Models for the detection of Diabetes

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1 Biological background

We shall first give a short introduction to the problem by presenting the biological basis of it, which is helpful in understanding the mathematical formulations.

Glucose is the main source of energy for our cells. We obtain it either directly from food or as a result of metabolism of other saccharides. All cells need glucose, but nerve cells are critical and there needs to be glucose available for them at every instant. As a result, the core of glucose metabolism goes like this: After a period of not eating, a constant level of glucose in the bloodstream should be established, some is consumed by cells and this loss is balanced by glucose in the form of glycogen released by liver. When we then ingest some saccharides, they shall be metabolised into glucose and as a result, it's concentration in the bloodstream increases. In this situation, the pancreas releases the hormone insulin, which sends a signal to cells (other than nerve cells) that they should now absorb more glucose from the bloodstream. At the same time, liver reacts to increased level of glucose in the bloodstream by absorbing it and converting it to glycogen for storage. Liver also decomposes the insulin. There are other hormones and factors which play a role in the metabolism of glucose, but we neglect them.

If the concentration of insulin in bloodstream is too high, then cells absorb most of the glucose and as a result, there may not be enough for the nerve cells, which may end up by coma or death. If the level of insulin is too low, then cells cannot obtain the energy they need for normal functioning. The later is the case which happens for people suffering by the disorder Diabetes Mellitus: Their bodies create insufficient amounts of insulin.

2 Bolie's diabetes model

Bolie's diabetes model is based on the following general assumptions, taken from [1]:

1. Insulin is being degraded by the liver.
2. A rise in the concentration of glucose in the bloodstream results in increased production of insulin by the pancreas.
3. With increasing concentration of insulin, the glucose is more easily absorbed by the cells, i.e. it leaves the bloodstream more quickly.
4. A rise in glucose concentration in the bloodstream results in increased glucose absorption by the liver.

The model, described by eq. 1, takes into account just two variables – glucose G and hormone insulin, denoted by H. Generally nonlinear functions on the right hand side of the equations follow directly from the assumptions above. The symbols with their corresponding meaning and units are summarized in Tab. 1.

$$\begin{aligned} V\frac{\mathrm{d}H}{\mathrm{d}t} &= -F_1(H) + F_2(G) + x \\ V\frac{\mathrm{d}G}{\mathrm{d}t} &= -F_3(H,G) - F_4(H,G) + y \end{aligned} \tag{1}$$

For changes around equilibrium H_0, G_0 we can rewrite the model to:

$$\begin{aligned} V\frac{\mathrm{d}h}{\mathrm{d}t} &= -F_1(H_0+h) + F_2(G_0+g) + x \\ V\frac{\mathrm{d}g}{\mathrm{d}t} &= -F_3(H_0+h, G_0+g) - F_4(H_0+h, G_0+g) + y \end{aligned} \tag{2}$$

For small changes around the equilibrium it is possible to use linearized model. By Taylor expanding the eq. 2 we get:

$$\begin{aligned}
\frac{\mathrm{d}h}{\mathrm{d}t} &= -\underbrace{\frac{1}{V}\frac{\partial F_1(H_0)}{\partial H}}_{\alpha} h + \underbrace{\frac{1}{V}\frac{\partial F_2(G_0)}{\partial G}}_{\beta} g + O(2) + \dots \\
\frac{\mathrm{d}g}{\mathrm{d}t} &= -\frac{1}{V}\frac{\partial F_3(H_0,G_0)}{\partial H} h - \frac{1}{V}\frac{\partial F_3(H_0,G_0)}{\partial G} g - \frac{1}{V}\frac{\partial F_4(H_0,G_0)}{\partial H} h - \frac{1}{V}\frac{\partial F_4(H_0,G_0)}{\partial G} g + \mathcal{O}(2) + \dots \\
&= -\underbrace{\left(\frac{1}{V}\frac{\partial F_3(H_0,G_0)}{\partial H} + \frac{\partial F_4(H_0,G_0)}{\partial H}\right)}_{\gamma} h - \underbrace{\left(\frac{1}{V}\frac{\partial F_3(H_0,G_0)}{\partial G} + \frac{\partial F_4(H_0,G_0)}{\partial G}\right)}_{\delta} g + \mathcal{O}(2) + \dots
\end{aligned}$$

By omitting the second and higher order terms we get the following linear model:

$$\begin{aligned}
\frac{\mathrm{d}h}{\mathrm{d}t} &= -\alpha h + \beta g \\
\frac{\mathrm{d}g}{\mathrm{d}t} &= -\gamma h - \delta g
\end{aligned} \tag{3}$$

All of the constants α, β, γ, δ are positive. Let's check that the signs correspond to Bolie's assumptions. If we put $g = 0$ we can see from the first equation that the concentration of insulin decreases in time, which is in agreement with the first assumption. On the other hand, if we put $h = 0$ we can see that increase in g leads to increase in h, which is in accordance with the second assumption. Assumptions 3 and 4 say that rise in each of the variables results in decrease of glucose concentration and the negative signs at both terms in the second equation reflect that.

Symbol	**Meaning**	**Dimension**
V	volume	L
x	rate of insulin injection	units h^{-1}
y	rate of glucose injection	$\mathrm{g\,h}^{-1}$
H	insulin concentration	units L^{-1}
H_0	insulin concentration equilibrium	units L^{-1}
h	insulin concentration changes	units L^{-1}
G	glucose concentration	$\mathrm{g\,L}^{-1}$
G_0	glucose concentration equilibrium	$\mathrm{g\,L}^{-1}$
g	glucose concentration changes	$\mathrm{g\,L}^{-1}$
$F_1(H)$	rate of insulin destruction	units h^{-1}
$F_2(G)$	rate of insulin production	units h^{-1}
$F_3(H,G)$	rate of liver accumulation of glucose	$\mathrm{g\,h}^{-1}$
$F_4(H,G)$	rate of tissue utilization of glucose	$\mathrm{g\,h}^{-1}$

Table 1: Diabetes model parameters.

3 Linearized model solution

We can reduce the linearized model from eq. 3 to a 2^{nd} order by differentiating the first equation and substituting $\dot{h}$ with the second equation. h is substituted with the expression for h derived from the first equation. We get:

$$\ddot{g} + (\alpha + \delta)\dot{g} + (\beta\gamma + \delta\alpha)g = 0, \tag{4}$$

The solutions are found by solving the characteristic polynomial

$$\lambda^2 + (\alpha + \delta)\lambda + (\beta\gamma + \delta\alpha) = 0 \tag{5}$$

$$\lambda_{1,2} = \frac{1}{2}\left(-(\alpha+\delta) \pm \sqrt{(\alpha-\delta)^2 - 4\beta\gamma}\right) \tag{6}$$

Since both $(\alpha+\delta)$ and $(\beta\gamma+\delta\alpha)$ are positive, the solutions are always stable, going to zero with $t \to \infty$. If the discriminant is lower than zero then the solutions go to zero periodically, otherwise aperiodically.

4 Bolie's diabetes test

predpoklada kriticky tlumene reseni

bod 4, povidani o testu

ploty reseni g,h, diskuze viz. 4

nabizi se vlozit reseny priklad, napr. 4 na str. 108

5 Ackermann's diabetes test

predpoklada kmitave reseni

opsat par rovnic ze strany 105/106

vyresit ten stejny priklad jako vyse

References

[1] G. Fulford, *Modelling with Differential and Difference Equations*. Cambridge University Press, Jun. 1997.