U.S.N.										

B.M.S. College of Engineering, Bengaluru-560019

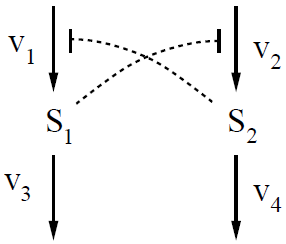
Autonomous Institute Affiliated to VTU

June 2025 Semester End Main Examinations

Programme: B.E. **Semester: VI**
Branch: BIOTECHNOLOGY **Duration: 3 hrs.**
Course Code: 23BT6PESYB / 22BT6PESYB **Max Marks: 100**
Course: SYSTEMS BIOLOGY

Instructions: 1. Answer any FIVE full questions, choosing one full question from each unit.
2. Missing data, if any, may be suitably assumed.

Important Note: Completing your answers, compulsorily draw diagonal cross lines on the remaining blank pages. Revealing of identification, appeal to evaluator will be treated as malpractice.

		UNIT - I	CO	PO	Marks
1	a)	Given a biochemical network in which each species allosterically inhibits the production of the other, formulate the model equations for species S1 and S2. Illustrate the dynamic behavior of the system as it approaches steady state. 	CO2	PO3	05
	b)	Evaluate the accuracy of the finite difference approach by approximating the absolute sensitivity coefficient using the given equation at the nominal value of V_{max} = 5 mM/min. Calculate approximations with $\Delta p_0 = 0.2$ (5% deviation) and $\Delta p_0 = 0.04$ (1% deviation). Data: V_0=4 mM/min and K_m=1.5. $$\frac{ds^{ss}}{dp} \approx \frac{s^{ss}(p_0 + \Delta p_0) - s^{ss}(p_1)}{\Delta p_0}$$	CO2	PO3	05
	c)	Demonstrate the dynamic model to design an engineered genetic toggle switch.	CO2	PO3	10
		OR			
2	a)	Demonstrate how a dynamic model can be used to investigate the origin of oscillations in the NF-κB signaling pathway that drives the expression of cellular response genes.	CO2	PO3	10
	b)	Consider the network $\xrightarrow{k_1} S_1 \xrightarrow{k_2} S_2 \xrightarrow{k_3}$ Suppose that the degradation rate k_3 = 4mM/min has been measured directly, and that observations are made in two conditions, but only the pooled concentration of S_1 and S_2 can be	CO2	PO 3	10

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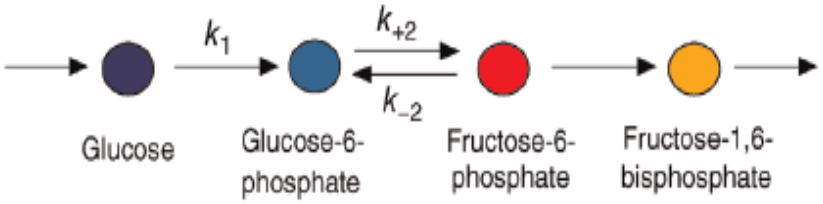
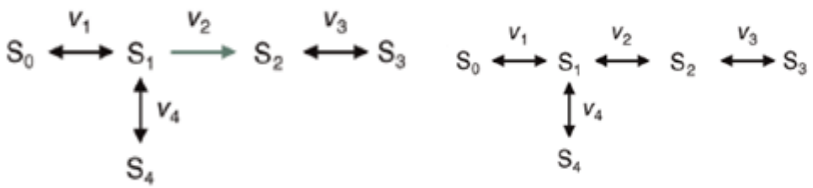
			measured. Perform a least square fit for the following two conditions. Compare and contrast between condition (i) and (ii) i. Suppose that in the control condition $S_1^{obs} + S_2^{obs} = 6$ mM , while in the experimental condition, the production rate k_1 has been reduced by 90% and the resulting observation is $S_1^{obs} + s_2^{obs} = 0.6$mM. ii. Suppose that in the control condition $S_1^{obs} + S_2^{obs} = 6$mM , while in the experimental condition, the production rate k_2 has been reduced by 90% and the resulting observation is $S_1^{obs} + S_2^{obs} = 18$mM.			
			UNIT - II			
	3	a)	Describe how different model reduction strategies can be applied to streamline a biochemical model, especially in the context of a branched metabolic or signaling pathway	***CO2***	***PO3***	**10**
		b)	Using a schematic representation, distinguish between identifiable and non-identifiable parameters in the context of parameter identifiability analysis based on maximum likelihood estimation. Highlight how identifiable parameters can be uniquely estimated from the data, whereas non-identifiable parameters lead to ambiguity due to insufficient or redundant information.	***CO2***	***PO3***	**10**
			OR			
	4	a)	Perform the quasi-steady state and quasi-equilibrium approximation for the following simple model of upper glycolysis  	***CO2***	***PO3***	**10**
		b)	Illustrate how the cross-validation technique can be applied to identify overfitting in a predictive model.	***CO2***	***PO3***	**10**
			UNIT - III			
	5	a)	Consider the following metabolic network reactions and answer the following: a. How many reactions are present in the network? b. Construct the stoichiometric matrix for the given reactions. c. Determine the elementary flux modes (or simply flux modes) involving metabolites i and ii. d. Identify all possible metabolic pathways or routes that the system can take based on the reactions. i. ii.  	***CO2***	***PO3***	**10**

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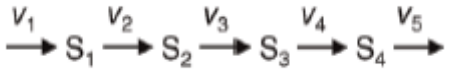
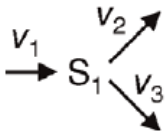
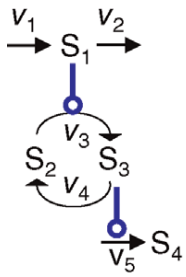
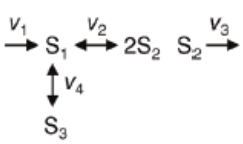
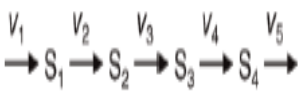
		b)	In pharmacokinetics, the decay of a drug in the body often follows first-order kinetics, where the rate of elimination is directly proportional to the drug concentration. Write a MATLAB code to represent first order kinetics of drug used to model drug elimination.	***CO2***	***PO3***	**05**
		c)	Write a MATLAB code to represent Michelis Menten Kinetics represented by the reaction S+E↔ ES↔ E+P for any Km and Vmax values.	***CO2***	***PO3***	**05**
			OR			
	6	a)	What is a flux cone? Determine the flux cone for the following on the basis of vectors of kernel matrix K. a) A higher dimensional system with r-Rank(N)=4 b) An unbranched reaction chain of arbitrary length  c) A metabolic network  d) Consider the metabolic network given in **c** and answer the following i. Compute the stochiometric matrix. ii. Formulate the ODE. iii. Compute the possible vectors of kernel matrix k.	***CO2***	***PO3***	**10**
		b)	Consider the following metabolic networks and answer the following for each network: a. Construct the stoichiometric matrix (N). b. Determine the number of reactions and compute the rank of the stoichiometric matrix (rank(N)). c. Formulate the corresponding ordinary differential equations (ODEs) for each stoichiometrically active (SA) metabolite. d. Compute the kernel matrix (K) and list its possible basis vectors i.  ii.  iii. 	***CO2***	***PO3***	**10**

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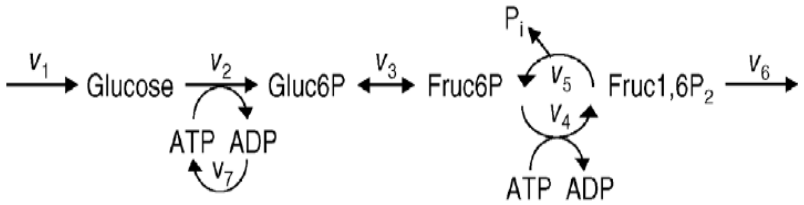
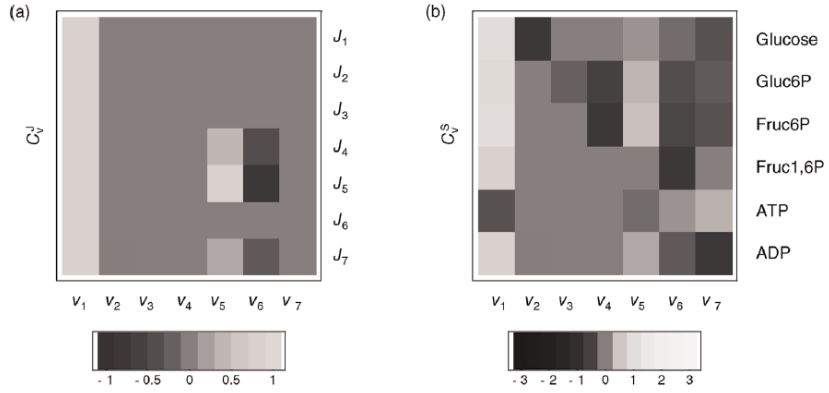
			UNIT - IV			
	7	a)	Design and demonstrate a state transition diagram to represent a given state of a species.	***CO3***	***PO1, 5***	**05**
		b)	Discuss the features of KEGG database.	***CO1***	***PO***	**05**
		c)	Discuss the major features of Cell Designer tool to build a model and COPASI tool for simulation and analysis for biochemical networks and their dynamics.	***CO3***	***PO1, 5***	**10**
			OR			
	8	a)	Design a SBGN diagram and develop a model in BIOPAX format for AKT pathway	***CO3***	***PO1, 5***	**10**
		b)	Discuss the features of Reactome database.	***CO3***	***PO1, 5***	**05**
		c)	Design and demonstrate an entity-relation diagram to represent the gene regulation and transcription of a gene.	***CO3***	***PO1, 5***	**05**
			UNIT - V			
	9	a)	Consider the following model for Upper Glycolysis and answer the following  a) Compute the stochiometric matrix. b) How many reactions are there and what is the rank(N)? c) Formulate the ordinary differential equations to develop system biology model. d) Plot the dynamic behavior of the model. e) Compute the possible vectors of kernel matrix K. Flux and concentration control coefficients for the above model are represented in grey scale. Analyze the following grey scale diagram and interpret the flux and concentration control coefficients for the upper glycolysis model.  	***CO4***	***PO2***	**10**

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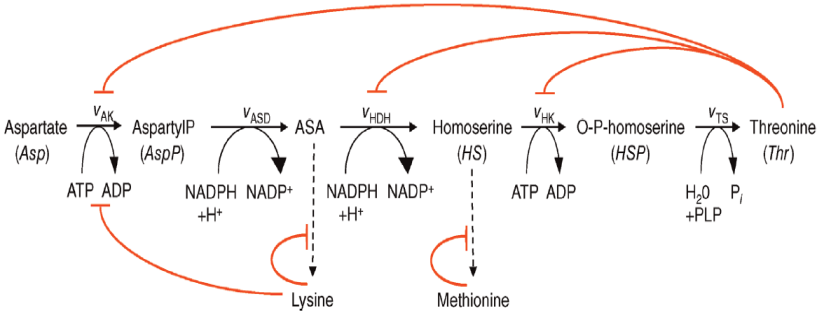
		b)	Illustrate the sequential steps involved in a signaling pathway cascade that begins with receptor activation by an external stimulus. Use a schematic diagram to explain how the signal is transmitted through intracellular components to elicit a specific cellular response.	***CO4***	***PO2***	**10**
			OR			
	10	a)	How can we mathematically model the Aspartate-derived Threonine biosynthesis pathway to study the flux regulation and feedback inhibition by lysine, methionine, and threonine? Derive the system of ordinary differential equations (ODEs) representing the dynamics of each metabolite in the pathway, and use appropriate kinetic expressions for enzyme-catalyzed reactions, including the feedback-inhibited rate law for AK I and III. 	***CO4***	***PO2***	**10**
		b)	Develop the signal transduction cascades for the following, accompanied by schematic diagrams: i. MAP kinase cascade. ii. The phosphorelay mechanism in the yeast HOG signaling pathway	***CO4***	***PO2***	**10**

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