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Assignment 2: Performing simulations with existing models and making a formalization

Question #1a

❖ Change the initial settings in such a way that glucose is externally present from the start, while lactose is also present. Use the first Excel sheet (tab ‘exercise a-b’). Describe and explain the changes that you observe.

		external glucose
t	**Dt**	*EG*
0	1	0
1	1	0
2	1	0
3	1	0
4	1	0
5	1	0
6	1	0
7	1	0
8	1	0
9	1	0

		external glucose
t	**Dt**	*EG*
0	1	1
1	1	1
2	1	1
3	1	1
4	1	1
5	1	1
6	1	1
7	1	1
8	1	1
9	1	1

Figure 1.0 Table of implication(Left table is the original. Right table is the changed version.)

Figure 1.0 has been able to show the changes in the graphs mentioned below. Figure 1.2 has glucose externally present from the start till t = 27. On the other hand, Figure 1.1 only has glucose to be externally present at t = 10 till t = 27. Figure 1.2 has glucose externally present for t = 9 more than Figure 1.1.

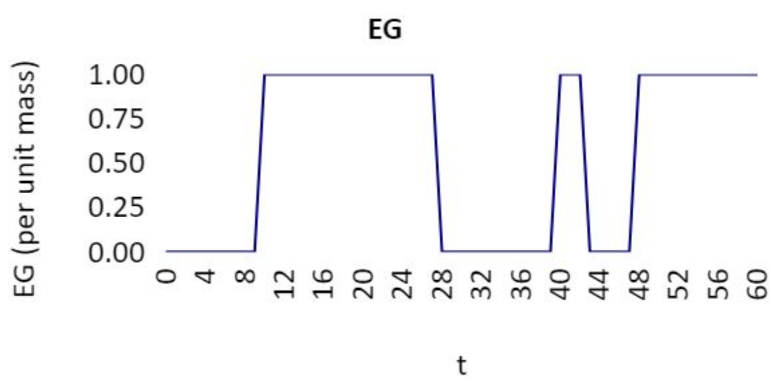


Figure 1.1 Original EG

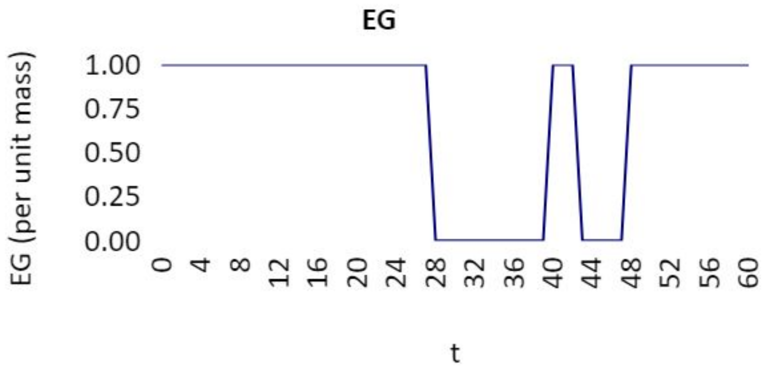


Figure 1.2 Adjusted EG

Due to the implication of Figure 1.0, the glucose indicator also shows that there is 1.00 GI(per unit mass) at t = 1. Thus there is an additional 9 [GI(per unit mass) × t] area below the line in Figure 1.4, in comparison to Figure 1.3.

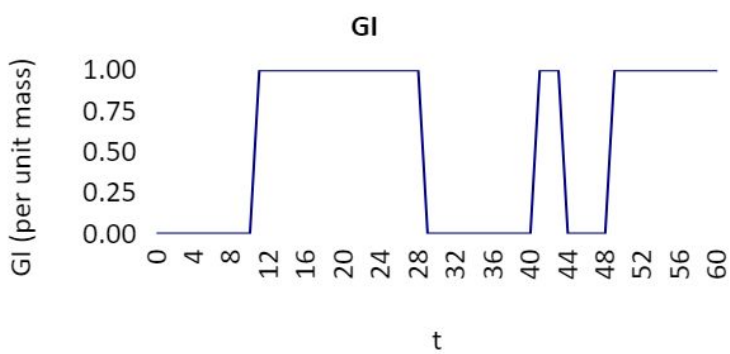


Figure 1.3 Original GI

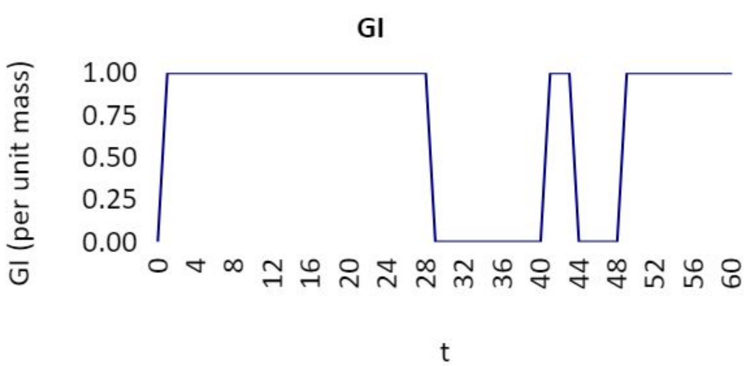


Figure 1.4 Adjusted GI

Figure 1.5 is lacking 9 [GIE(per unit mass) × t] of the total area below the line, in comparison to Figure 1.6. Figure 1.5's graph is lacking the area when GIE(per unit mass) = 1 from t = 2 till t = 11.

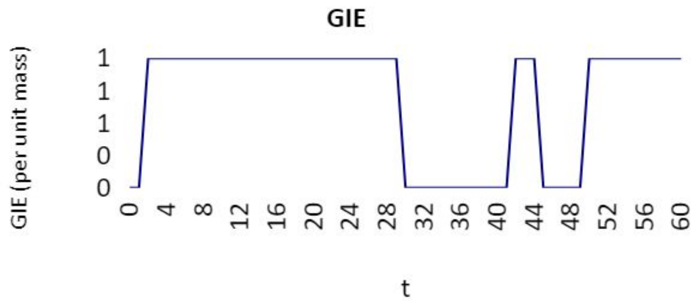


Figure 1.5 Original GIE

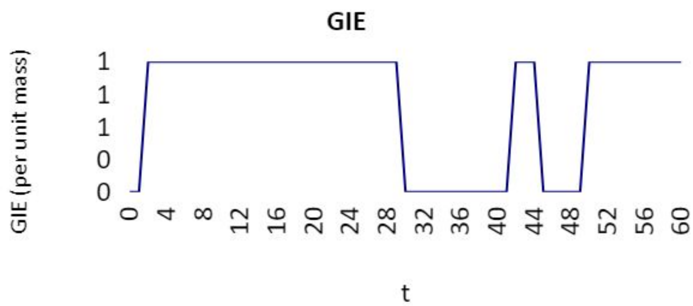


Figure 1.6 Adjusted GIE

The difference between the original LIE and adjusted LIE is the opposite of what has been shown in the graphs above. Figure 1.7 has LIE(per unit mass) = 1 from t = 2 till t = 11. On the other hand Figure. 1.8 does not have LIE(per unit mass) =1, before it reaches t = 39. Thus, when glucose is externally present from the start the amount of LIE(per unit mass) decreases.

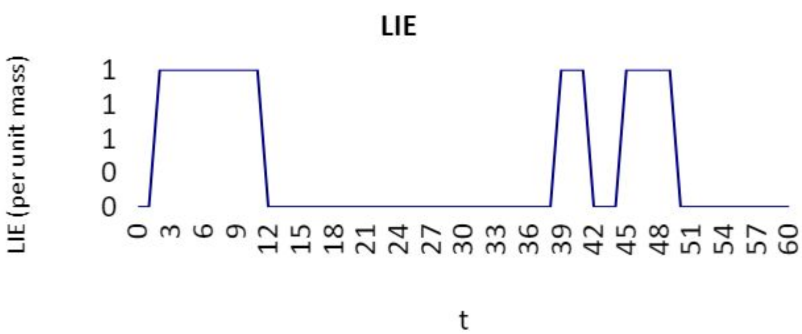


Figure 1.7 Original LIE

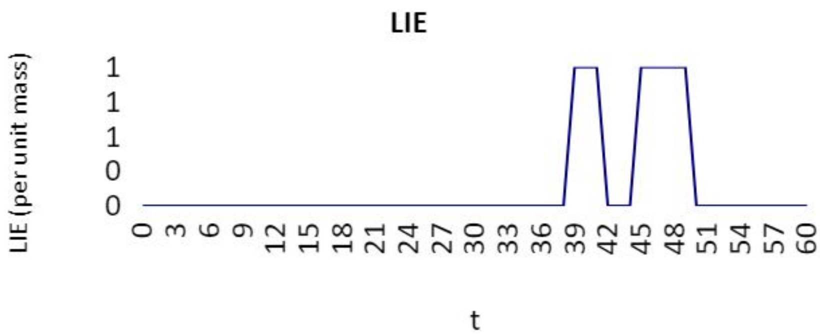


Figure 1.8 Adjusted LIE

In Figure 2.0 GIM(per unit mass) is present from t = 3, whereas GIM(per unit mass) for Figure 1.9 is only present from t = 13. Thus, Figure 2.0 has a GIM(per unit mass) = 1 for t = 10 more than Figure 1.9.

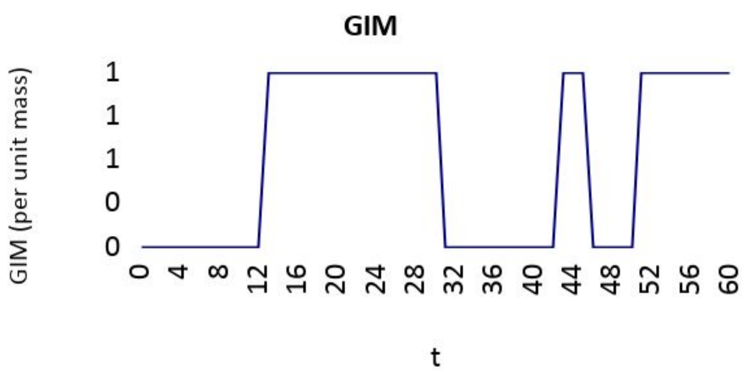


Figure 1.9 Original GIM

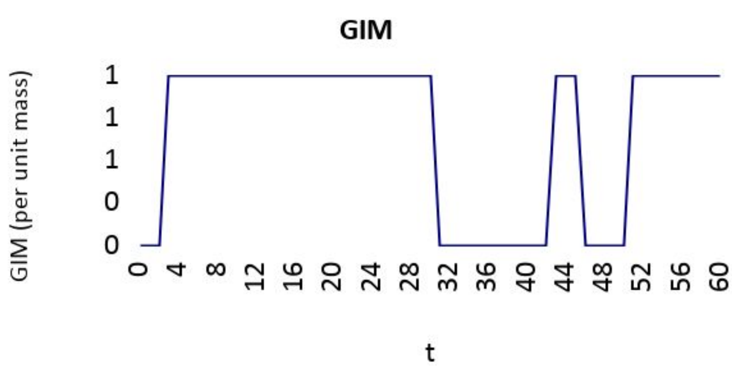


Figure 2.0 Adjusted GIM

Figure 2.2 is lacking LIM(per unit mass) = 1 from t = 3 till t = 12. Therefore, when glucose is externally present from the start the amount of LIM present increases.

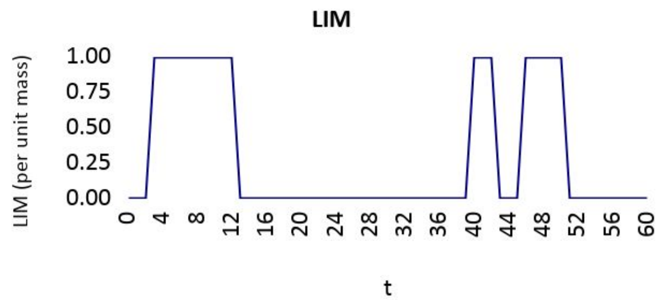


Figure 2.1 Original LIM

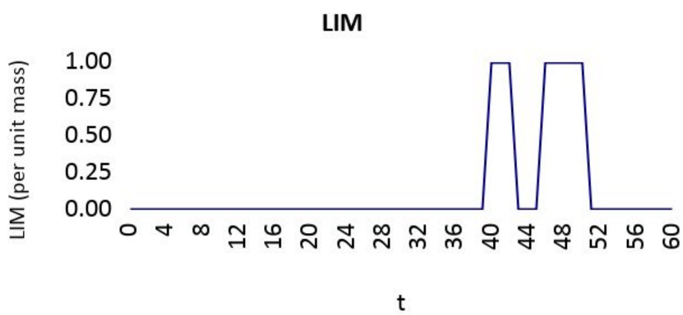


Figure 2.2 Adjusted LIM

The external glucose present from the start seems to have an impact on the IG. As illustrated in Figure 2.4 the IG(per unit mass) is at 1.00 from t = 4 till t = 13, but Figure 2.3 is missing this area. Thus, suggesting that the external glucose present from the start has an impact on the IG.

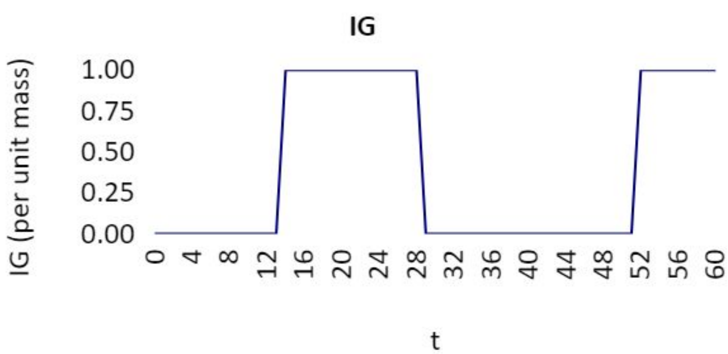


Figure 2.3 Original IG

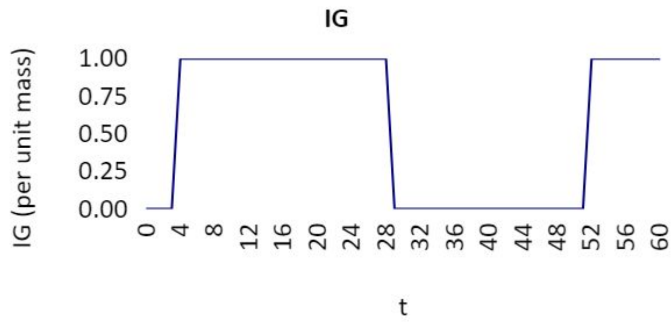


Figure 2.4 Adjusted IG

For IL, it seems that the external glucose being present from the start has decreased the amount of IL. This can be portrayed in the comparison of Figure 2.5 and Figure 2.6. Figure 2.5 has IL(per unit mass) = 1.00 present from t = 4 till t = 13. However, Figure 2.6 has IL(per unit mass) = 0.00 from t = 4 till t = 13. The rest of the graph matches with each other, but unfortunately it lacks the IL(per unit mass) from t = 4 till t = 13. Thus, it can be hypothesized that the presence of external glucose from the start decreases the amount of IL.

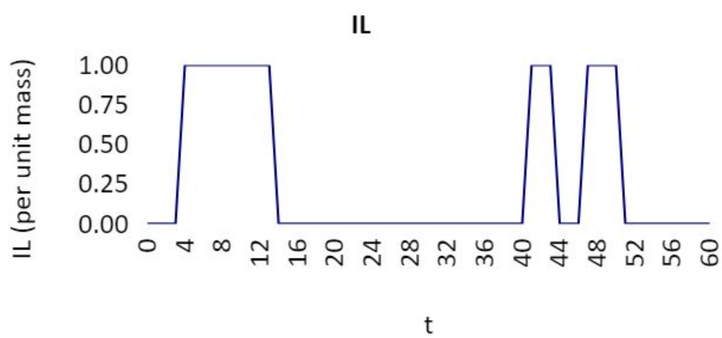


Figure 2.5 Original IL

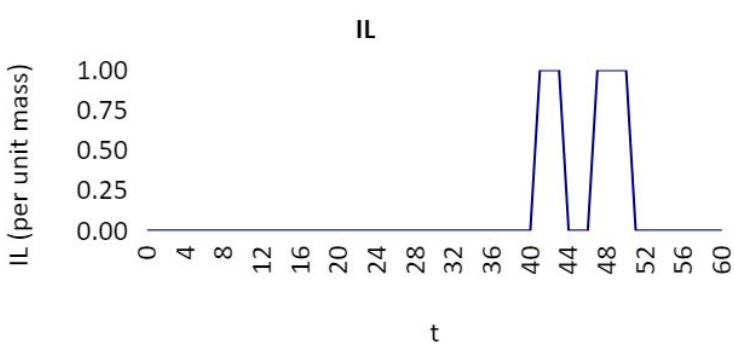


Figure 2.6 Adjusted IL

Question #1b

- As can be seen in the current model, there is a small period when glucose is externally present at time points 40 to 42. This leads to the presence of the glucose import enzyme from time point 42 to 44; however, glucose will not make it inside. Why does the glucose not get inside the E.coli?

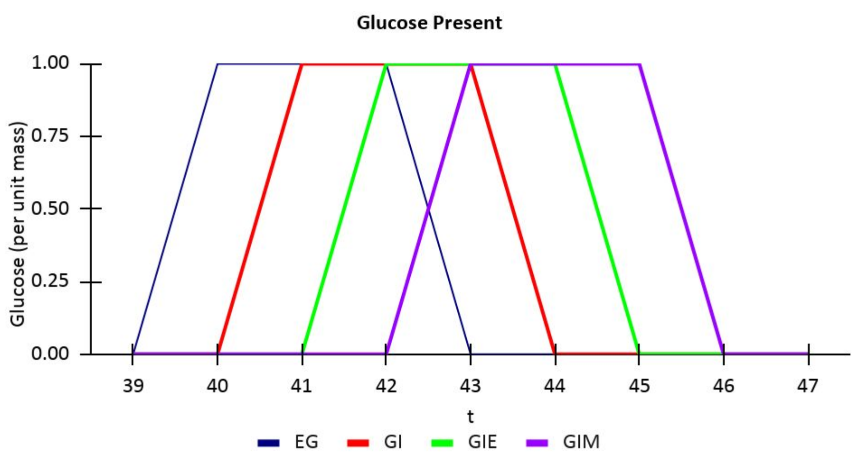


Figure 2.7 Glucose Present

As displayed in Figure 2.7, glucose is externally present, thus has a Glucose (per unit mass) = 1 at t = 40 till t = 42 when referring to the EG within Figure 2.7. As a result, the glucose enzyme is only present at Glucose (per unit mass) = 1 for t = 42 till t = 44 as illustrated in GIE from Figure 2.7. Glucose is only imported at Glucose (per unit mass) = 1 and t = 43 to t = 45, as shown in Figure 2.7. Despite the fact that the glucose has been imported, there is no glucose being internally shown. This is caused due to the lack of glucose that must be present for a longer time. The internal glucose is influenced by the equation, shown in Figure 2.8.

$$INTgluc(t + \Delta t) \ = \ glucIMP(t) \times EXTgluc(t)$$

Figure 2.8 Effect of glucose import taking place

One of the variables that influence the equation is the amount of glucose being internally present. Through Figure 2.8, the relationship between the impact that the amount of internally present glucose has upon the glucose import reaction to succeed. In this specific situation(displayed in Figure 2.7) because the import of glucose is at t = 43 and the glucose is not externally present at t = 43, as a result at t = 43 no internal glucose is present.

Question #1c

❖ Use the second Excel sheet (tab ‘exercise c’) for this exercise. Try to adjust the input values (i.e.the external presence of glucose and lactose) such that food is always available inside the E. coli, while there are still changes between the presence of glucose and lactose outside the E. coli and glucose and lactose are never present externally at the same time point. Explain your answer.

To achieve the state that food is always available inside the E.coli, the external availability of glucose and lactose needed to be changed. This was achieved by repeating a value in periods of three throughout the whole time stamp. The particular reason for this situation of repeating the three values is caused by the internal glucose checking whether the external glucose and glucose import are true in the previous step, thus not counting the internal glucose as a step. Therefore, it repeats the three values throughout the whole time stamp. It is important to check that the availability of glucose or lactose do not overlap. For instance, if glucose were to be externally available at t = 4 and t = 6 lactose must have to be available at t = 5.

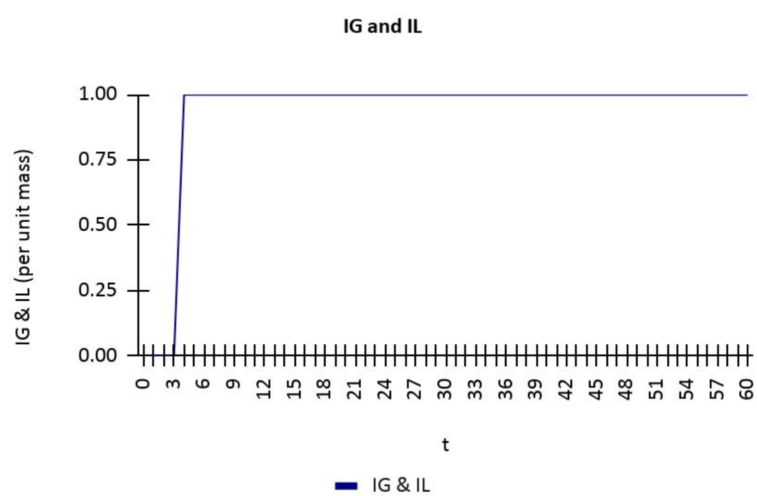


Figure 2.9 Internal glucose and internal lactose graph data combined discluding the gaps

When looking at the table[1] the glucose being internally present is t = 1 behind the glucose being externally present. For example, if glucose was externally present at t = 6, it will be internally present at t = 7. The same goes for lactose being internally present, it is always t = 1 behind the actual t value. Thus, to calculate when it will be internally present the t value that the glucose was externally present must be subtracted by one.

[1] Please refer to the excel document, Assignment2-ecoli-model.xlsx, exercise c Adjusted.

In Figure 3.1, it actively demonstrates that the mass increases at an exponential rate as the t value increases by looking at the curve of the graph. When referring to the table[2] values, it is clear that only when food is present there will be an added mass larger than zero. The reason towards Figure 3.0 not having a smooth exponential increase is a matter caused due to the fact that glucose or lactose was not internally present at some time points(t). Thus, it illustrates no change in the value for a period of t, but increases again when glucose or either lactose is internally present. Moreover, as can be seen in both Figure 3.0 and 3.1, Figure 3.1 has been able to achieve higher mass values when looking at the same time stamp. For example, Figure 3.0 only reached 1469.77(mass) at t = 60 when Figure 3.1 was able to reach 27173.76(mass) at t = 60. The difference between these values is 25703.99(mass).

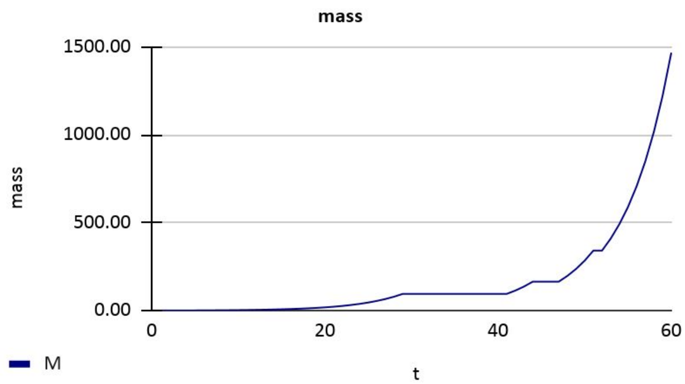


Figure 3.0 Original mass

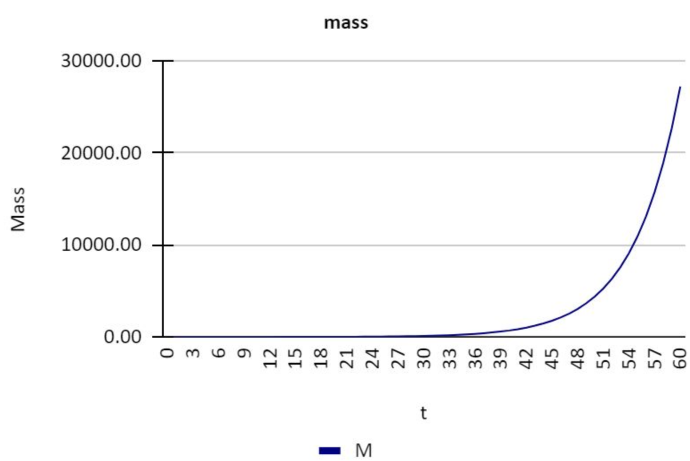
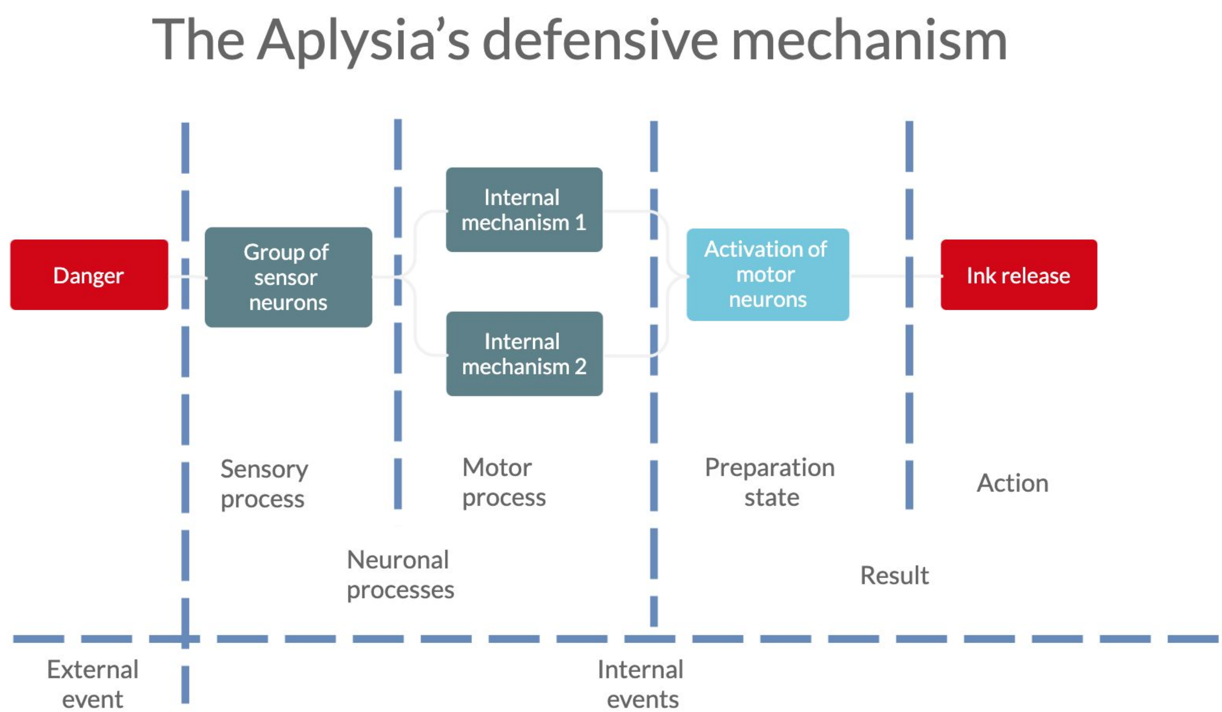


Figure 3.1 Adjusted mass

[2] Please refer to the excel document, Assignment2-ecoli-model.xlsx, exercise c Adjusted.

Question #2a

❖ Draw a figure to show the dynamic relations of this model. You can use figure 2 in Chapter 4 as an example. Make sure to include the dotted line, that indicates the boundary between external and internal concepts, in your picture.



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Question #2b

❖ Complete the following table of dependencies between the variables. Draw arrows between the active cells to show the dependencies (see table 2 in Chapter 4 of the reader).

t	danger	sensory process	mechanism 1	mechanism 2	motor process	ink release
0	0	0	0	0	0	0
1	1	0	0	0	0	0
2	0	1	0	0	0	0
3	0	0	1	1	0	0
4	0	0	0	0	1	0
5	0	0	0	0	0	1

Question #2c

- Now give the formulas for the activation of the sensory process (*SP*), the mechanisms (*M1* and *M2*), the motor process (*MP*) and the ink release (*IR*) using the table from the previous question. Give the formulas in two languages: one using natural language to describe your formulas, one using the style of the syllabus (see section 3.2 of chapter 4).

The first line is 0, so each cell is equal to 0, no influence on internal mechanisms. In the next line appeared a danger, external event (1 in the "danger" cell) and 0 everywhere else. In the next one, the danger disappeared and influenced only the sensory process (1 in the "sensory process" cell). Afterwards, the t3 line, sensory processes influenced motor processes, two internal mechanisms (1 in the "mechanism 1" cell and "mechanism 2" cell). These two are succeeding the reaction, firstly the preparation for it, motor process (1 in motor process cell). Finally, we see the result, the ink released (1 for the last cell in the "ink release" column).

Neuronal Processes

<u>From danger to activation of sensory process:</u>

If a danger occurs, then sensory process will be activated:

SensoryProcess(t) = 1 if Danger(t-1)=1

0 if Danger(t-1)=0

<u>From sensory process to activation of mechanism 1 and mechanism 2:</u>

If a sensory process occurs, then mechanism 1 and mechanism 2 will be activated:

Mechanism1(t) and Mechanism2(t) = 1 if SensoryProcess(t-1)=1

0 if SensoryProcess(t-1)=0

The result

From mechanism 1 and mechanism 2 to activation of motor process:

If a mechanism 1 and mechanism 2 occurs, then motor process will be activated:

$$\text{MotorProcess}(t) = \begin{cases} 1 & \text{if } \text{Mechanism1}(t-1) = 1 \text{ and } \text{Mechanism2}(t-1) = 1 \\ 0 & \text{if } \text{Mechanism1}(t-1) = 0 \text{ or } \text{Mechanism2}(t-1) = 0 \end{cases}$$

From motor process to activation of ink release:

If a motor process occurs, then ink release will be activated:

$$\text{InkRelease}(t) = \begin{cases} 1 & \text{if } \text{MotorProcess}(t-1)=1 \\ 0 & \text{if } \text{MotorProcess}(t-1)=0 \end{cases}$$

Question #2d

This part of exercise is represented in the excel file "Assignment2-ecoli-model.xlsx", the last sheet "exercise 2d" attached here