Diabetes Modeling and Sensitivity Analysis

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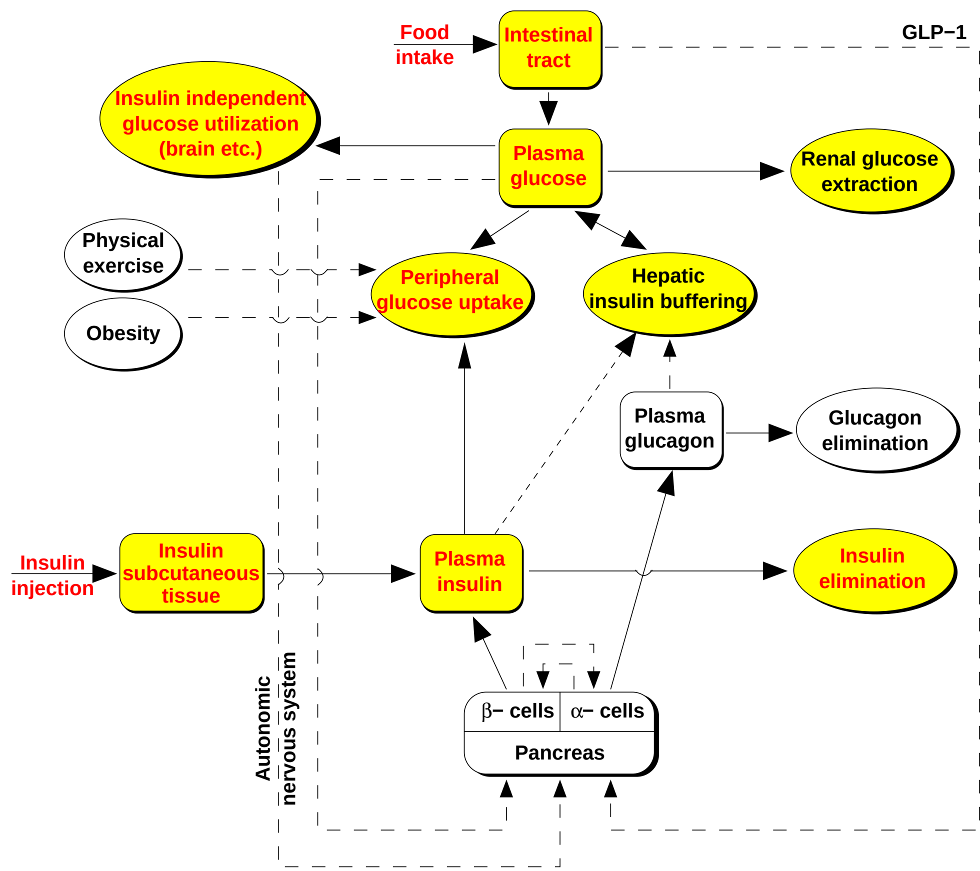
  - $\sim$ Fast healthy Insulin Glucose System

Completes System for IGS

- Insulin-Glucose System (IGS)



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- Sensors
  - samples glucose every 5min

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$$\dot{G}(t) = -(b_1 + X(t))G(t) + b_1 G_b, G(0) = b_0,$$

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$$\dot{I}(t) = b_4(G(t) - b_5)^+ t - b_6(I(t) - I_b), I(0) = b_7 + I_b.$$

where $(G(t) - p_5)^+ = G(t) - p_5$ if $G(t) \geq p_5$ and 0 otherwise.

- $X(t)$ denotes an auxiliary function representing **insulin-excitable tissue** glucose uptake activity.

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- Simple example

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$$x(s) = 1, -1 \leq s \leq 0.$$

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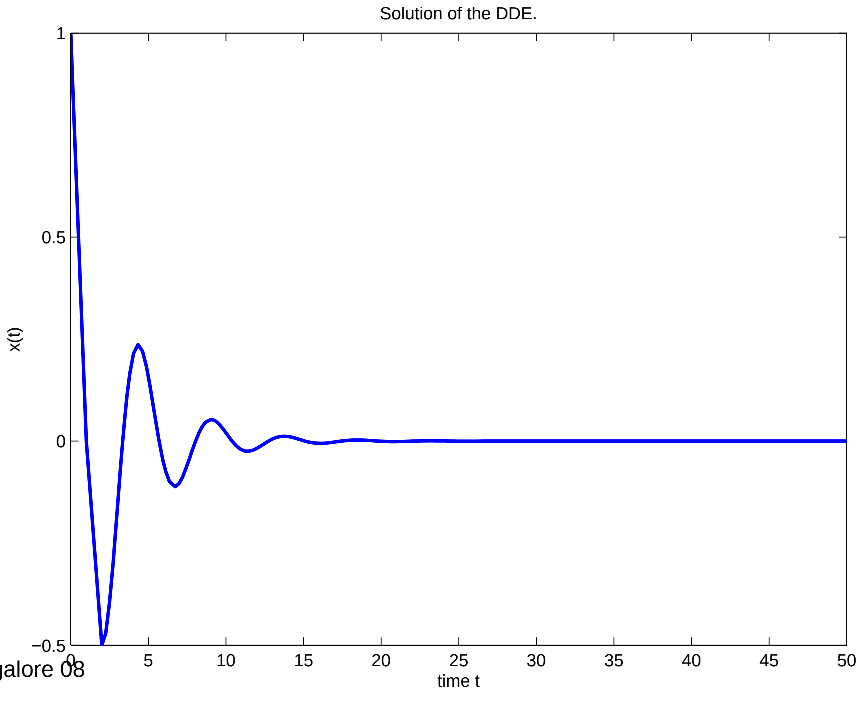

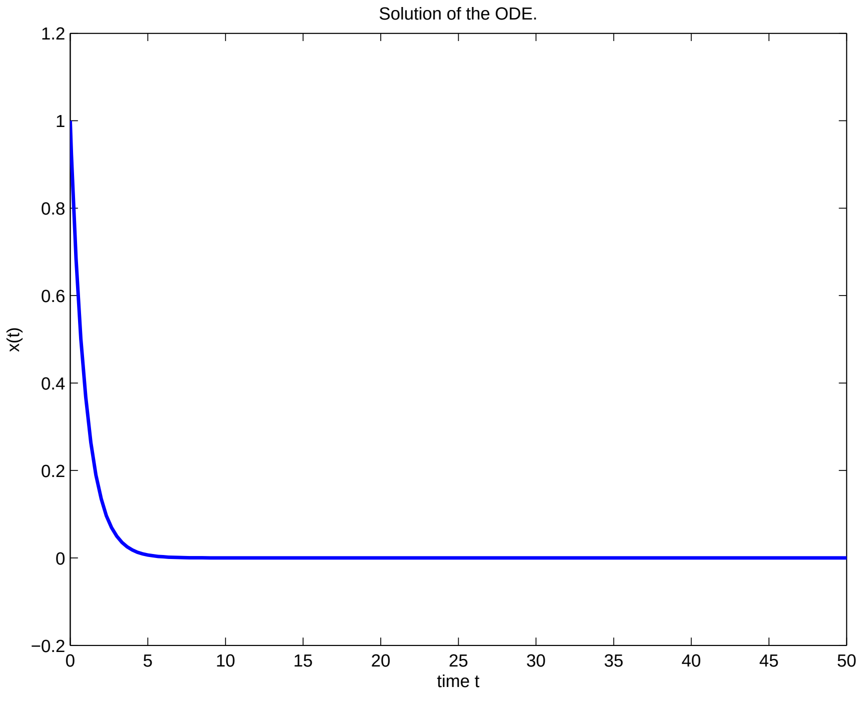

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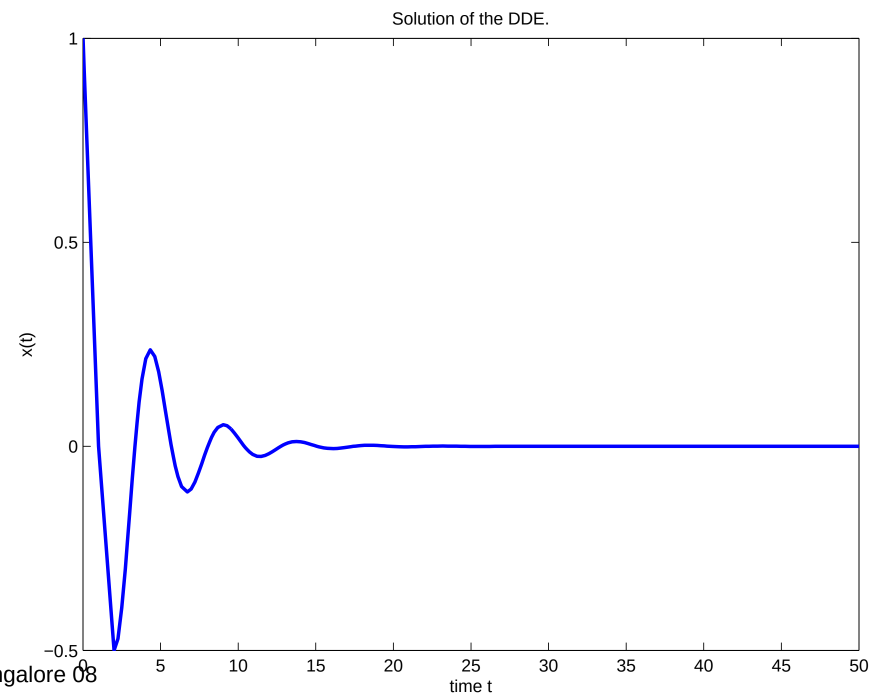

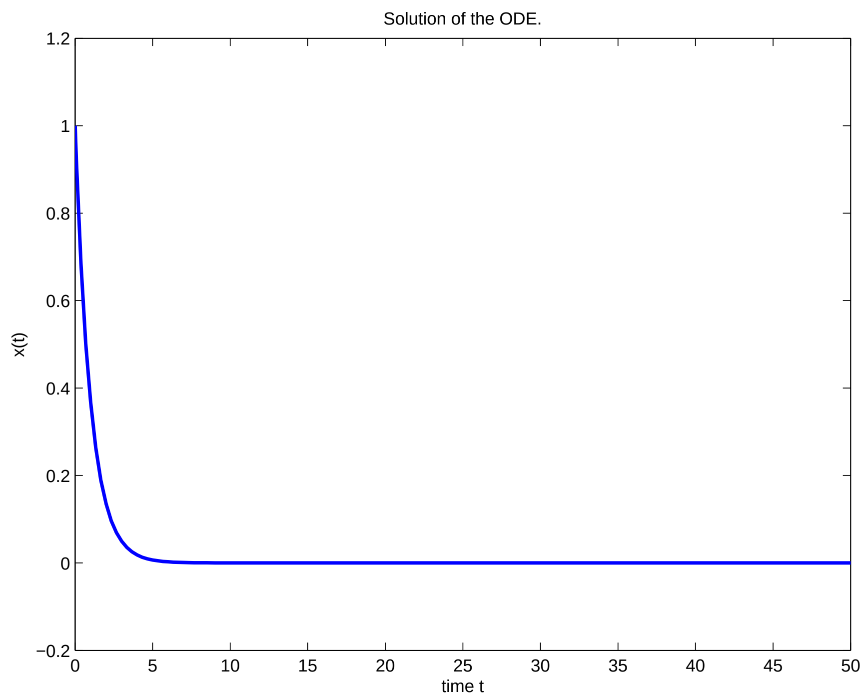

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- J. Hale, 1977.

$$\dot{x}(t) = F(t, x(t), x(t+\theta)), t \geq 0,$$
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- This model have positive, bounded solution, and to be globally asymptotically stable around equilibrium.

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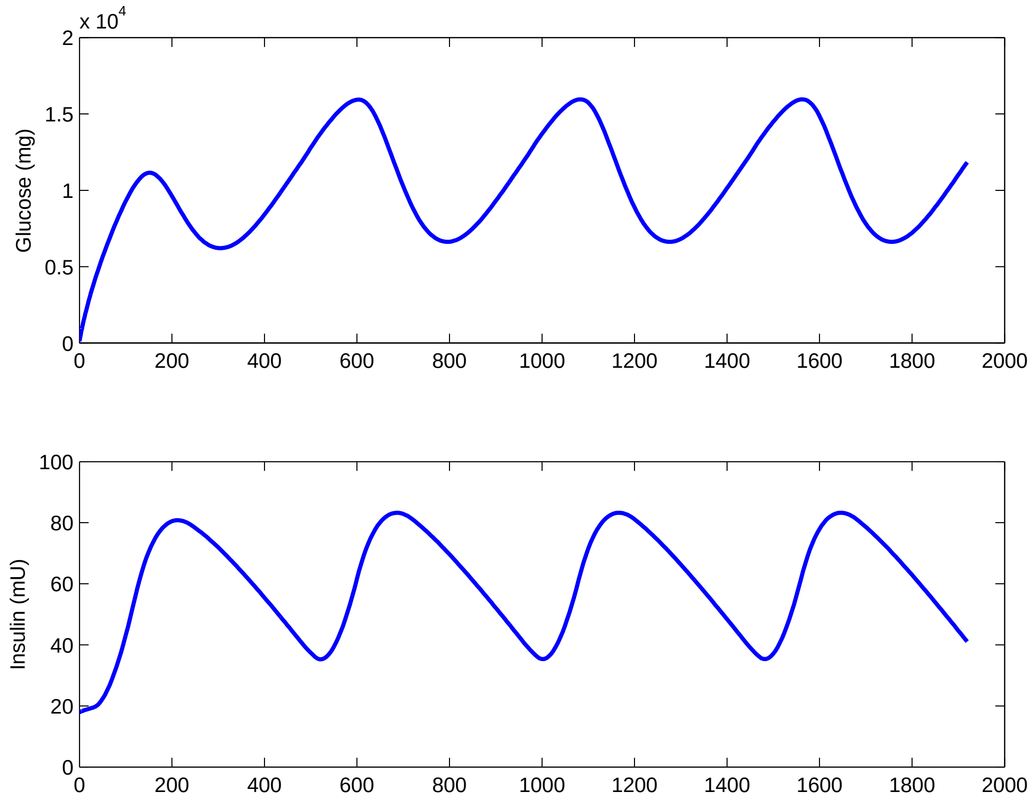

Model reduction

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Sensitivity Analysis

$$y = y(p) = f(t, p), \quad p \in D,$$

where D is some open interval and y is differentiable on D. Let $p_0 \in D$ be given and assume that $p_0 \neq 0$, $y_0 = y(p_0) \neq 0$. In view of our assumption on p_0 and y_0 it makes sense to consider the relative errors $\Delta p/p_0$ and $\Delta y/y_0$. The sensitivity $\sigma_{y,p}(p_0)$ of y with respect to p at p_0 is defined by

$$\sigma_{y,p}(p_0) = \lim_{\Delta p \to 0} \frac{\Delta y/y_0}{\Delta p/p_0} = \frac{p_0}{y_0}\, y'(p_0).$$

Simple impulses Model

$$\dot{Q}_f(t) = -K_{fq} Q_f(t) + \sum_{i=1}^{n} \delta(t - t_{f,i}) D_{f,i}\,, \quad Q_f(0) = Q_{f,0},$$

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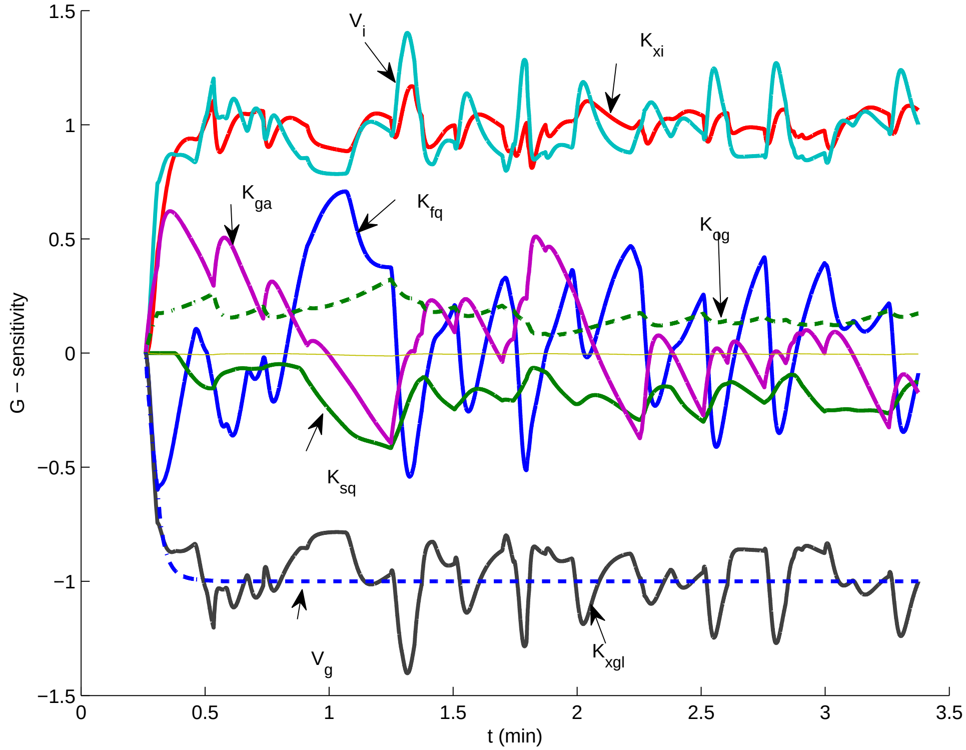

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- $f_i(x)_{i=2,3,4} \in C^1$ are positive, $f_2(0) = f_3(0) = 0$.
- $f_i^{'}(x)_{i=2,3,4}$ are positive on $[0, \infty]$.
- $f_5 > 0$ and $f_5^{'}$ is negative.

Mathematical Modeling

- $0 \leq f_2 \leq b_2 x$ and $a_3 x \leq f_3(x) \leq b_3 x$

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Mathematical Modeling

This model can be written formally as DDE:

$$\dot{X}(t) = F(t, X(t), X(t-\tau_2), X(t-\tau_3)), t \geq 0,$$
$$X(s) = \varphi(s), -\tau \leq s \leq 0, \tau = \max(\tau_2, \tau_3).$$

Sensitivity analysis

Lemma 1 *There exist a solution to:*

$$\dot{v}(t) = D_X F(t, X(t,p), X_t)(v(t)) + D_{X_t} F(t, X(t,p), X_t)(v_t) \quad (1)$$

$$+ D_p F(t, X(t,p), X_t)(1), t \geq 0; \quad (2)$$

$$(v(0), v_0) = (\varphi(0), \varphi) \in \mathbb{R}^2 \times C(-r, 0, \mathbb{R}) \quad (3)$$

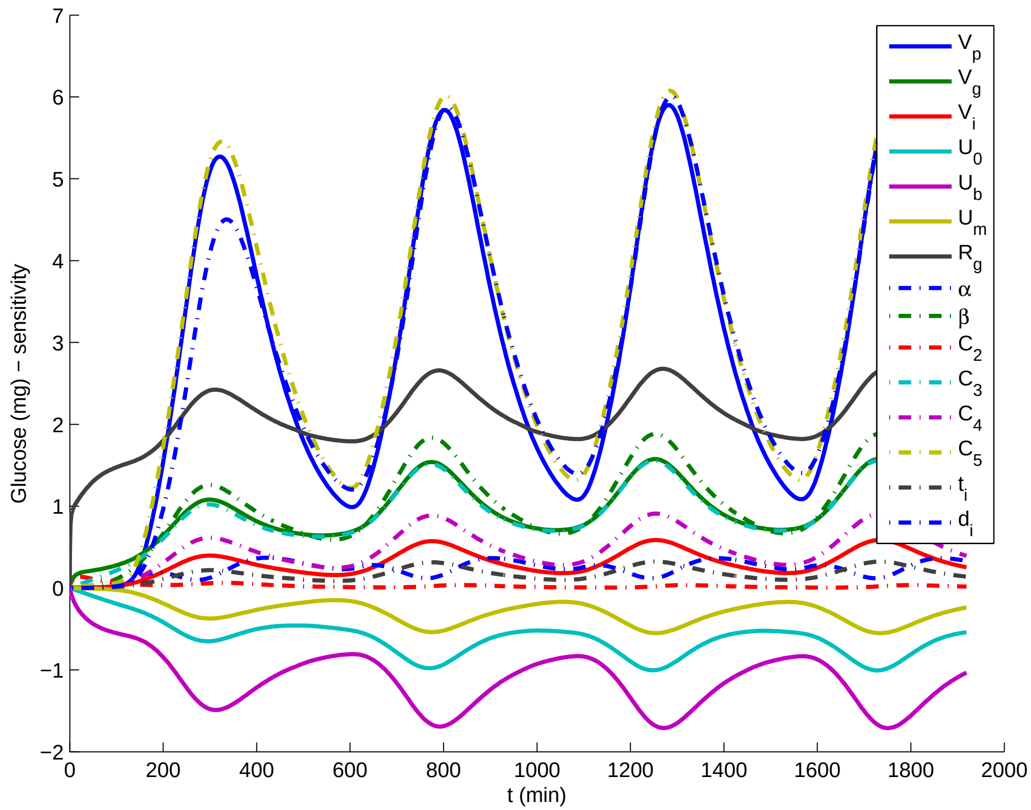
for X the solution to H. Wang Model.

Sensitivity analysis

Theorem 1 *For the solution* $X = (G, I)$ *of H. Wang Model,* X *has a derivative with respect to the parameter* p*, this derivative* $D(t) = \frac{\partial X(t,p)}{\partial p}$ *satisfies (1-3) with initial condition* $(\varphi(0), \varphi) = (0, 0) \in \mathbb{R}^2 \times C(-r, 0; \mathbb{R}^2)$.

Sensitivity analysis

- Insulin-Glucose System (IGS)



Sensitivity analysis

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