BEL 413
Modelling and Simulation of Bioprocesses
Major Examination

Time :Two hour
Max. Marks: 40

Please attempt all the questions -

1. What do you understand by the term Model? Define structured and unstructured model. What are the assumptions with respect to cells in the unstructured model? What are the advantages and disadvantages of using an unstructured model? 5

2. Write short notes on
(a) Assumptions of Monod's model (b) Balanced growth(c) Discrete time model 3

3. If the specific growth rate (μ) is described by Monod's model ($\mu = \mu_m S/(S + K_S)$) (where μ_m = Maximum specific growth rate S = Substrate concentration and K_S = saturation constant) and Specific substrate consumption rate (q_s) is represented by $q_s = 1/Y (\mu) + m$ (where "Y" is the yield coefficient and "m" is maintenance coefficient), it leads to a conceptual problem, What is it? How it can be addressed? 5

4. What peculiar inhibitions (substrate or product) can be normally eliminated by the fed-batch cultivation? What are the main considerations (at least four) which need to be kept in mind for the design of the fed-batch cultivation? 1+2

5. Why are transients of continuous cultivation important? Briefly describe (with reasons) if the Monod Model can (or can't) describe the transient conditions arising out of "Shift up in the dilution rates" in continuous cultivation. 3

6. What do you understand by the **"Gateway sensor approach"** List & very briefly describe few Gateway sensor parameters used in the fermentation. 2

7. What are the specific assumptions in the model development for plant cell cultivation? Neem (*A. indica*) cells grow using Glucose, Nitrate & Phosphate as limiting nutrients. The growth is inhibited (not killed) by over addition of above substrates. The major nutrient (glucose) is consumed for the growth & maintenance of the cells, while the product azadirachtin is produced due to growth as well as non growth activities of the cell. Propose the mathematical model and extrapolate it for the fed-batch cultivation conditions. 3

8. Describe Physiological State Marker? Describe how RNA can be incorporated as Physiological State marker in the Mathematical model. What benefits will be achieved by incorporation of Physiological State Marker in the mathematical model

Demonstrate the procedure for incorporating the structural component RNA in the mathematical model for the following example.

Growth rate equation $\mu = Y\ Q\ G(S)$, where **Y** is the yield factor, **Q** is the metabolic activity functional and **G(S)** is some function of substrate concentration **(S)** For the calculation of **G(S)**, use the steady state kinetics and the following example. Sorbose fermentation is a typical fermentation process limited by sorbitol availability and inhibited by higher initial substrate concentration and accumulated product concentrations. μ for the growth becomes –

$$\mu = \mu_m \left(\frac{S}{S+K_s}\right)\left(1-\frac{S}{S_{max}}\right)^n \left(\frac{K_I}{K_I+P_t}\right)$$

Where μ = specific growth rate of microorganism with inhibitor (h^{-1}) μ_{max} = Maximum substrate concentration at zero inhibition (h^{-1}) S = Substrate concentration gL^{-1} S_{max} = Maximum substrate concentration at which there is no growth gL^{-1} . n = exponent. P_t = Product concentration gL^{-1} K_I = Product inhibition constant gL^{-1}

Assume $Q_0/Q_m = c$ and $\mu_m = Y\ Q_m$ and

$$Qa = (Q_m - Q_o)\ \mu/\mu_m \quad + \quad Q_o$$

Where Qa is the steady state value of Bottleneck substance 'Q' and Q_m and Q_o are the upper and lower limits of Qa. 5

9. Briefly describe (No mathematical treatment) how NADH (amount and rates) production can be established by using metabolic pathway rates by Reardon- Bailey procedure. 3

10. (a) Briefly describe the extracellular culture metabolism of *Clostridium acetobutylicum* at pH 4.5 and pH 6.0 Does it grow in aerobic or anaerobic conditions ? 2

(b) Name the products associated with the ATP production in the metabolism of *Clostridium aceotbutylicum* at pH 4.5 and pH 6.0 Define Y_{ATP} How does it changes during the cultivation of pH 4.5 ? 3

(c) Explain how the culture regenerates its NADH in the two phases of cultivation (at pH 4.5) 2

(b) Carbon dioxide and Hydrogen are produced as gaseous products during the cultivation of *C. acetobutylicum*. Describe the trend of H_2/CO_2 during the cultivation period of above microorganism at pH 4.5 1