A relevant glucose-insulin dynamics model for type 1 diabetes

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Objective

A new model of glucose insulin dynamics for type 1 diabetes **without non desired equilibria**.

A standard identification algorithm provides a long term fit over two days with constant parameters.

As a byproduct, **the parameters** of the relevant model **provide the computation of the tools for the functional insulin therapy (FIT):**

- the **basal infusion rate** (**BR**),
- the **insulin sensitivity factor** (**ISF**) and
- the **insulin to carbo ratio** (**I:C**).

This is a major outcome as they can be used for the education of type 1 diabetic patients.

Methods

Glucose dynamics

Increase of glycemia includes:
• the liver endogenous glucose production k_l
• the digestion of CHO $D(t)$.

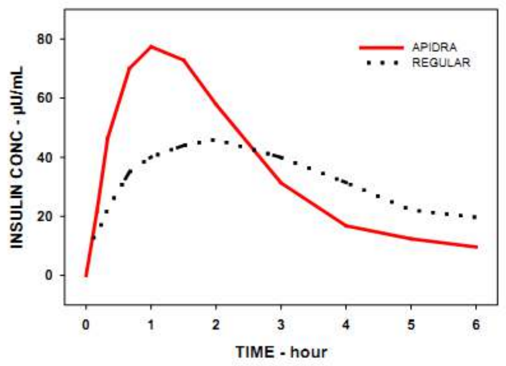
The glucose absorption rate includes:
• an insulin-independent term k_b
• an insulin-dependent term $-k_{si}.I(t)$

The dynamics of the blood glucose level (BG) $G(t)$ is:

$$\begin{cases} \dot{G}(t) = -k_{si}.I(t) + k_l - k_b + D(t) \\ \dot{G}(t) = 0 \text{ if } G(t) = 0 \text{ for positivity} \end{cases}$$

Insulin dynamics

A second order from the pharmacokinetic profile :



$$I(s) = \frac{k_u/V_i}{(1+T_u.s)^2} U(s)$$

Digestion dynamics

A second order with a single time constant

Six free parameters to be identified.

Insulin sensitivity k_{si} is one major parameter which has to be identified for each patient as it reflects the well-known variability of the metabolic effect of insulin.

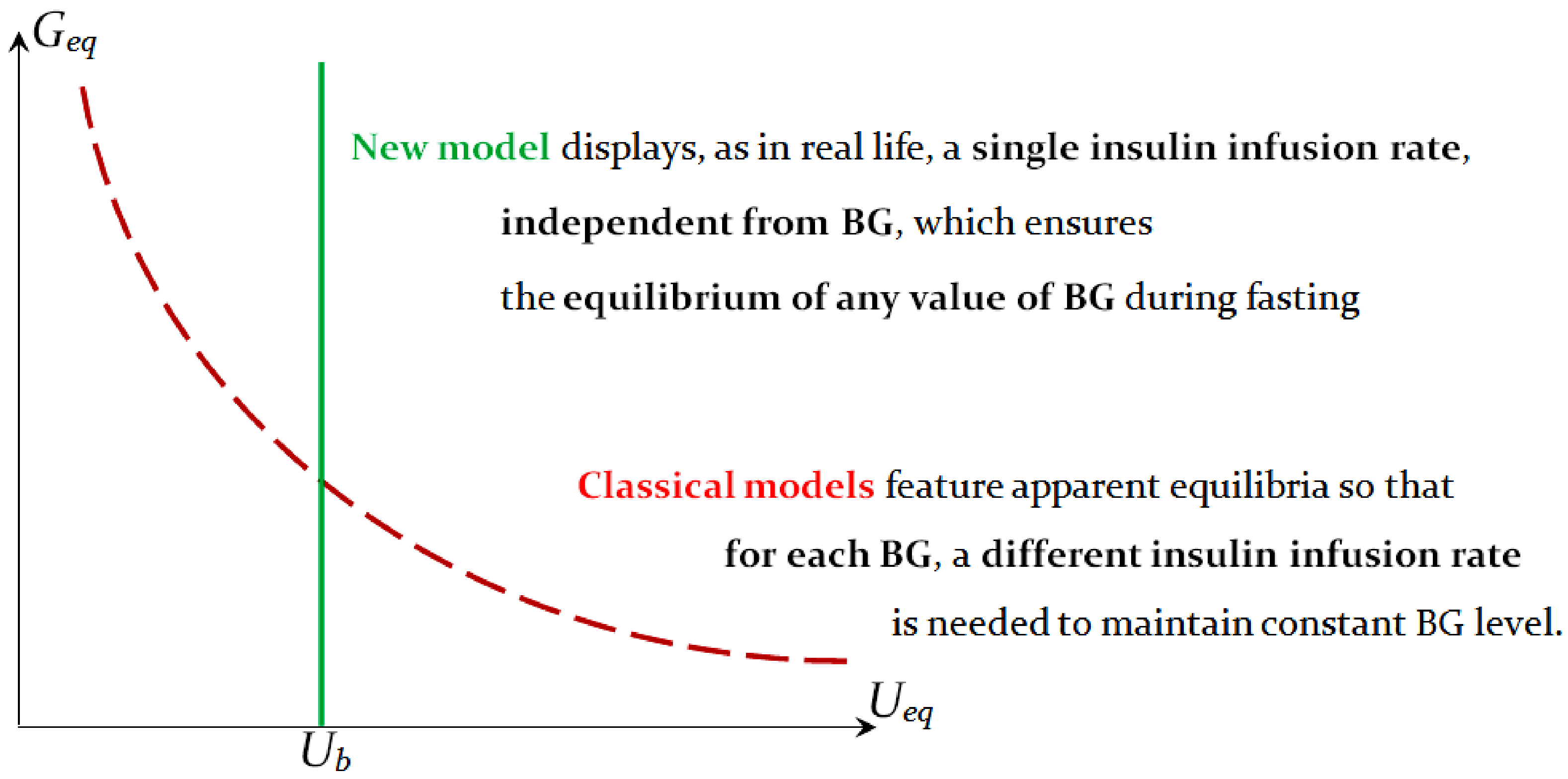
Classical models

R.N. Bergman et *al.* "Quantitative estimation of insulin sensitivity," *Am. J. Physiol. Endocrinol. Metab.*, 236:667-677, 1979.

A. De Gaetano and O. Arino, "Mathematical modelling of the intravenous glucose tolerance test," *J. Math. Biol.*, vol. 40, no. 2, pp. 136–168, Feb. 2000.

Results

1. **Equilibrium** during fasting ($D(t)$=0) :



2. Computed tools for the functional insulin therapy :

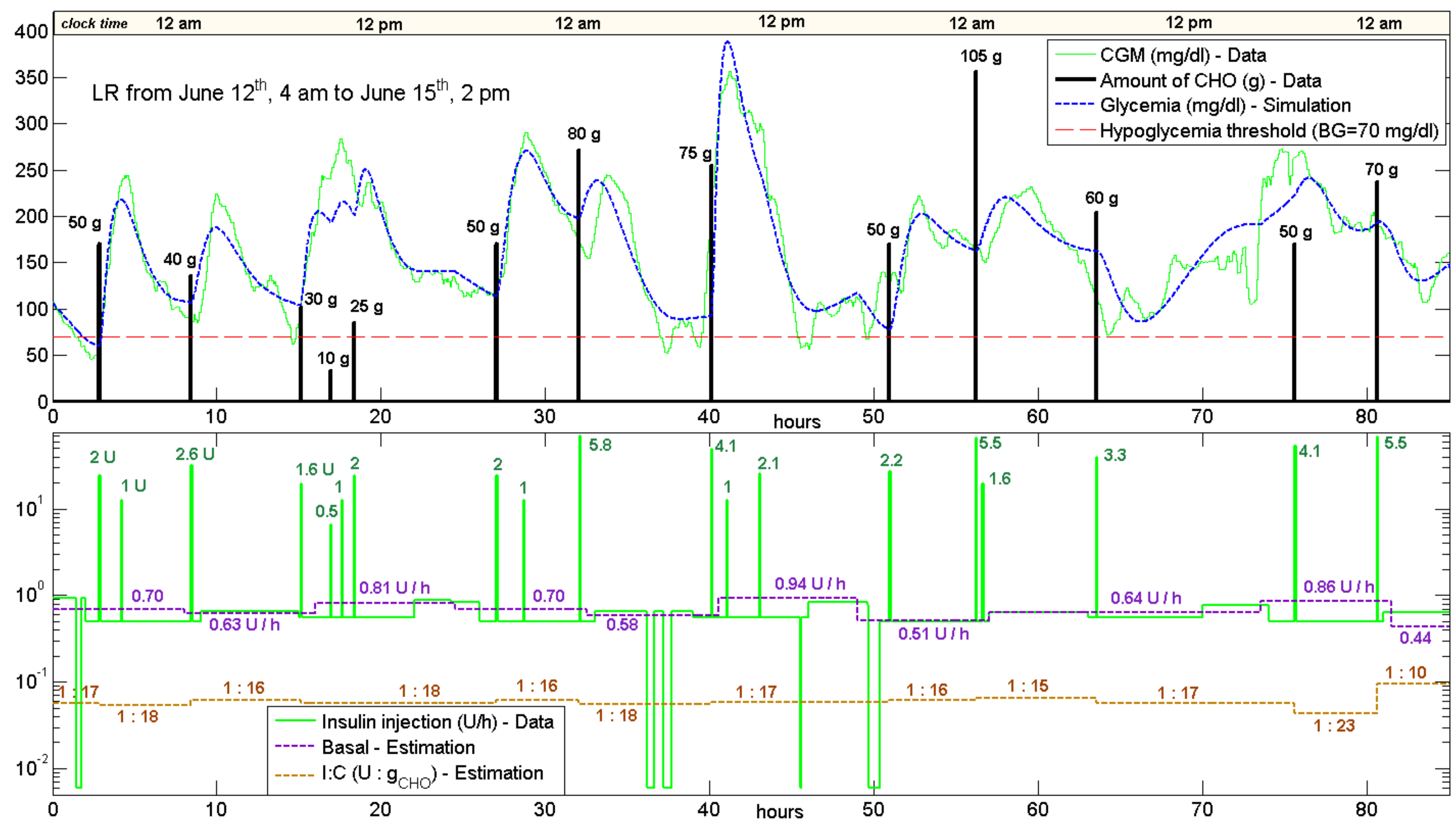
$$U_b = \frac{k_l - k_b}{k_{si}} \frac{V_i}{k_u} \qquad ISF = k_{si}\frac{k_u}{V_i} \qquad I:C = \frac{V_i}{k_{si}k_u}\frac{k_r}{V_B}$$

3. Estimation algorithm

An off-line estimation, wih the least square method on the output error, using standard clinical data (CGM, Injection, CHO) of a type 1 diabetic patient provides a fit over two days and the constant parameters allow to compute the tools for the FIT:

U_b	ISF	I:C
0.7 U/h	83 mg/dl/U	1: 17 U:g_{CHO}

The method is extended to a picewise time varying model, improving the fit on an even longer period. k_{si} is assumed to be constant. The time varying parameter k_r reflects the glycemic index depending on the meal composition and the variations of the liver glucose production k_l displays a basal rate pattern as used by some patients.



Conclusion

This new model has realistic asymptotic properties. Its relevant parameters provide the tools for FIT. An adaptative estimation algorithm displays a long-term fit. This new model could impact the design of a control algorithm for the artificial pancreas.