CS CM 182 Homework 5

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

Exercise 7.1 - Specifying State Variables, Parameters & v Fluxes for MC Models

Part (a) & Part (b)

1. **Figure 7.4 - Blood / Urine Measurement MC Submodel**

   Let Compartment 1 = X in Blood
   Let Compartment 2 = X in Urine
   Let 0 = environment outside of blood and urine

   a. **State Variables :**
      i. q_B (*compartment of X in blood*) , number of substance X in blood
      ii. q_U (compartment of X in urine), number of substances X in urine
      iii. q_O (outside environment), number of substances X in outside environment

   b. **V fluxes :**
      i. u k_u (influx of substance X to blood)
      ii. $k_{UB}q_B$ (rate of exchange of X from blood to urine)
      iii. $k_{BO}q_O$ (rate of exchange of X from other compartments to blood)
      iv. $k_{OB}q_B$ (rate of exchange of X from blood to other compartments)

   c. **Parameter :**
      i. k_u
      ii. k_{UB}
      iii. k_{BO}
      iv. k_{OB}

2. **Figure 7.5 - Hormone metabolism MC submodel**

   Let Compartment 1 = T4 in Cell
   Let Compartment 2 = T3 in Cell
   Let 0 = environment outside of T4 and T3 in Cell

   a. **State Variables :**
      i. q_{T4} (*compartment of T4 in cell*) , number of T4 in cell
      ii. q_{T3} (*compartment of T3 in cell*) , number of T3 in cell
      iii. $q_{outside}$ (outside environment)

b. V fluxes :

i. u k_u (influx of T4 to cell u)

ii. $k_{34}q_{T4}$ (metabolic flux from T4 in cell to T3 in cell)

iii. $k_{4CO}q_{outside}$ (flux of T4 from other compartment to cell)

iv. $k_{4OC}q_{T4}$ (flux of T4 from cell to other compartment)

c. Parameter

i. k_u

ii. k_{34}

iii. k_{4CO}

iv. k_{4OC}

3. Figure 7.6 - MC model with metabolism of X1 in liver

Let Compartment 1 = X1 in Blood
Let Compartment 2 = X1 in Liver
Let Compartment 3 = X2 in Liver
Let Compartment 4 = X2 in Gut
Let Compartment 5 = X2 in Feces
Let Compartment 0 = environment outside of all blood, liver, gut and feces compartments

a. State Variables :

i. q_{1B} (number of substance X1 in blood)

ii. q_{1L} (number of substance X1 in liver)

iii. q_{2L} (number of substance X2 in liver)

iv. q_{2G} (number of substances X2 in Gut)

v. q_{2F} (number of substances X2 in Feces)

vi. $q_{outside}$ (outside environment)

b. V fluxes :

i. u k_{u1} (input flux of substances X1)

ii. $k_{O1B}q_{1B}$ (rate of exchange of X1 from blood to other compartments)

iii. $k_{1BO}q_{outside}$ (rate of exchange of X1 from other compartment to blood)

iv. $k_{1L1B}q_{1B}$ (rate of exchange of X1 from blood to liver)

v. $k_{1B1L}q_{1L}$ (rate of exchange of X1 from liver to blood)

vi. $k_{2L1L}q_{1L}$ (rate of exchange from X1 in liver to X2 in liver)

vii. $k_{2G2L}q_{2L}$ (rate of exchange from X2 in liver to X2 in gut)

viii. $k_{2F2G}q_{2G}$ (rate of exchange from X2 in gut to X2 in feces)

c. Parameters :

i. k_{u1}
ii. k_{O1B}
iii. k_{1BO}
iv. k_{1L1B}
v. k_{1B1L}
vi. k_{2L1L}
vii. k_{2G2L}

4. Figure 7.7 - X1 in blood & X1 in liver as one lumped "central compartment"

Let Compartment 1 = X1 in Blood
Let Compartment 2 = X1 in Liver
Let Compartment 3 = X1 in Blood and X1 in Liver together
Let Compartment 0 = environment outside of blood and liver compartments

1. Left Diagram

a. State variables :

i. q_{1B} (number of substances X1 in blood)
ii. q_{1L} (number of substances X1 in liver),
iii. $q_{outside}$ (outside environment)

b. Fluxes :

i. $k_{u1}u_1$ (input flux of substances X1)
ii. $k_{O1B}q_{1B}$ (rate of exchange of X1 from blood to outside environment)
iii. $k_{1BO}q_{outside}$ (rate of exchange of X1 from outside environment to blood)
iv. $k_{1L1B}q_{1B}$ (rate of exchange of X1 from blood to liver)
v. $k_{1B1L}q_{1L}$ (rate of exchange of X1 from liver to blood)
vi. $k_{O1L}q_{1L}$ (rate of exchange of X1 from liver to outside environment)

c. Parameters :

i. k_{u1}
ii. k_{O1B}
iii. k_{1BO}
iv. k_{1L1B}
v. k_{1B1L}

vi. k_{O1L}

2. **Right Diagram**
   a. **State variables :**
      i. q_{1B1L} (number of substances X1 in blood and liver)

   b. **Fluxes :**
      i. $k_{u1}\,u_1$ (input flux of substances X1)
      ii. $k_{O1BL}q_{1B1L}$ (rate of exchange of X1 from blood and liver to outside environment)
      iii. $k_{1BLO}q_{outside}$ (rate of exchange of X1 from outside environment to blood and liver)
      iv. $k_{O1BL\,(metabolism\ pathway)}q_{1B+1L}$ (rate of exchange of X1 from blood and liver to outside environment, the metabolic pathway)

   c. **Parameter :**
      i. k_{u1}
      ii. k_{O1BL}
      iii. k_{1BLO}
      iv. $k_{O1BL\,(metabolism\ pathway)}$

Part (c)

Figure 7.4 - Blood / Urine Measurement MC Submodel

Let Compartment 1 = X in Blood
Let Compartment 2 = X in Urine
Let 0 = environment outside of blood and urine

(c) If ~~the~~ fluxes are non-linear M-M type, write the ODE

(Figure 7.4) Based from assumption from part(c) ~~part(b)~~

Given the primary v fluxes are not linear.

$$\frac{dq_{blood}}{dt} = u - V_{21} - V_{01} + V_{10}$$

$$= \boxed{u - \frac{C_{21}}{K_{21} + q_{blood}} q_{blood} - K_{01} q_{blood} + k_{10} q_{outside}}$$

$$\frac{dq_{urine}}{dt} = \underbrace{\boxed{\frac{C_{21}}{K_{21} + q_{blood}} q_{blood}}}_{\text{transfer pathway}} = V_{21}$$

Figure 7.5 - Hormone metabolism MC submodel

Let Compartment 1 = T4 in Cell
Let Compartment 2 = T3 in Cell
Let 0 = environment outside of T4 and T3 in Cell

(c) <u>cont.</u>

(Figure 7.5) Based from assumption from part (c)

Given the primary v flux are not linear

$$\frac{dq_{T4}}{dt} = u - V_{21} - V_{01} + V_{10}$$

$$= \boxed{u - \frac{C_{21}}{K_{21} + q_{T4}} q_{T4} - K_{01} q_{T4} + K_{10} q_{outside}}$$

$$\frac{dq_{T3}}{dt} = V_{21} = \underbrace{\boxed{\frac{C_{21}}{K_{21} + q_{T4}} q_{T4}}}_{\text{metabolism pathway}}$$

Part (d)

Figure 7.4 - Blood / urine measurement MC submodel (Based from ODE from part c)

Parameter : C_{21} , K_{21} (constants from the non-linear elimination rate from all the compartment)

State Variable : q_{blood} $(compartment\ of\ X\ in\ blood)$, q_{urine} (compartment of X in urine), $q_{outside}$ (outside environment)

Figure 7.5 - Hormone metabolism MC submodel

Parameter : C_{21} , K_{21} (constants from the non-linear elimination rate from all the compartment)

State Variable : q_{T4} $(compartment\ of\ T4\ in\ cell)$, q_{T3} $(compartment\ of\ T3\ in\ cell)$, $q_{outside}$ (outside environment)

Part (e)

Let Compartment 1 = X1 in Blood

Let Compartment 2 = X1 in Liver

Let Compartment 3 = X2 in Liver

Let Compartment 4 = X2 in Gut

Let Compartment 5 = X2 in Feces

Let Compartment 0 = environment outside of all blood, liver, gut and feces compartments

Exercise 1: Specifying state Variables, Parameters & V Fluxes for MC Models (Figure 7.6)

(e) → Based from relation & assumption from part (a)

$$\frac{dq_{blood\,1}}{dt} = u_1 - V_{01} + V_{10} - V_{21} + V_{12}$$

$$= \boxed{u_1 - k_{01} q_{blood\,1} + k_{10} q_{outside} - k_{21} q_{blood\,1} + k_{12} q_{liver\,1}}$$

$$\frac{dq_{liver\,1}}{dt} = V_{21} - V_{12} - V_{32}$$

$$= \boxed{k_{21} q_{blood\,1} - k_{12} q_{liver\,1} - k_{32} q_{liver\,1}}$$

$$\frac{dq_{liver\,2}}{dt} = V_{32} - V_{43}$$

$$= \boxed{k_{32} q_{liver\,1} - k_{43} q_{liver\,2}}$$

$$\frac{dq_{feces\,2}}{dt} = V_{54} = \boxed{k_{54} q_{gut\,2}}$$

Part (f)

1. **Models in Part C (Figure 7.4 and Figure 7.5)**
    a. **Figure 7.4 - Blood/Urine measurement**

Let q_{blood} = concentration/masses of X in blood
Let V_b = volume of X in blood
Let q_{urine} = concentration/masses of X in urine
Let V_u = volume of X in feces

$$y_{Blood} = \frac{q_{blood}}{V_b}$$
$$y_{Urine} = \frac{q_{urine}}{V_u}$$

    b. **Figure 7.5 - Hormone metabolism MC submodel**

Let $q_{4\,cell}$ = concentration/masses of T4 in cell
Let $V_{4\,cell}$ = volume of T4 in cell
Let $q_{3\,cell}$ = concentration/masses of T3 in cell
Let $V_{3\,cell}$ = volume of T3 in cell

$$y_{4\,cell} = \frac{q_{4\,cell}}{V_{4\,cel}}$$
$$y_{3\,cell} = \frac{q_{3\,cell}}{V_{3\,cell}}$$

2. **Models in Part E (Figure 7.6 - MC model with metabolism of X1 in liver)**

Let $q_{blood\,1}$ = concentration/masses of X1 in blood
Let V_1 = volume of X1 in blood
Let $q_{feces\,2}$ = concentration/masses of X2 in feces
Let V_2 = volume of X2 in feces

a. $y_1 = \frac{q_{blood\,1}}{V_1}$

b. $y_2 = \frac{q_{feces\,2}}{V_2}$

Exercise 2
Part (a)

Exercise 2: Measuring and Unknown Doses

(a) According to lecture, let the injected drug dose into the bloodstream be an impulse function

Let the function be represented as $u(t) = \underbrace{Q_0}_{\text{Doses}} \delta(t)$

After drug dose D_0 get into the bloodstream, the measured concentration at time is 0 $(t = 0)$

is $\underbrace{y_{blood}(0^+)}_{\text{measurement of output } y} = \frac{Q_0}{\underbrace{V_{blood}}_{\text{volume of blood}}}$

The measurement take place by assuming the drug immediate dissolve & mix with the blood once it get in.

In order to estimate the volume of the blood, we can take our measurement first time at a place very close to $t = 0$. $\rightarrow \hat{y}_{blood}(0^+)$

This means that $y_{blood}(t)$ still haven't change that much

$$\boxed{V_{blood} \approx \frac{\hat{y}_{blood}(0^+)}{Q_0}}$$

Part (b)

(b) The experiment could collect the patient urine for a period of time until the patient body has completely eliminated the injected drug dose X. We are able to measure the concentration of substance X sequentially because we know when it become zero we know the drug is completely eliminated from the body.

$$M_{drug} = C_{drug} \times V_{drug}$$

mass of drug

concentration of drug through measurement

volume of drug eliminated from the body

Exercise 3

Part (a)

Exercise 3 : Mammillary Compartment Model

(a) Here the ODEs

$$\frac{dq_3}{dt} = V_{31} - V_{13} - V_{03} = \boxed{k_{31} q_1 - k_{13} q_3 - k_{03} q_3}$$

$$\frac{dq_1}{dt} = u_1 - V_{01} + V_{13} - V_{31} + V_{12} - V_{21}$$

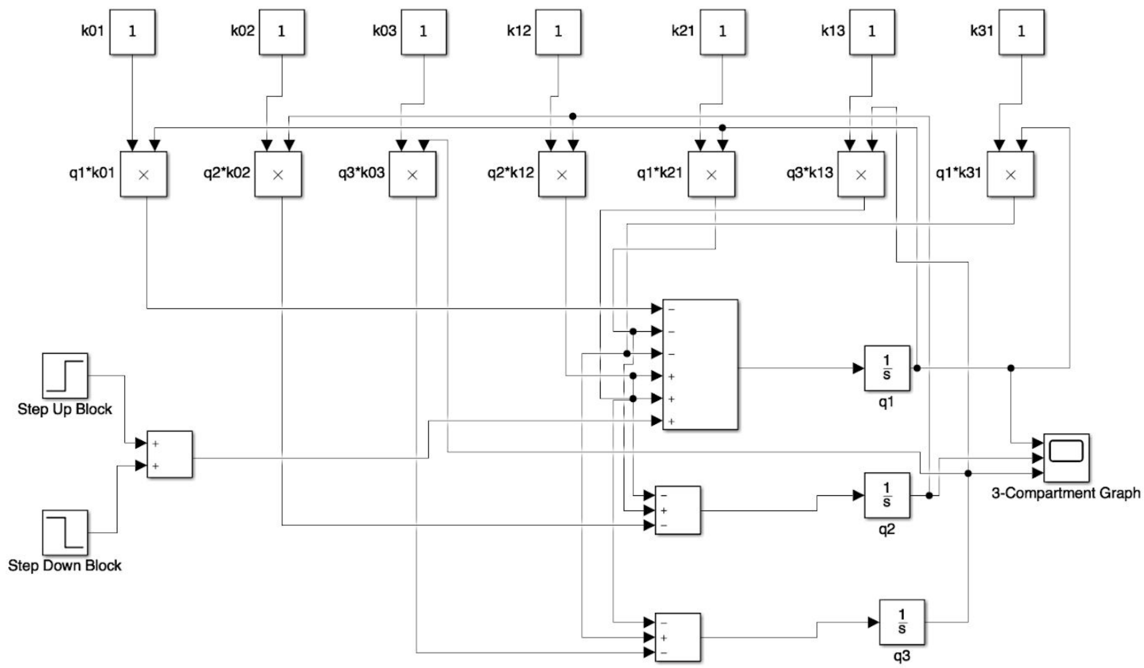
$$= \boxed{u_1 - k_{01} q_1 + k_{13} q_3 - k_{31} q_1 + k_{12} q_2 - k_{21} q_1}$$

$$\frac{dq_2}{dt} = V_{21} - V_{12} - V_{02}$$

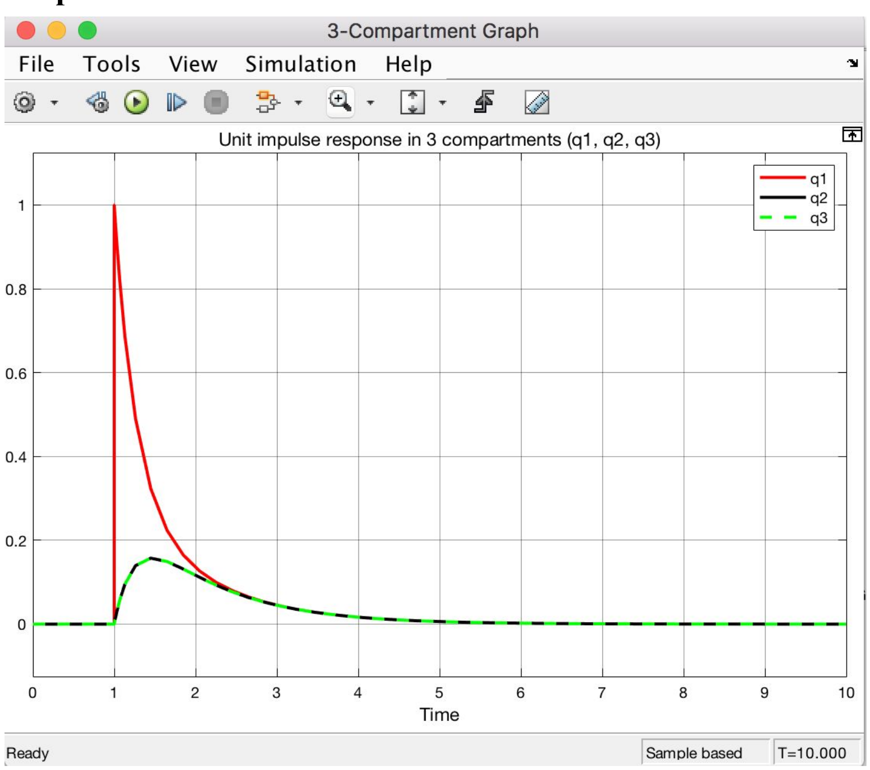
$$= \boxed{k_{21} q_1 - k_{12} q_2 - k_{02} q_2}$$

$$\boxed{y_1 = \frac{q_1}{V_1}}$$

Part (b)
Simulink



Graph

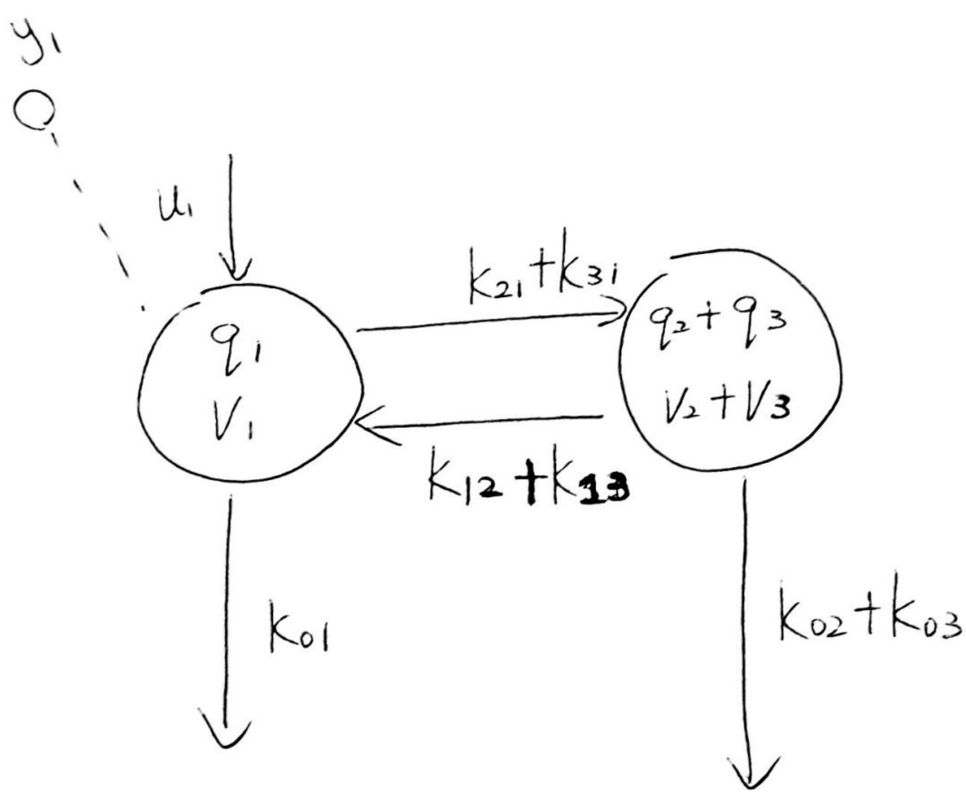


Q2 and Q3 overlap with each other

Part (c)

According to the simulink diagram and the corresponding scope graph, compartment 2 and 3 can be combined into one single compartment. The reason behind the similar property is both compartment 2 and 3 have a single influx from compartment 1 and a single outflux to compartment 1. They also have a leak to the outside environment. Under consumption that all rate constants equal to one, all of the parameters from compartment 2 are the same as the parameters from compartment 3.

Here is the new model :



Part (b) - All models are linear compartmental (Based from notation in Part a)

1. **Blood / Urine measurement MC submodel**

   Let Compartment 1 = X in Blood
   Let Compartment 2 = X in Urine
   Let 0 = environment outside of blood and urine

   a. Parameter : u(input flux, influx), k_{21} (rate of exchange of X from blood to urine, efflux), k_{01} (rate of exchange of X from blood to outside environment, efflux), k_{10} (rate of exchange of X from outside environment to blood, influx)

2. **Hormone metabolism MC submodel**

   Let Compartment 1 = T4 in Cell
   Let Compartment 2 = T3 in Cell
   Let 0 = environment outside of T4 and T3 in Cell

   a. Parameter : u(input flux, influx), k_{21} (rate of exchange from T4 in Cell to T3 in Cell, efflux), k_{01} (rate of exchange from T4 in Cell to outside environment, efflux), k_{10} (rate of exchange from outside environment to T4 in Cell, influx)

3. **MC model with metabolism of X1 in liver**

   Let Compartment 1 = X1 in Blood
   Let Compartment 2 = X1 in Liver
   Let Compartment 3 = X2 in Liver
   Let Compartment 4 = X2 in Gut
   Let Compartment 5 = X2 in Feces
   Let Compartment 0 = environment outside of all blood, liver, gut and feces compartments

   a. Parameter : u (input flux, influx), k_{01} (rate of exchange of X1 from blood to outside environment, efflux), k_{10} (rate of exchange of X1 from outside environment to blood, influx), k_{21} (rate of exchange of X1 from blood to liver, efflux), k_{12} (rate of exchange of X1 from liver to blood, influx), k_{32} (rate of exchange from X1 in liver to X2 in liver, efflux), k_{43} (rate of exchange from X2 in liver to X2 in gut, efflux), k_{54} (rate of exchange from X2 in gut to X2 in feces, efflux)

4. X1 in blood and X1 in liver as one lumped "central" compartment

Let Compartment 1 = X1 in Blood
Let Compartment 2 = X1 in Liver
Let Compartment 3 = X1 in Blood and X1 in Liver together
Let Compartment 0 = environment outside of blood and liver compartments

a. Parameter : u_1 (input flux, influx), k_{21} (rate of exchange of X1 from blood to liver, efflux), k_{12} (rate of exchange of X1 from liver to blood, influx), k_{01} (rate of exchange of X1 from blood to outside environment, efflux), k_{10} (rate of exchange of X1 from outside environment to blood, influx), k_{02} (rate of exchange of X1 from liver to outside environment, efflux), $k_{03\,(\textit{other compartment exchanges})}$ (rate of exchange of X1 from blood and liver to outside environment, efflux), $k_{30\,(\textit{other compartment exchanges})}$ (rate of exchange of X1 from outside environment to blood and liver, influx), $k_{03\,(\textit{metabolism pathway})}$ (rate of exchange of X1 from blood and liver to outside environment, efflux, the metabolism pathway)