Linear Control Systems
Master 1

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LCS - HW2 - Control of blood sugar concentration

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1 Detailed schematic of the open loop system

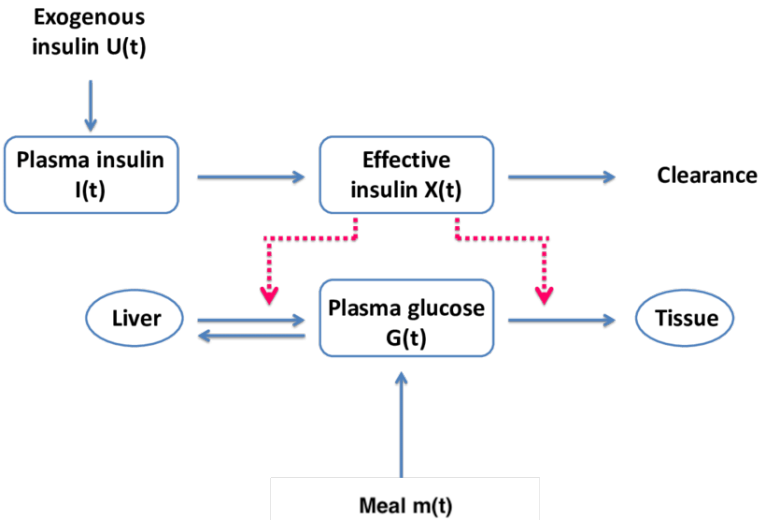

FIGURE 1 – Schematic of the open loop system

All the state and input variables are present in this diagram. The Bergman minimal model, on which our dynamical system is based, also considers hypoglycemia but we will focus on hyperglycemia for this project.

2 Constraints, assumptions, limitation

We based our work on the Bergman [5] model adapted by Gillis [4] to the type 1 diabetic patient.

•We assume that during a period of hypoglycemia, the patient will eat and the liver will not have to produce glucagon. In other words, the input m(t) will always be accessible. We will therefore focus on hyperglycemia, which is the major issue for patients who suffer from type 1 diabetes.

•The main constraint we have to face is the time delay that appear in the dynamic system. On the one hand, after a meal (input m(t)), the process of digestion takes place and the rise of blood sugar happens a long period following the meal. There is no typical value but as an example, for patients suffering a type 1 diabete, a normal glycemic level during fasting must be in the interval [70-120] mg/dl and 2 hours after a meal it should be lower than 160 mg/dl. It shows that glycemia can be high even 2 hours later. On the other hand, the insulin ejected takes some time to arrive at certain parts of the human body. It is not instantaneous and the propagation of insulin follows the blood flow.

•One of the limitations of this method is that it doesn't take all the dynamics of the metabolism into account. In particular, the long term effect of an external insulin ejection.

3 State-space representation

	Notation	Signification
Inputs		
u_1	U	Injected insulin
u_2	m	Ingested glucose
State		
x_1	G	Glucose level in the blood
x_2	X	Concentration of insulin in a distant compartment
x_3	I	Concentration of insulin in the blood
Output		
y	G	Glucose level in the blood

TABLE 1 – State-space representation

The system that we will consider is the following :

$$\begin{cases} \dot{G}(t) = f_1(G(t), X(t), m(t)) = -p_1 G(t) - X(t)G(t) + p_1 G_b + \dfrac{m(t)}{V_G} \\ \dot{X}(t) = f_2(X(t), I(t)) = -p_2 X(t) + p_3(I(t) - I_b) \\ \dot{I}(t) = f_3(I(t), U(t)) = -nI(t) + \dfrac{U(t)}{V_I} \end{cases} \tag{1}$$

The parameters [6] of this system are :

•$p_1 = 0.035 min^{-1}$, rate at which glucose is removed from the plasma independently of action of insulin

•$p_2 = 0.05 mU/l min^2$, rate of disappearance of insulin from the remote insulin compartment

•$p_3 = 23 * 10^{-6} min^{-1}$, insulin's appearance's rate in the remote insulin compartment

•n = 0.142 l/min, clearance of plasma insulin

•Ib = 0 mg/dl, the basal insulin value around 0 for a diabetic patient and around 15 for a non-diabetic person.

•Vg = 117 dl, the volume of the gut

•Vi = 10.2041 dl, the insulin distribution volume

•$G_b = 200 mg/dl$, the basal glucose concentration, around 200 for a diabetic patient and around 80 for a non-diabetic person.

Our system is not linear since the level of glucose does not depend linearly on the injection of insulin, indeed, the change in concentration of glucose will not be directly proportional to the insulin injected This is due to the term $X(t)G(t)$ in the equation of $\dot{G}(t)$.

The system can be evaluated at equilibrium points. First, we will find those points and we will then analyse if they are stable or not. In fact, if they are not stable, a small perturbation would lead the system far from the equilibrium point. The potential equilibrium points can be found at points where the state variables do not vary (i.e. $\dot{x_i} = 0$) : By doing this, we obtain :

$$\begin{cases} 0 = -p_1 G_{eq} - X_{eq} G_{eq} + p_1 G_b + \dfrac{m(t)}{V_G} \\ 0 = -p_2 X_{eq} + p_3 \left(I_{eq} - I_b\right) \\ 0 = -n I_{eq} + \dfrac{U_{ieq}}{V_I} \end{cases} \tag{2}$$

The values of inputs and state variables are taken at the equilibrium. In our case, we focus on type 1 diabetic patients so G_{eq} will normally have a higher value than a normal person would have. $m(t)$ is really discontinuous over time as there are only "peaks" during a small period of time. We will consider, for our equilibrium, that the person is not eating ($m(t) = 0$) and so the equilibrium is taken during the digestion period. However, our constraints suppose that there are some delays, including the time it takes for the ejected insulin to be effective or the time for glucose to reach blood plasma. Therefore, at equilibrium, there is a constant flux of glucose going in blood due to digestion and there must be a constant injection of insulin U_{eq} to maintain G_{eq} constant.

By injecting $m_{eq} = 0$, the equilibrium point becomes :

$$\begin{cases} G_{eq} = \dfrac{G_b p_2}{p_2 + \frac{p_3 I_b}{p_1} - \frac{U_{eq} p_3}{p_1 V_I n}} \\ X_{eq} = \dfrac{p_3}{p_2}\left(\dfrac{U_{eq}}{V_I n} - I_b\right) \\ I_{eq} = \dfrac{U_{eq}}{V_I n} \end{cases} \tag{3}$$

The matrix A can be computed by deriving each dynamical equation f_1, f_2 and f_3 with respect to the state variables at the equilibrium point.

$$A = \begin{bmatrix} -p_1 - X_{eq} & -G_{eq} & 0 \\ 0 & -p_2 & p_3 \\ 0 & 0 & -n \end{bmatrix} = \begin{bmatrix} -p_1 + \frac{p_3}{p_2}\left(\frac{U_{eq}}{V_I n} - I_b\right) & -\frac{G_b p_2}{p_2 + \frac{p_3 I_b}{p_1} - \frac{U_{eq} p_3}{p_1 V_I n}} & 0 \\ 0 & -p_2 & p_3 \\ 0 & 0 & -n \end{bmatrix} \tag{4}$$

The matrix B can be computed by deriving each dynamical equation f_1, f_2 and f_3 with respect to the input variables at the equilibrium point.

$$B = \begin{bmatrix} \frac{\delta f_1}{\delta m} & \frac{\delta f_1}{\delta U} \\ \frac{\delta f_2}{\delta m} & \frac{\delta f_2}{\delta U} \\ \frac{\delta f_3}{\delta m} & \frac{\delta f_3}{\delta U} \end{bmatrix} = \begin{bmatrix} \frac{1}{V_g} & 0 \\ 0 & 0 \\ 0 & \frac{1}{V_I} \end{bmatrix} \tag{5}$$

The matrix C and D are equal to

$$C = \begin{bmatrix} 1 & 0 & 0 \end{bmatrix} \qquad D = \begin{bmatrix} 0 & 0 \end{bmatrix} \tag{6}$$

In fact, the output equation can be written as $y = Cx + D$ and we are seeking for the output $y = G$ so matrices C and D must have these values. Such matrices show us that we will need one sensor (by looking at matrice C), this sensor is our glucometer.

4 System simulations without controller

We choose the initial conditions such as $G(0) = G_b$, $I(0) = I_b$ and $X(0) = 0$. Since we consider that there is no controller for those simulations, we took $U(t) = 0$. For a diabetic patient, we can consider that $I_b = 0$ since the patient's pancreas does not release insulin. The basal glucose concentration of a diabetic patient is high, we set $G_b = 200$. We can see the results in the figure 2.

Since there is no insulin in the system, the glucose level stays at the basal concentration. Indeed, we have :

$$\begin{cases} \dot{G}(t) = -p_1 G(t) - X(t)G(t) + p_1 G_b + \dfrac{m(t)}{V_G} = -p_1(G(t) + G_b) = 0 \\ \dot{X}(t) = -p_2 X(t) + p_3(I(t) - I_b) = 0 \\ \dot{I}(t) = -nI(t) + \dfrac{U(t)}{V_I} = 0 \end{cases} \tag{7}$$

We also wanted to test the affect of a meal in those conditions, considered that the patent is eating at time = 100. Theses choices lead to the simulation represented in the figure 3.

After the meal, the concentration of glucose increases and then decreases to go back to the basal concentration. Indeed, even if there is no insulin, the organism is going to use the glucose for its basic functions thanks to the parameter p_1.

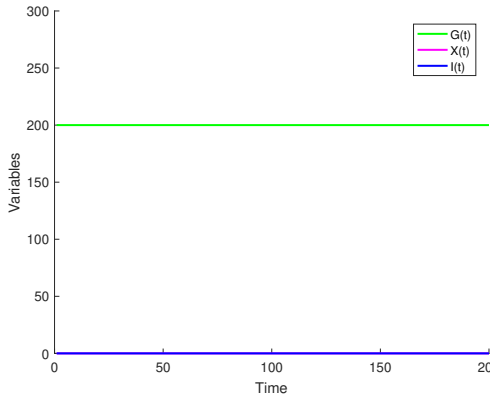

FIGURE 2 – Evolution of variables when $U(t) = 0$ and $I_b = 0$ when the patient doesn't eat

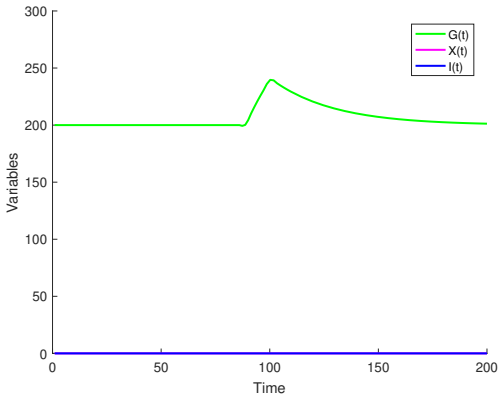

FIGURE 3 – Evolution of variables when $U(t) = 0$ and $I_b = 0$ when the patient eat at time 100

5 State-space representation analysis (computations and result interpretation

5.1 Stability

We can find the stability by computing the eigenvalues of the A matrix (4).

The eigenvalues are :

$$\begin{cases} \lambda_1 = -n \\ \lambda_2 = -p_2 \\ \lambda_3 = -p_1 - X_e \quad = -p_1 + \dfrac{p_3}{p_2}(I_b - \dfrac{U_e}{V_I n}) \end{cases} \tag{8}$$

By checking the results of the three lambdas, we can assume that the system is stable because the three eigenvalues are real and negatives if we make the assumption that $I_b = 0$ as said in the list of the parameters.

5.2 Observability

To access the observability of the system, the observability matrix W_r has to be computed, we found :

$$W_r = \begin{bmatrix} C \\ CA \\ CA^2 \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 \\ -p_1 - X_e & -G_e & 0 \\ (p_1 + X_e)^2 & G_e(p_1 + p_2 + X_e) & -p_3 G_e \end{bmatrix} \tag{9}$$

Since all the rows of the matrix are linearly independent, the matrix is full row rank and we know that the system is observable.

5.3 Controllability

To access the controllability of the system, the controllability matrix W_r has to be computed, we found :

$$W_r = \begin{bmatrix} B & AB & A^2B \end{bmatrix} = \begin{bmatrix} \frac{1}{V_g} & 0 & -\frac{p_1+X_e}{V_g} & 0 & \frac{(p_1+X_e)^2}{V_g} & -\frac{p_3 G_e}{V_I} \\ 0 & 0 & 0 & \frac{p_3}{V_I} & 0 & -\frac{p_3}{V_I}(p_2+n) \\ 0 & \frac{1}{V_I} & 0 & \frac{-n}{V_I} & 0 & \frac{n^2}{V_I} \end{bmatrix} \tag{10}$$

Since all the rows of the matrix are linearly independent, the matrix is full row rank and we know that the system is controllable.

Références

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[3] Bergman, R. N., Ider, Y. Z., Bowden, C. R., and Cobelli, C. (1979). *Quantitative estimation of insulin sensitivity. American Journal of Physiology - Endocrinology and Metabolism, 236(6) :E667–677*

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