Exercise 6: Glucose and Insulin Dynamics

November 22, 2013

1. Insulin Sensitivity: The minimal model is used to estimate the insulin sensitivity $S_I = \partial^2 \dot{G} / \partial G \partial I$ from an Intraveneus Glucose Tolerance Test (IVGTT). The minimal model is:

$$\frac{dX(t)}{dt} = -p_2 X(t) + p_3(I(t) - I_b), \quad X(0) = 0, I(0) = I_b \tag{1}$$

$$\frac{dG(t)}{dt} = -(p_1 + X(t))G(t) + p_1 G_b + U_G(t)/V_G, \quad G(0) = G_b \tag{2}$$

   - $U_G(t)$: Intravenous Glucose Injection.
   - V_G: Distribution volume for plasma glucose.
   - $X(t) = (k_4 + k_6)I_{ISF}$ represents 'remote insulin'.

   According to the model developers, S_I can be calculated as:

$$S_I = -\frac{p_3}{p_2} \tag{3}$$

   assuming steady state conditions of insulin. Derive this expression given this assumption. Do you see any problems with this assumption considering the IVGTT experiment?

2. Minimal Model Simulation: Create a Simulink model of the minimal model and simulate it with 1-minute interpolated (see e.g. `interp1`) plasma insulin data from Table 1, acting as input, together with the glucose injection at time 0 min of 30 grams of glucose into a distribution volume V_g of 5.45 l, to produce the glucose response data. You may assume that we start in steady state conditions with $I = I_b = 7.3$ and $G = G_b = 85$. The parameters are: $p_1 = 0.0308$, $p_2 = 0.0209$ and $p_3 = 1.06 \cdot 10^{-5}$.

3. Digestion Modeling: Consider the digestion model in the Padova simulation model:

$$q_{sto}(t) = q_{sto1}(t) + q_{sto2}(t) \tag{4}$$

$$\dot{q}_{sto1}(t) = -k_{gri} \cdot q_{sto1}(t) + C(t) \tag{5}$$

$$\dot{q}_{sto2}(t) = k_{gri} \cdot q_{sto1}(t) - k_{empt} \cdot q_{sto}(t) \cdot q_{sto2}(t) \tag{6}$$

$$\dot{q}_{gut}(t) = -k_{abs} \cdot q_{gut}(t) + k_{empt} \cdot q_{sto}(t) \cdot q_{sto2}(t) \tag{7}$$

$$R_a(t) = \frac{f \cdot k_{abs} \cdot q_{gut}(t)}{M_{BW}} \tag{8}$$

   - $C(t)$ is the amount of ingested carbohydrates.

Time	Plamsa Insulin
0	11
2	26
4	130
6	85
8	51
10	49
12	45
14	41
16	35
19	30
22	30
27	27
32	30
42	22
52	15
62	15
72	11
82	10
92	8
102	11
122	7
142	8
162	8
182	7

- q_{sto1} is the solid stomach compartment, and q_{sto2} represents the liquid phase.
- q_{gut} is the glucose mass in the intestine.
- k_{gri} the rate of grinding.
- k_{empt} is the rate constant of gastric emptying.
- k_{abs} is the rate constant of intestinal absorption.
- $R_a(t)$ is the appearance rate of glucose in the blood.

The model parameters are different for different types of meals. Which parameters would you expect to change between for example cooked potatos and potato mash, and how would those values change?

4. Subcutaneous Delay: Show that the interstitial glucose value is a first-order low-pass filtered version of the plasma glucose value considering the kinetics according to Fig. 2, i.e., that the transfer function is of the form $G = K\frac{1}{1+s\tau}$.

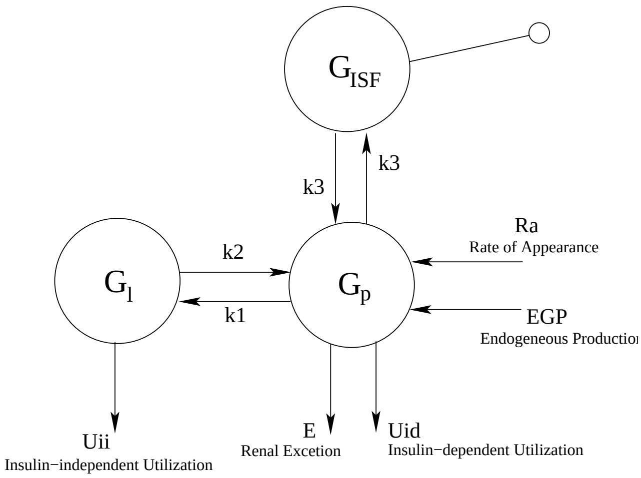

Figure 1 Interstitial and Plasma Glucose compartment kinetics.