βcell Mass, Insulin, Glucose.

Topp et al (2000) JTB 206: 605–619

Blood Glucose:

$$\frac{dG}{dt} = \text{production rate} - \text{uptake rate}$$

(G: mg/dl (deciliter)
t: days

production rate: released into blood by liver, kidney

uptake rate: removed from blood by all cells (for nutrient consumption)

$$\frac{dG}{dt} = P_0 - (E_{G0P} + S_{IP} I)G - \{U_0 + (E_{G0U} + S_{IU} I)G\}.$$

$$\frac{dG}{dt} = R_0 - (E_{G0} + S_I I)G$$

R_0: (mg dl^{-1} d^{-1}) E_{G0}: d^{-1} S_I: μU^{-1} ml d^{-1}

$$\begin{cases} R_0 = P_0 - U_0 \\ E_{G0} = E_{G0P} - E_{G0U} \\ S_I = S_{IP} + S_{IU} \end{cases}$$

Insulin:

I: $\mu U\, d^{-1}$

$$\frac{dI}{dt} = \text{secretion rate} - \text{clearance rate}$$

$$\frac{dI}{dt} = \beta\, \sigma \frac{G^2}{\alpha + G^2} - kI$$

β: βcells mg σ: μU ml^{-1} d^{-1} k: d^{-1}

α: units of $(mg/dl)^2$

βcells:

β: mg

$$\frac{d\beta}{dt} = \text{Formation (replication, neogenesis)} - \text{loss}$$

$$= (r_{1r} G - r_{2r} G^2)\beta - (d_0 - r_{1a} G + r_{2a} G^2)\beta$$

$$\frac{d\beta}{dt} = (-d_0 + r_1 G - r_2 G^2)\beta$$

$$\begin{cases} r_1 = r_{1r} + r_{1a} \\ r_2 = r_{2r} + r_{2a} \end{cases}$$

d_0: per day d^{-1} r_1: mg^{-1} dl d^{-1} r_2: mg^{-2} dl^2 d^{-1}

$$\begin{cases} \dfrac{dG}{dt} = R_0 - (E_{G0} + S_I I)G \\ \dfrac{dI}{dt} = \beta\sigma\left(\dfrac{G^2}{\alpha + G^2}\right) - kI \\ \dfrac{d\beta}{dt} = (-d_0 + r_1 G - r_2 G^2)\beta \end{cases}$$

Exercise 1: Put the model into dimensionless form.

Exercise 2: Use values of parameters in Table 1 of Topp et al (2000) to estimate the (dimensionless) parameters. Thereby show that this model operates on two timescales, a fast one (GI system) and a slower one (β system).

Exercise 3: Analyze the GI subsystem with β as a parameter using a phase-plane diagram.

Exercise 4: Find conditions for: β static, β growing, vs $\beta \to 0$ using the eqn for β cell mass.
Under what conditions does the β eqn have three relevant steady states?

Exercise 5: Use XPP to simulate this 3 eqn system with the param values given in Topp et al.

Exercise 6: Use XPPauto to produce a bifurcation diagram for G with bifurc. parameter r_1 in the range $0 \le r_1 \le 0.002$.