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Research paper

Mathematical analysis of successive approximation to identify the blood glucose regulation using picards iteration method

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Abstract

Diabetes affects millions of peoples all over the world, and the correct identification of Glucose of individuals affected with this disease, especially of those in early stages or in progression towards diabetes, remains an active area of research. This Picard's Mathematical model is useful to identify the glucose-insulin interactions. In this system we used a couple of ordinary differential equations prevails as an important tool for interpreting data collected during an intravenous glucose tolerance test.(IVGTT). In this study we extract the solution to the Picard's method and for identifying patient-specific parameters of glucose trajectories form IVGTT. As illustrated with patient data, our approach seems to have an edge over nearly an accurate approximate value using this method. Additionally, we also present an application of our method to prediction of the time to baseline glucose and calculation of glucose effectively, two quantities regarded as significant in diabetes diagnostics.

Keywords: *Diabetes; Glucose-insulin interactions; Picard's Mathematical model; Intravenous glucose tolerance test (IVGTT);Patient-specific parameters*

1. Introduction

To conduct a mathematical model it is necessary to follow the following well known facts from the elementary biology-

1) Glucose is a source of energy for all tissue and organs and has an important role in the metabolism of vertebrate. The blood glucose concentration has an optimal level for each individual.
2) The blood glucose levels tend to be auto regulatory but they are also susceptible to a wide variety of hormones and some hormones here we have mentioned-

a) Insulin:- Screted by beta cell of pancreas, It reduce the blood sugar concentration.
b) Glycigen:- It secreted by alpha cell of pancreas. Any excessive glucose is stored in the liver in the form of glycogen and this glycogen is converted back into glucose in terms of need for low blood sugar
c) Thyroxin- thyroxin is the major hormone secreted by the follicular cells of the thyroid gland.It is important to note that is involved in controlling the rate of metabolic processes in the body and influencing physical development.Diabetic patients have a higher prevalence of thyroid disorders compared with the normal person. The presence of thyroid dysfunction may affect diabetic control. Hyperthyroidism is typically associated with worsening glycaemia control and increased insulin requirements. In patients without any thyroid dysfunction it normally segregated the thyroxim hormone which influence in the metabolism of the body ergo it can either increased or decreased blood sugar levels.

2. Mathematical model

Mathematical models have provided one of the understanding Diabetes dynamics. There are various models based on glucose and insulin distributions and those models have been used to explain glucose/insulin interaction. But this model are valid under certain conditions and assumptions.Although these models may be useful in research setting, they all have limitations in predicting blood glucose in real-time clincal situation because of the inherent requirement of frequently updated information about the models variable like glucose loads and insulin availability(4). Consider a mathematical model comprised of glucose level G, glucose uptake activity X and insulin level I. Many parameters have been taken and on the basis of these parameters values a mathematical model "Picard's Iteration Method"is formed. This model includes the basal values also G_b and I_b This model is defined as:

$$\frac{dG}{dt} = -m_1 G + m_2 I + m_1 G_b \quad (1)$$

$$\frac{dG}{dt} = f\left(G, I, G_b\right)$$, where $f\left(G, I, I_b\right) = -m_1 G + m_2 I + m_1 G_b$

Integrating on both sides with respect to t, we get

$$\int_{t_0}^{t} dG\left(t\right) = \int_{t_0}^{t} \left(-m_1 G + m_2 I + m_1 G_b\right) dt$$

$$G\left(t\right) - G\left(t_0\right) = \int_{t_0}^{t} \left(-m_1 G + m_2 I + m_1 G_b\right) dt$$

$$G\left(t\right) = G\left(t_0\right) + \int_{t_0}^{t} \left(-m_1 G + m_2 I + m_1 G_b\right) dt$$

$$G\left(t\right) = G_0 + \int_{t_0}^{t} f\left(G, I, G_b\right) dt$$, where $G_0 = G\left(t_0\right)$ (2)

Differentiating equation (2), we get

$$\frac{dG}{dt} = f\left(G, I, G_b\right)$$

Putting $t = t_0$ in equation (2) yields

$$G\left(t_0\right) = G_0 + 0$$

$$G\left(t_0\right) = G_0$$

Conversely equation (2) has been obtained from equation (1) by integrating over the interval $\left(t_0, t\right)$ and employing the initial condition

$$G\left(t_0\right) = G_0$$

Since the information concerning the expression of y in terms of x is absent, the integral on the R.H.S of (2) cannot be evaluated. Hence the exact value of y cannot be obtained. Therefore we determine a sequence of approximation to the solution (2) as follows.

$$G_1\left(t\right) = G_0 + \int_{t_0}^{t} f\left(G_0, I, G_b\right) dt \quad (3)$$

Where $G_1\left(t\right)$ the corresponding is value of $G\left(t\right)$ and is called first approximation and is better approximation of $G\left(t\right)$ at any t. To determine still better approximation we replace G_0 by G_1 in the R.H.S in (2). We obtain the second approximation as

$$G_2\left(t\right) = G_0 + \int_{t_0}^{t} f\left(G_1, I, G_b\right) dt \quad (4)$$

Proceeding in this way, the nth approximation is given by

$$G_n\left(t\right) = G_0 + \int_{t_0}^{t} f\left(G_{(n-1)}, I, G_b\right) dt$$, where $f\left(G_{(n-1)}, I, G_b\right) = -m_1 G_{(n-1)} + m_2 I + m_1 G_b$ (5)

Thus we arrive at a sequence of approximation solutions $G_1\left(t\right), G_2\left(t\right), \ldots\ldots, G_n\left(t\right)$.

3. Simultaneous differential equations

Picard's Method of solving simultaneous differential with initial conditions is as follows

$$\left.\begin{aligned}\frac{dG}{dt} &= f\left(G, I, G_b\right)\\ \frac{dI}{dt} &= g\left(I, G, I_b\right)\\ \frac{dX}{dt} &= h\left(X, I, I_b\right)\end{aligned}\right\}, \quad (6)$$

Where

$$G\left(t_0\right)=G_0,\ I\left(t_0\right)=I_0 \text{ when } X\left(t_0\right)=X_0 \quad (6)$$

Then the nth approximation $\left(G_n, I_n, X_n\right)$ to the initial value problem (1) is given by

$$G_n\left(t\right)=G_0+\int_{t_0}^{t} f\left(G_{(n-1)}, I, G_b\right)dt \quad (7)$$

$$I_n\left(t\right)=I_0+\int_{t_0}^{t} g\left(G_{(n-1)}, I, G_b\right)dt \quad (8)$$

$$X_n\left(t\right)=X_0+\int_{t_0}^{t} h\left(X_{(n-1)}, I, G_b\right)dt \quad (9)$$

To construct a mathematical model it is necessary to follow the following well known facts from the elementary biology-
Uniqueness Theorem
Let $f\left(G, I, G_b\right)$ be continuous in a domain D of the $\left(X=G\left(t\right), Y=I\left(t\right)\right)$ plane and let M be the constant such that

$$f\left(G, I, G_b\right) \le M \text{ in D} \quad (10)$$

Let $f\left(G, I, G_b\right)$ satisfy in D the Lipchitz condition in G namely

$$\left|f\left(G_1, I, G_b\right)-f\left(G_2, I, G_b\right)\right| \le K\left|G_1-G_2\right| \quad (11)$$

Where the constant K is independent of I, G_1, G_2
Let the rectangle R defined by $\left|G-G_0\right| \le h$ and $\left|I-I_0\right| \le k$ lie in D, where $Mh<k$. Then for $\left|G-G_0\right| \le h$, the differential equation $\frac{dG}{dt}=f\left(G, I, G_0\right)$ has a unique solution $I=I\left(t\right)$ for which $I\left(t_0\right)=I_0$
Step 1
We prove that for $t_0-h \le t \le t_0+h$ the curve $G=G_n\left(t\right)$ lies in the XY plane that is to say $I_0-k \le I \le I_0+k$
Now $I_1-I_0=\left|\int_{t_0}^{t} g\left(G_0, I, G_b\right)dt\right| \le \int_{t_0}^{t}\left|g\left(G_0, I, G_b\right)\right|\left|dt\right|$ using (8)
$\Rightarrow \left|I_1-I_0\right| \le M\left|G-G_0\right| \le Mh<k$ using (10), (11) and the given result viz $Mk<k$
This proves the desired result for n=1
Assume that $I=I_{n-1}\left(t\right)$ lies in XY-plane and so $f\left(G, I_{n-1}\right)$ is defined and continuous ans satisfies $\left|f\left(G, I_{n-1}\right)\right| \le M$ on $\left[t_0-h, t_0+h\right]$
From (8) we have

$$\left|I_n-I_0\right|=\left|\int_{t_0}^{t} f\left(G, I_{n-1}\right)dt\right| \le \int_{t_0}^{t}\left|f\left(G, I_{n-1}\right)\right|\left|dt\right| \le M\left|G-G_0\right| \le Mh<k$$

As before which shows that $I_n\left(t\right)$ lie in XY plane and hence $f\left(G, I_n\right)$ is defined and continuous on $\left[t_0-h, t_0+h\right]$. Thus the above arguments show that the desired result holds for all n by induction.ep
Step 2

4. Numerical solution

The analysis is done on the normal person as well as on different types of diabetic patient. That is patient 1, patient 2, patient 3 and patient 4. Basically there are patients who are suffering from Diabetes mellitus but the results from each patient is different and it is explained with the help of graphs and parameters values. Glucose is given to the patients then we studied the plasma glucose concentration, plasma insulin concentration and generalized insulin variable in the body of patients. The graph for these types of patients is obtained by MATLAB.
There are some variables and symbols used in the graphs: G (t)-The plasma glucose concentration at time t (mg/dl)"*".X (t) - The generalized insulin variable for the remote compartment (min-1) ,"." I(t)-The plasma insulin concentration at time t $\left(\mu U/ml\right)$,"O"

Table 1: Parametric Values of the Four Patients

Parameters	Patent 1	Patent 2	Patent 3	Patent 4
m_1	0.0317000	0	0	0
m_2	0.0123	0.017	0.072	0.0142
m_3	0.00000492	0.0000053	0.000216	0.00000994
m_4	0.0039	0.0042	0.0038	0.0046
m_5	79.0353	80.25	77.5783	82.9370
m_6	0.2659	0.264	0.2465	0.2814
G_b	80	80	80	80
I_b	7	7	7	7

5. Data for normal person

The study of normal person shows that initially when glucose is given glucose concentration become very high and as time passes the level become stable, the values of parameters are given in Table 1

$$\frac{dG}{dt} = -m_1 G + m_2 I + m_1 G_b + \sin(t)$$

Or

$$\frac{dG}{dt} = f\left(m_1, m_2, I, G, G_b\right)$$

$$\frac{dI}{dt} = -m_3 I + m_4 G + m_4 m_5 - m_6 I + m_6 I_b$$

$$\frac{dI}{dt} = h\left(m_3, m_4, m_5, m_6, I, I_b\right)$$

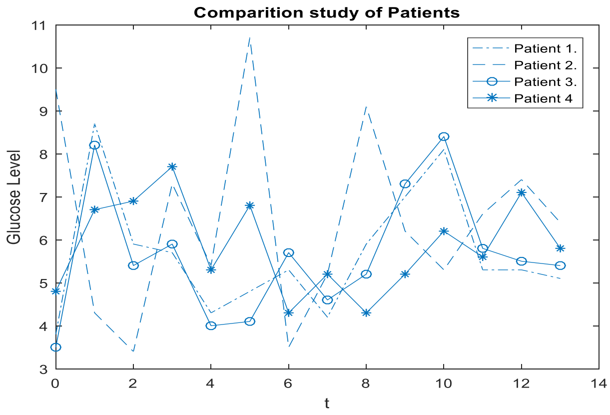
$$\frac{dX}{dt} = -m_2 X + m_3 I - m_3 I_b + m_6 I_b$$

$$\frac{dX}{dt} = g\left(m_2, m_3, I, I_b\right)$$

Table 2: Patients Glucose level

Time	0	1	2	3	4	5	6	7	8	9	10	11	12	13
Glucose/Patient 1	3.8	8.7	5.9	5.7	4.3	4.8	5.3	4.2	5.9	7.0	8.1	5.3	5.3	5.1
Glucose/Patient2	9.5	4.3	3.4	7.3	5.4	10.7	3.5	5.2	9.1	6.2	5.3	6.6	7.4	6.4
Glucose/Patient 3	3.5	8.2	5.4	5.9	4.0	4.1	5.7	4.6	5.2	7.3	8.4	5.8	5.5	5.4
Glucose/Patient 4	4.8	6.7	6.9	7.7	5.3	6.8	4.3	5.2	4.3	5.2	6.2	5.6	7.1	5.8

```
% -------------------------------------------------------------------
% Generated by MATLAB on 23-Jan-2022 13:45:00
% MATLAB version: 9.0.0.341360 (R2016a)
% -------------------------------------------------------------------
t=0:13
y1=[3.8 8.7 5.9 5.7 4.3 4.8 5.3 4.2 5.9 7.0 8.1 5.3 5.3 5.1];
y2=[9.5 4.3 3.4 7.3 5.4 10.7 3.5 5.2 9.1 6.2 5.3 6.6 7.4 6.4];
y3=[3.5 8.2 5.4 5.9 4.0 4.1 5.7 4.6 5.2 7.3 8.4 5.8 5.5 5.4];
y4=[4.8 6.7 6.9 7.7 5.3 6.8 4.3 5.2 4.3 5.2 6.2 5.6 7.1 5.8];
plot(t,y1,'linestyle','-.')
line(t,y2,'linestyle','--')
line(t,y3,'marker','o')
line(t,y4,'marker','*')
xlabel('t')
ylabel('Glucose Level')
title('Comparition study of Patients')
legend('Patient 1.','Patient 2.','Patient 3.','Patient 4')
```



The MATLAB picture shows that '-.' line indicates the patient 1, '—'line indicates the patient 2, '0' line indicates the patient 3 and '*' line indicates the patient 4 flow chart. This chart shows the patient 2 glucose levels are abnormal, patient 1 and patient 3 are more are less the same condition and patient 4 condition is controllable (It can be controlled either by medicine or by diet control).

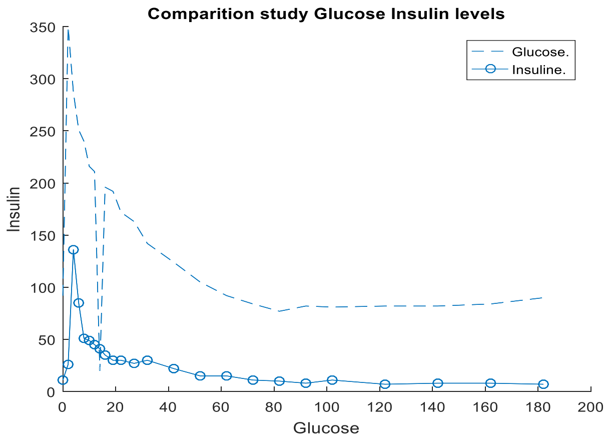
6. Example

Table 3: Insulin and Glucose Plasma Levels During an FSIGT Test

Time	Glucose	Insulin	Age	Time	Glucose	Insulin	Age	Time	Glucose	Insulin	Age
0	92	11	50	16	196	35	53	72	84	11	31
2	350	26	31	19	192	30	54	82	77	10	31
4	287	136	32	22	172	30	30	92	82	08	33
6	251	85	21	27	163	27	34	102	81	11	32
8	240	51	33	32	142	30	57	122	82	07	27
10	216	49	30	42	124	22	59	142	82	08	50
12	211	45	26	52	105	15	51	162	84	08	41
14	20	41	29	62	92	15	32	182	90	07	29

```
% -------------------------------------------------------------------
% Generated by MATLAB on 13-Feb-2022 10:45:00
% MATLAB version: 9.0.0.341360 (R2016a)
% -------------------------------------------------------------------
g=[92 350 287 251 240 216 211 20 196 192 172 163 142 124 105 92 84 77 82 81 82 82 84 90];
i=[11 26 136 85 51 49 45 41 35 30 30 27 30 22 15 15 11 10 08 11 07 08 08 07];
line(t,g,'linestyle','--')
line(t,i,'marker','o')
xlabel('Glucose')
ylabel('Insulin')
title('Comparition study Glucose Insulin levels')
legend('Glucose.','Insuline.')
```

There are some variables and symbols used in the graphs: G (t). The plasma glucose concentration at time t (mg/dl) "--".X(t). The generalized insulin variable for the remote compartment (min-1) ,"o" I(t).



7. Conclusion

This model shows the difference of glucose-insulin regulatory system, between a normal person and diabetic person. The glucose concentration of diabetic patient does not come down after a certain time which shows the evidence that the person suffer from diabetes. This model makes the accurate level of glucose-insulin in the patient's body by using the Iterative method, which is useful for clinical purposes through a careful assessment of the relevant parameter. From the above observation, that when insulin level increases the Glucose level also increases. When the insulin level lies between the intervals of 90 to100, the patient may have normal Glucose level. We did not care about the time and age factor(diabetic person).

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