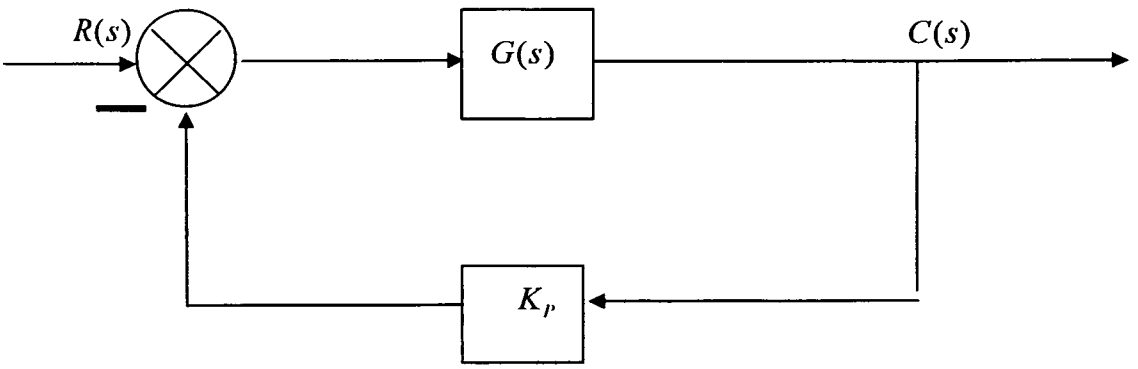

Figure 2. Alternative control System

7.

a) Discuss the use of microbial vs. mammalian cells for production of recombinant therapeutics. [10]

b) Briefly explain the current most popular manufacturing strategies for production of therapeutic antibodies by mammalian cells. [5]

c) Describe the sources of mammalian cells for tissue engineering applications and discuss the advantages and disadvantages associated with each cell source and the key processing challenges. [10]

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