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On the dynamics of the discrete delay models of Glucose-Insulin systems

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Abstract.
In this paper, we study the dynamics of the discrete delay models of Glucose-Insulin systems

\[ G_{n+1} = \alpha G_n - \beta G_n I_{n-m} + \Gamma \quad (0.1) \]
\[ I_{n+1} = \lambda I_n + \Delta f(G_{n-m}) \quad (0.2) \]

We are interested in providing sufficient conditions guaranteeing the fact that all positive solutions of this systems converge to the positive equilibrium.

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Introduction and Preliminaries

Our main motivation in studying the dynamics of the systems (0.1-0.2) is the dynamics of the differential version systems of (0.1-0.2), namely of the system

\[
\dot{G}(t) = -K_{xg}G(t) - K_{xgi}G(t)I(t - \tau_i) + \frac{T_{gh}}{V_G} \tag{0.3}
\]

\[
\dot{I}(t) = -K_{xi}I(t) + \frac{T_{iG_{\text{max}}}}{V_I} f(G(t - \tau_g)) \tag{0.4}
\]

investigated in [3].

However, it is very interesting to see the connection of (0.3-0.4) to (0.1-0.2). In practice, when formulating (0.3-0.4), we actually replace the first derivative \(\dot{G}(t)\) and \(\dot{I}(t)\) of \(G\) and \(I\) at \(t\) by their first right approximation

\[
\frac{G(t + h) - G(t)}{h}, \quad \frac{I(t + h) - I(t)}{h}
\]

for \(h > 0\) sufficient small. Thus, formally, system (0.3-0.4) comes from

\[
\frac{\ddot{G}(t + h) - \ddot{G}(t)}{h} = -K_{xg}G(t) - K_{xgi}G(t)I(t - \tau_i) + \frac{T_{gh}}{V_G}
\]

\[
\frac{\ddot{I}(t + h) - \ddot{I}(t)}{h} = -K_{xi}I(t) + \frac{T_{iG_{\text{max}}}}{V_I} f(G(t - \tau_g)),
\]

for small \(h\). If we set

\[
G_h(t) := \ddot{G}(ht), \quad I_h(t) := \ddot{I}(ht), \quad t = nh, \frac{\tau_i}{h} = m_i, \frac{\tau_g}{h} = m_g,
\]

then preceding system becomes

\[
G_h(n + 1) = \alpha G_h(n) - \beta G_h(n)I_h(n - m_i) + \Gamma
\]

\[
I_h(n + 1) = \lambda I_h(n) + \Delta f(G_h(n - m_g)),
\]

or

\[
G_{n+1} = \alpha G_n - \beta G_nI_{n-m_i} + \Gamma
\]

\[
I_{n+1} = \lambda I_n + \Delta f(G_{n-m_g}),
\]
where

\[ \alpha = 1 - hK_{xg}, \beta = hK_{xgi}, \Gamma = h\frac{T_{gh}}{V_G}, \lambda = 1 - hK_{zi}, \Delta = h\frac{T_{gmax}}{V_I}. \]

2. The results

We consider the following discrete system of Glucose and Insulin

\[ G_{n+1} = \alpha G_n - \beta G_n I_{n-m_i} + \Gamma \]
\[ I_{n+1} = \lambda I_n + \Delta f(G_{n-m_g}), \]

where

\[ f(G) = \frac{G^\gamma}{G^\gamma + G^*_\gamma} \]

defined on positive reals, \( \alpha, \lambda \in (0, 1) \) and \( \beta, \Gamma, \lambda, \Delta \) are positive parameters. The derivative of \( f \) is

\[ f'(G) = \frac{\gamma G^*_\gamma G^{\gamma-1}}{(G^\gamma + G^*_\gamma)^2} > 0, \]

so \( f \) is increasing. We have

\[ \sup_{G \geq 0} f(G) = 1 \]

and

\[ f''(G) = 2G^*_\gamma G^{\gamma-2} \frac{(\gamma - 1)G^*_\gamma - (\gamma + 1)G^\gamma}{(G^\gamma + G^*_\gamma)^2} \]

so, if \( \gamma \leq 1 \), \( f' \) is decreasing, and if \( \gamma > 1 \), \( f' \) is unimodal. Thus,

\[ \sup_{G \geq 0} f'(G) = f'(G_0) = \frac{(\gamma + 1)^2(\gamma - 1)}{4\gamma G_0}, \quad \text{if } \gamma > 1, \quad \text{where } G_0 = \sqrt[\gamma]{\frac{\gamma - 1}{\gamma + 1}}, \]

\[ \sup_{G \geq 0} f'(G) = f'(0) = \frac{1}{G_*}, \quad \text{if } \gamma = 1, \]

\[ \sup_{G \in [0, G]} f'(G) = \infty, \quad \text{if } \gamma < 1, \]

\[ \sup_{G \in (G, \infty)} f'(G) = f'(\overline{G}), \quad \text{if } \gamma < 1. \]
System \((0.5-0.6)\) has a unique positive equilibrium \((\bar{G}, \bar{I})\), which consists of the basal levels of glucose and insulin concentrations. These levels satisfy the following system

\[
\bar{G}(1 - \alpha + \beta \bar{I}) = \Gamma \\
\bar{I} = \frac{\Delta}{1 - \lambda} f(\bar{G}).
\]

We now let

\[
G_m = \lim\inf_{n \to \infty} G_n, \quad G_M = \lim\sup_{n \to \infty} G_n, \quad I_m = \lim\inf_{n \to \infty} I_n, \quad I_M = \lim\sup_{n \to \infty} I_n.
\]

**Proposition.** For every persistent solution \((G_n, I_n)\) of the system \((0.5-0.6)\), we have

\[
I_m \leq \bar{I} \leq I_M \leq \frac{\Delta}{1 - \lambda} \sup_{G \geq 0} f(G)
\]

\[
G_m \leq \bar{G} \leq G_M \leq \frac{\Gamma}{1 - \alpha + \beta I_m}.
\]

**Proof.** First, we construct four full time solutions \((\bar{G}_n, \bar{I}_n), (\tilde{G}_n, \tilde{I}_n), (\bar{G}_n, \tilde{I}_n), (\tilde{G}_n, \bar{I}_n)\) such that

\[
\bar{I}_0 = I_M, \quad \bar{I}_n \geq I_m, \quad G_m \leq \bar{G}_n \leq G_M, \quad \forall n \in \mathbb{Z},
\]

\[
\tilde{G}_0 = G_m, \quad \tilde{G}_n \leq G_M, \quad I_m \leq \tilde{I}_n \leq I_M, \quad \forall n \in \mathbb{Z},
\]

\[
\tilde{I}_0 = I_m, \quad \tilde{I}_n \leq I_M, \quad G_m \leq \tilde{G}_n \leq G_M, \quad \forall n \in \mathbb{Z},
\]

\[
\bar{G}_0 = G_M, \quad \bar{G}_n \geq G_m, \quad I_m \leq \bar{I}_n \leq I_M, \quad \forall n \in \mathbb{Z}.
\]

We have the following inequality

\[
I_M = \tilde{I}_0 = \lambda \bar{I}_0 + \Delta f(\bar{G}_{-1-m_0}) \leq \alpha \bar{I}_0 + \Delta f(\bar{G}_{-1-m_0})
\]

\[
I_M = \bar{I}_0 \leq \frac{\Delta}{1 - \lambda} f(\bar{G}_{-1-m_0}).
\]
If $\tilde{G}_{-1-m} < \overline{G}$, then $G_m < \overline{G}$ and
\[
I_M \leq \frac{\Delta}{1-\lambda} f(\tilde{G}_{-1-m}) < \frac{\Delta}{1-\lambda} f(\overline{G}) = \overline{I}.
\]

On the other hand,
\[
G_m = \tilde{G}_0 = \alpha \tilde{G}_{-1} - \beta \tilde{G}_{-1-1-m} + \Gamma \\
\geq \alpha \tilde{G}_0 - \beta \tilde{G}_0 \tilde{I}_{-1-m} + \Gamma \\
\tilde{G}_0 (1 - \alpha + \beta \tilde{I}_{-1-m}) \geq \Gamma \\
G_m (1 - \alpha + \beta \tilde{I}_{-1-m}) \geq \Gamma.
\]

But in this case $G_m < \overline{G}$ and $I_M < \overline{I}$, so we have
\[
\Gamma \leq G_m (1 - \alpha + \beta \tilde{I}_{-1-m}) < \overline{G} (1 - \alpha + \beta \tilde{I}) = \Gamma,
\]
which is a contradiction. Therefore, the hypothesis that $\tilde{G}_{-1-m} < \overline{G}$ is false.

So we have $\tilde{G}_{-1-m} \geq \overline{G}$, and consequently, $I_M \geq \overline{I}$ and $G_M \geq \overline{G}$. By using two full time solutions $\tilde{G}_n, \tilde{I}_n$, $\tilde{G}_n, \tilde{I}_n$ we will get $I_m \leq \overline{I}$ and $G_m \leq \overline{G}$. The proof is complete.

**Theorem 1.** Assume that $(G_n, I_n)$ is a persistent solution of the system (0.5-0.6). If one of $\{G_n\}_n$ and $\{I_n\}_n$ does not oscillate around its basal level, then both of them converge to their basal levels.

**Proof.** From the proof of Proposition 1 we have
\[
\frac{\Delta}{1-\lambda} f(G_m) \leq I_m \leq \overline{I} \leq I_M \leq \frac{\Delta}{1-\lambda} f(G_M) \\
G_M (1 - \alpha + \beta I_m) \leq \Gamma \leq G_m (1 - \alpha + \beta I_M).
\]

From the inequality $\Gamma \leq G_m (1 - \alpha + \beta I_M)$, it follows that if $I_M = \overline{I}$, then $\Gamma = \overline{G} (1 - \alpha + \beta \overline{I}) \leq G_m (1 - \alpha + \beta \overline{I})$, this implies $\overline{G} \leq G_m$. Therefore $G_m = \overline{G}$. Now, the inequality $\frac{\Delta}{1-\lambda} f(G_m) \leq I_m$ will give $\overline{I} \leq I_m$ so that $I_m = \overline{I}$, that is $\lim_{n \to \infty} I_n = \overline{I}$. Again by $G_M (1 - \alpha + \beta I_m) \leq \Gamma$ we have $G_M = \overline{G}$, or equivalently, $\lim_{n \to \infty} G_n = \overline{G}$.

Similarly, if $I_m = \overline{I}$, then $G_M = \overline{G}$. We can conclude that both $\{I_n\}_n$ and $\{G_n\}_n$ converge to their basal levels. The proof is complete.
Now, we let \((G_n, I_n)\) be an oscillated solution of the system of equation (0.5-0.6). Here, the oscillation means the oscillation around the basal levels.

**Theorem 2.** Put

\[
L_1 = \frac{\Delta}{1 - \lambda} \sup_{\mathcal{E}} f'(G), \quad L_2 = \frac{\Delta}{1 - \lambda} \sup_{G \in [0, \mathcal{E}]} f'(G),
\]

\[
L_3 = \frac{\Gamma \beta}{(1 - \alpha + \beta I)(1 - \alpha + \beta I_M)}, \quad L_4 = \frac{\Gamma \beta}{(1 - \alpha + \beta I)(1 - \alpha + \beta I_M)}.
\]

If \(L_1 L_2 L_3 L_4 < 1\), then every positive solution of the (0.5-0.6) converge to the positive equilibrium, or equivalently, their basal levels are globally attractive.

**Proof.** We construct two full time solutions \((\tilde{G}_n, \tilde{I}_n)\), \((\tilde{G}_n, \tilde{I}_n)\) such that

\[
\tilde{I}_0 = I_M, \quad \tilde{I}_n > I_m, \quad G_m \leq \tilde{G}_n \leq G_M, \quad \forall n \in \mathbb{Z},
\]

\[
\tilde{G}_0 = G_m, \quad \tilde{G}_n \leq G_M, \quad I_m \leq \tilde{I}_n \leq I_M, \quad \forall n \in \mathbb{Z}.
\]

As before, we have

\[
I_M = \tilde{I}_0 \leq \frac{\Delta}{1 - \lambda} f(\tilde{G}_{1-m}).
\]

It follows that

\[
I_M - \tilde{I} \leq \frac{\Delta}{1 - \lambda} \left( f(\tilde{G}_{1-m}) - f(G) \right) \leq L_1 (G_M - \tilde{G}),
\]

and

\[
\tilde{I} - I_m \leq \frac{\Delta}{1 - \lambda} \left( f(G) - f(G_m) \right) \leq L_2 (G - G_m).
\]

On the other hand,

\[
G - G_m \leq \frac{\Gamma}{1 - \alpha + \beta \tilde{I}} - \frac{\Gamma}{1 - \alpha + \beta I_M} \leq L_3 (I_M - \tilde{I}),
\]

and

\[
G_M - G \leq \frac{\Gamma}{1 - \alpha + \beta I_m} - \frac{\Gamma}{1 - \alpha + \beta \tilde{I}} \leq L_4 (\tilde{I} - I_m).
\]

Therefore, we get
\[ I_M - \bar{I} \leq L_1 L_2 L_3 L_4 (I_M - \bar{I}), \]
\[ G_M - \bar{G} \leq L_1 L_2 L_3 L_4 (G_M - \bar{G}), \]

so \( I_M = \bar{I} = I_m, G_M = \bar{G} = G_m \) and this completes the proof.

Remark. Theorem 2 is still true in the case \( \alpha = 1 \). Indeed, in this case the system (0.5-0.6) becomes

\[
G_{n+1} = G_n - \beta G_n I_{n-m} + \Gamma \\
I_{n+1} = \lambda I_n + \Delta f(G_{n-m}),
\]

and the basal levels satisfy the following system

\[
\bar{G} \beta \bar{I} = \Gamma \\
\bar{I} = \frac{\Delta}{1 - \lambda} f(\bar{G}).
\]

It is proved in [3] that if

\[
\gamma > \frac{G'_1 + (\bar{G})^\gamma}{G'_1},
\]

there are \( m_* \) an \( M_* \) such that \( m_* < \bar{G} < M_* \) and

\[
m_* f(M_*) = M_* f(m_*) = \bar{G} f(\bar{G}).
\]

Moreover, we conclude that

\[
m_* \leq G_m \leq \bar{G} \leq G_M \leq M_*,
\]

\[
\bar{I} \cdot \frac{1}{M_*} \leq I_m \leq \bar{I} \leq I_M \leq \bar{I} \cdot \frac{1}{m_*}.
\]

Since

\[
\frac{G_m}{G} \geq \frac{\bar{I}}{\bar{I} - 1 - m_i} \geq \frac{\bar{I}}{I_M},
\]

so

\[
\bar{G} - G_m = \bar{G} \left(1 - \frac{G_m}{G}\right) \leq \bar{G} \left(1 - \frac{\bar{I}}{I_M}\right) \leq \bar{G} \left(\frac{I_M - \bar{I}}{I}\right) \leq \frac{\bar{G}}{I} (I_M - \bar{I}).
\]
On the other hand, we have

\[ G_M - \overline{G} \leq M_0 - \overline{G} = \frac{M_0}{\bar{I}} \left( \bar{I} - \frac{\bar{I} \cdot \overline{G}}{M_0} \right) \leq \frac{M_0}{\bar{I}} (\bar{I} - I_m). \]

Therefore, if

\[ \frac{\overline{G}}{\bar{I}} \cdot \frac{M_0}{\bar{I}} < 1, \]

then \( G_M = \overline{G} = G_m \). So, the proof is complete.

References

