CS CM 182 Homework 3

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I completed this written part of the homework, lab report, or exam entirely on my own.

Exercise 4.1 : Membrane Models

(a) **Bilipid membranes** are formed by **phospholipid molecules** arranging themselves into a double-layer sheet, with their **polar hydrophilic heads** interacting with the aqueous surrounding water while their **nonpolar, hydrophobic tails** within the membrane interior and protected from its aqueous environment. The heads are pointed outward to the cell while the tail points inward. The membranes are **semipermeable** because nonpolar interior provides no opportunity for hydrogen bonding, therefore large polar molecules cannot flow through. **Simple diffusion** only allows small nonpolar or polar molecules to pass through the semipermeable membrane such as **oxygen, carbon dioxide, nitrogen, nitric oxide**. We need **active transport** and **facilitated diffusion** to transport the larger molecules.

Most molecules transfers across membranes occur by diffusion such as movement from a region of higher to a region of lower concentration. **Diffusion** is driven by a gradient in concentration of solvent or solute. **Osmosis** is the passive mechanism for moving solvent molecules through a selectively permeable membrane into a region of higher solute concentration in order to equalize the solute concentration on both sides. **Passive diffusion** of biomolecules means passive flow freely down a concentration gradient. **Facilitated diffusion** involves energy-independent flow control down a concentration gradient, facilitated by protein-channel membrane-bound transport molecules. **Active transport** involves energy-dependent passage and flow control against a concentration gradient or other resistance to flow.

(b) Osmosis

- State variables : concentration of solvent on the membrane
- Parameters : volume of high solute side, volume of low solute side, membrane permeability for solvent

Diffusion

- State variables : concentration of solute on the membrane
- Parameters : volume of left side, volume of right side, membrane permeability for solute

Facilitated Diffusion

- State variables : concentration of solute on the membrane
- Parameters : volume of left side of membrane, volume of right side of membrane, the number of membrane-bounded transporter molecules, the binding and separating rate of membrane-bounded transporter molecules

Active Transport

- State variables : volume of left side of membrane, volume of right side of membrane, concentration of solute on membrane, the number of ATP molecules, the number of ADP molecules
- Parameters : ATP, ADP, enzyme, the number of membrane-bounded transporter molecules, the binding and separating rate of membrane-bounded transporter molecules,

Exercise 4.5 - Symbols for ATP Dynamics modeling

State variables :

1. S, it is a substrate and refer to ATP molecules
2. E, it is an enzyme that is responsible for getting rid of the phosphate group
3. ADP, the output for the ATP Dynamics modeling
4. P* , the phosphate group that is responsible to provide energy for other molecules

Parameters :

1. a and b in function $v_2 = (aS)/(b+S)$ which is a variable rate used for transforming substrates to product. It is converting ATP to ADP and P* at a rate of v_2 .

Exercise 4.7 - Physiologically-based Model State Variables and Parameters

Figure 4.36 - A physiologically-based (PB) model paradigm

Let **X** be the substances flow in the model paradigm, such as drug dose or biochemical molecules

State variables :

1. x_1 = Concentration of substances in arterial and venous component of the blood
2. x_2 = Concentration of substances in heart
3. x_3 = Concentration of substances in veins
4. x_4 = Concentration of substances in lungs
5. x_5 = Concentration of substances in liver
6. x_6 = Concentration of substances in brain
7. x_7 = Concentration of substances in kidneys
8. x_8 = Concentration of substances in blood veins and vessels

Parameters :

1. r_1 = blood flow rate of substances between arterial blood and heart
2. r_2 = blood flow rate of substances between arterial blood and brain
3. r_3 = blood flow rate of substances between arterial blood and lungs
4. r_4 = blood flow rate of substances between arterial blood and liver
5. r_5 = blood flow rate of substances between arterial blood and kidneys
6. r_6 = blood flow rate of substances between arterial blood and intestines

1. w_1 = blood flow rate of substances between venous blood and heart
2. w_2 = blood flow rate of substances between venous blood and brain
3. w_3 = blood flow rate of substances between venous blood and lungs
4. w_4 = blood flow rate of substances between venous blood and liver
5. w_5 = blood flow rate of substances between venous blood and kidneys
6. w_6 = blood flow rate of substances between venous blood and intestines

Figure 4.37 - **Organ-compartmental PB model of the detoxifying action of the liver on toxic substances entering the body through the skin from where they are absorbed into blood**

State variables :

1. The amount of toxins (grams) in plasma
2. The amount of toxins (grams) in liver

Variable :

1. Arterial transfer flux (variable function of masses)
2. Venous return flux (variable function of masses)
3. Metabolic degradation in the liver (variable function of masses)
4. Exogenous toxin influx from skin (input variable)

Parameters :

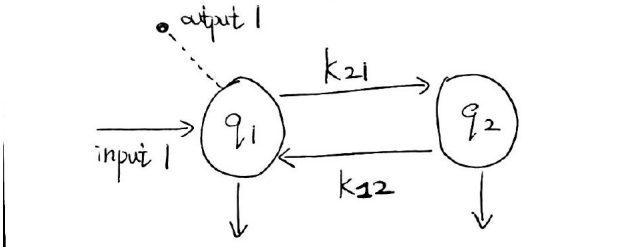
1. Constants in the model
2. Constants in the variables within this model

Exercise 5.1 : 2-compartment Model Candidate Experiment Designs

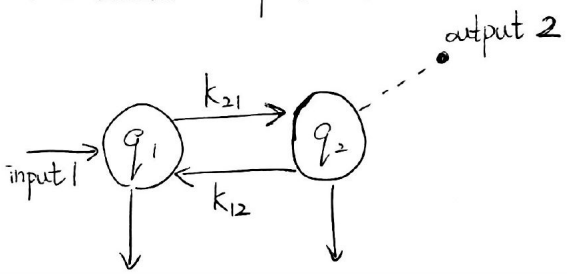
a)

E 5.1

a) The first compartmental model

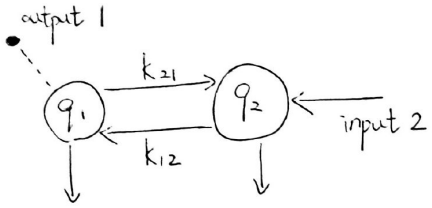


The second compartmental model

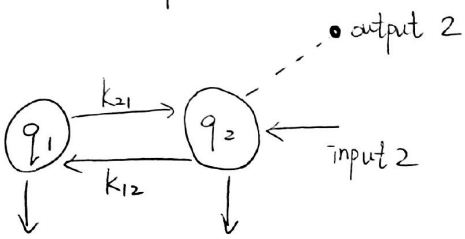


a) cont.

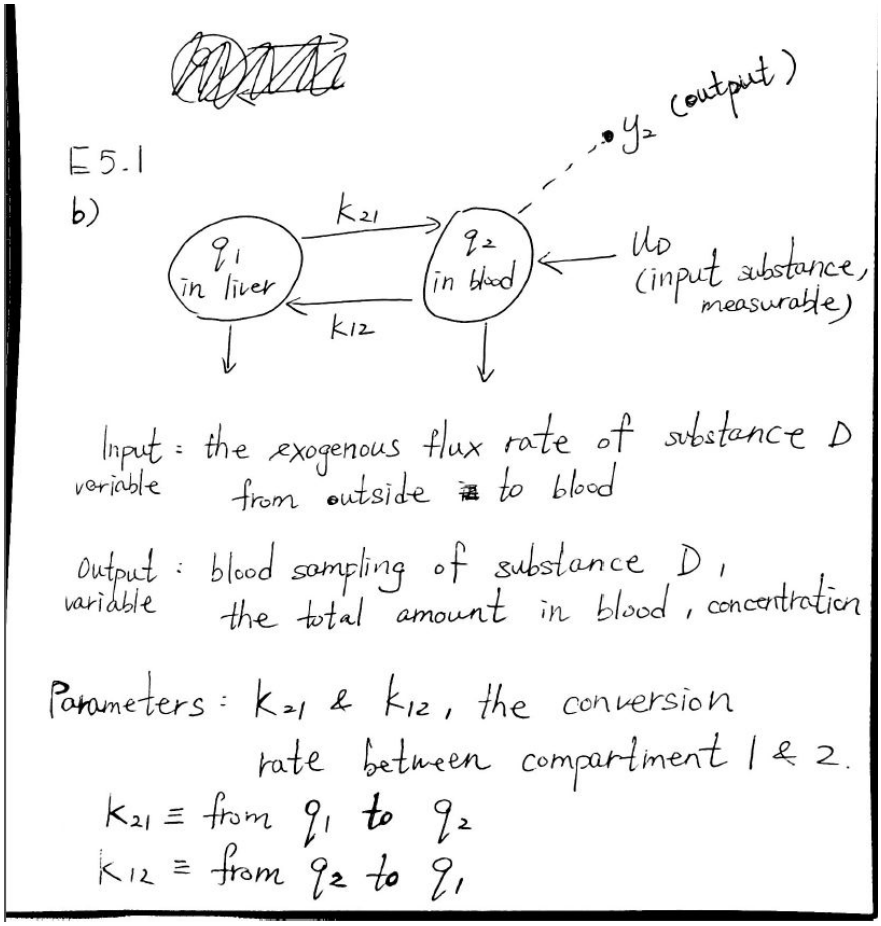
The third compartmental model



The fourth compartmental model



b)



c)

Both sampling from blood and liver are considered invasive diagnostic tests which requires medical instrumentation to enter the body. However, blood sampling is less invasive when compared with sampling from the liver. It is because liver sampling requires a larger scale of medical procedures and a longer recovery period for the patients.

Exercise 5.2 - Multi-organ model candidate experiment designs

a)

Single input ports (4) :

1. Through IV injection to the blood veins
2. Skin
3. Mouth
4. Airborn through nose

Single output ports (4):

1. Through IV sampling from blood stream
2. Urine
3. Faecal samples
4. Saliva

Total pair of single-input single-output = 4 * 4 = 16 pairs of (SISO) candidate experiment design models are feasible for I-O experiments conducted from the ports.

b)

The 16 combinations are listed as follow:

1. (IV, IV)
2. (IV, Urine)
3. (IV, Faecal samples)
4. (IV, Saliva)
5. (Skin, IV)
6. (Skin, Urine)
7. (Skin, Faecal samples)
8. (Skin, Saliva)
9. (Mouth, IV)
10. (Mouth, Urine)
11. (Mouth, Faecal samples)
12. (Mouth, Saliva)
13. (Airborn through nose, IV)
14. (Airborn through nose, Urine)
15. (Airborn through nose, Faecal samples)
16. (Airborn through nose, Saliva)

Exercise 5.6 - Complete model with discrete-time measurements

5.6 The complete model equations for this system experiment.

$z(t_1), z(t_2), z(t_3), \ldots, z(t_N)$ or

$z(t_i)$ for $i = 1, 2, \ldots, N$

General equations: $z(t) = y(t) + e(t)$,

$y(t) = q(t)/V$, $V > 0$,

$q(0) > 0$

Answers.

$z(t_1) = y_1(t) + e_1(t)$

$z(t_2) = y_2(t) + e_2(t)$

$\vdots$

$z(t_n) = y_n(t) + e_n(t)$

(y are the same, but varying with time

Exercise 5.7 - Quantifying the glycolysis pathway

a)

The essential features of the pathway :

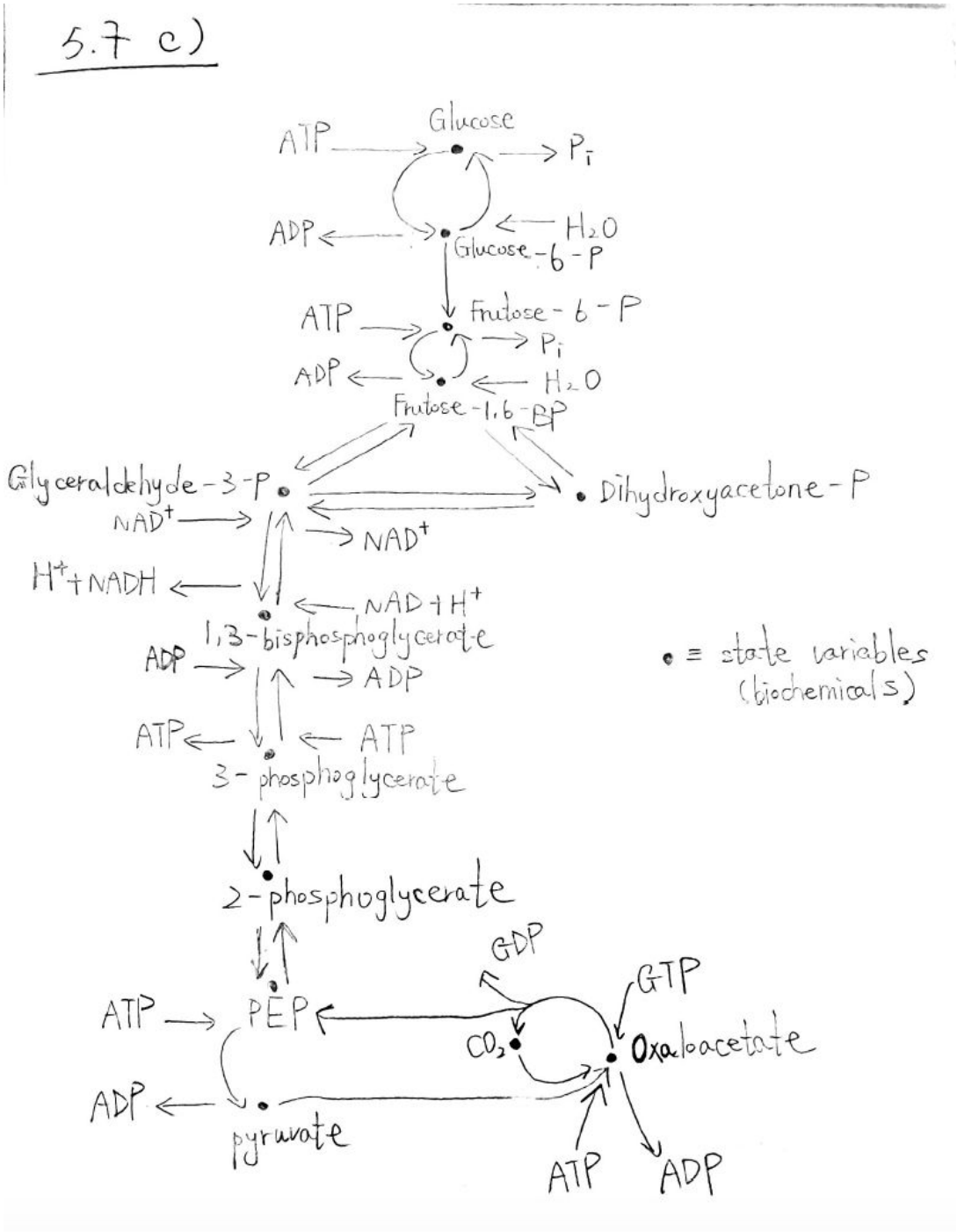
1. G (Glucose)
2. G6P (Glucose-6-Phosphatase)
3. F6P (Fructose-6-Phosphatase)
4. F1,6-BP (Fructose-1,6-Bisphosphatase)
5. G-3-P (Glyceraldehyde-3-P)
6. D-P (Dihydroxyacetone)
7. 1,3-B (1,3-bisphosphoglycerate)
8. 3-P (3-Phosphoglycerate)
9. 2-P (2-Phosphoglycerate)
10. PEP (PEP Carboxykinase)
11. Ox (Oxaloacetate)
12. Py (Pyruvate Carboxylase)

b)

State Variables of the pathway :

1. G (Glucose)
2. G6P (Glucose-6-Phosphatase)
3. F6P (Fructose-6-Phosphatase)
4. F1,6-BP (Fructose-1,6-Bisphosphatase)
5. G-3-P (Glyceraldehyde-3-P)
6. D-P (Dihydroxyacetone)
7. 1,3-B (1,3-bisphosphoglycerate)
8. 3-P (3-Phosphoglycerate)
9. 2-P (2-Phosphoglycerate)
10. PEP (PEP Carboxykinase)
11. Ox (Oxaloacetate)
12. Py (Pyruvate Carboxylase)

c)


5.7 c)
ATP
Glucose
P_i
ADP
H_2O
Glucose-6-P
ATP
Fructose-6-P
P_i
ADP
H_2O
Fructose-1,6-BP
Glyceraldehyde-3-P
Dihydroxyacetone-P
NAD^+
NAD^+
$H^+ + NADH$
$NAD + H^+$
1,3-bisphosphoglycerate
ADP
ADP
ATP
ATP
3-phosphoglycerate
2-phosphoglycerate
GDP
GTP
ATP
PEP
CO_2
Oxaloacetate
ADP
pyruvate
ATP
ADP
• = state variables (biochemicals)