The oral glucose minimal model

TO DO: look at fig 16.1 and relate the denoted parameters to the processes they describe (read text). Added some explanation in purple boxes.

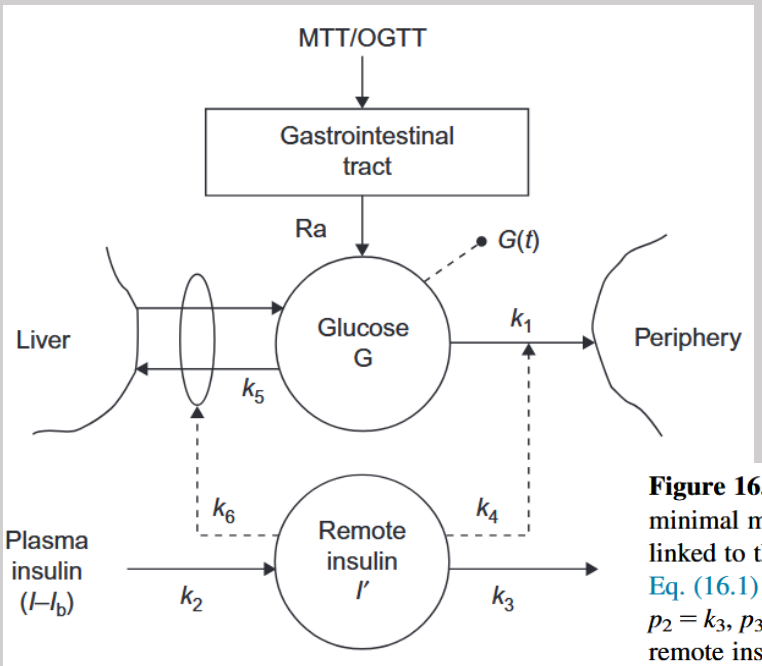
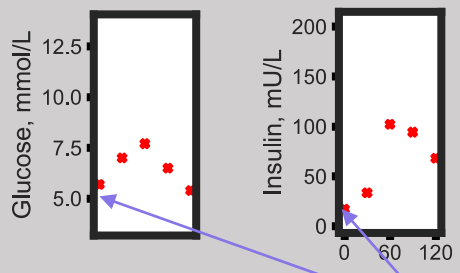


Figure 16.1 The oral glucose minimal model. Parameters k_i are linked to the parameters of Eq. (16.1) as follows: $S_G = k_1 + k_5$, $p_2 = k_3$, $p_3 = k_2 \cdot (k_4 + k_6)$. I' is remote insulin related to X as $X = k_2 \cdot (k_4 + k_6)I'$. Ra($t$) is the rate of appearance of the glucose in plasma after an oral ingestion.

example OGTT glucose and insulin responses (the data necessary to estimate the SI index of the OGMM)



basal refers to first measurement (Gb and Ib, respectively)

note! the measurement sampling schedule in the figure is different than what they used in the paper.

figure has 0,30,60,90,120
OGMM uses 0,13,25,35,60,90,120,180,420

$$\begin{cases} \dot{G}(t) = -[S_G + X(t)] \cdot G(t) + S_G \cdot G_b + \dfrac{\mathrm{Ra}(t, \alpha)}{V} & G(0) = G_b \\ \dot{X}(t) = -p_2 \cdot X(t) + p_3 \cdot [I(t) - I_b] & X(0) = 0 \end{cases} \quad (16.1)$$

where G is plasma glucose concentration, I is plasma insulin concentration, suffix "b" denotes basal (pre-test) values, X is insulin action on glucose production and disposal, V is distribution volume, and S_G, p_2, and p_3 are model parameters. Specifically, S_G is the fractional (i.e., per unit distribution volume) glucose effectiveness, measuring glucose ability *per se* to promote glucose disposal and inhibit glucose production; p_2 is the rate constant describing the dynamics of insulin action; and p_3 is the parameter governing the magnitude of insulin action like in Ref. [5]. The insulin sensitivity index is given by Ref. [7]:

*Initial values (starting values) of the **State variables:** Glucose concentration (G) and insulin action (X)*

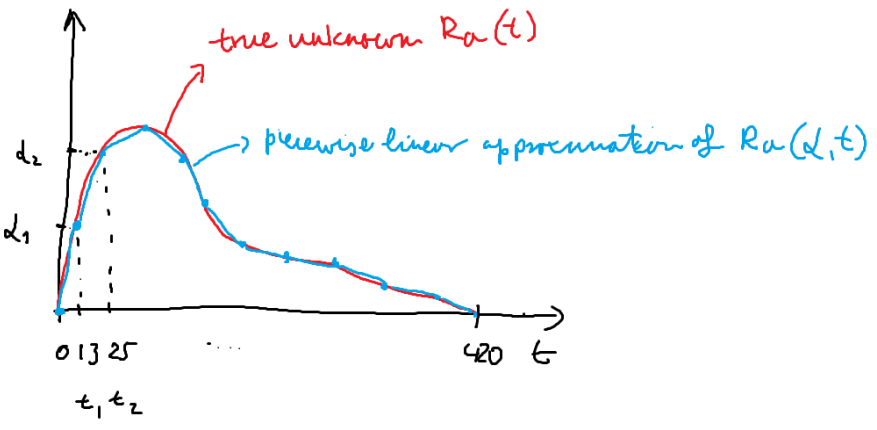
***Sg**: how glucose leaves the plasma on its own (irrespective of insulin action). This is a simplification of the biology. There exist some other types of glucose receptors that act without the need of insulin…. aaand biology is a leaky system. The glucose won't stay forever untouched in circulation even in diabetics who have no insulin secretion ☺. This modeling simplification allows for this property to be modeled realistically.*

$$S_I = \frac{p_3}{p_2} \cdot V \ (\mathrm{dL/kg/min\ per\ \mu U/mL}) \quad (16.2)$$

The model describes Ra as a piecewise-linear function with a given number of break points. Since the rate of glucose absorption varies more rapidly in the first portion of the test (Figure 16.3), intervals are shorter at the beginning and longer toward the end. A preliminary analysis indicated that eight intervals—and thus eight break points—are a good compromise between model flexibility and the number of parameters to be estimated from the data. The break points are allocated at 0, 13, 25, 35, 60, 90, 120, 180, and 420. The expression for Ra is thus given by

$$\mathrm{Ra}(t, \alpha) = \begin{cases} \alpha_{i-1} + \dfrac{\alpha_i - \alpha_{i-1}}{t_i - t_{i-1}} \cdot (t - t_{i-1}) & \text{for } t_{i-1} \le t < t_i, \ \ i = 1, \ldots, 8 \\ 0 & \text{otherwise} \end{cases} \quad (16.3)$$

***Ra:** this is a flexible function that allows the shape of glucose appearing in plasma to be approximated. Note! we do not know the true Ra curve (red in fig below). By estimating the alpha parameters the model is fitted to **plasma glucose** and **plasma insulin** measurements. The estimated Ra is the blue curve. (we do not usually look at this, as our interest is in the estimated insulin sensitivity and not how glucose appeared in plasma.)*



I heard from the tutors that there were some questions about running code already in the tutorial. Don't worry about that, we will look at the code together on Thursday!

If you have any questions, email me!
– Best wishes, Balazs