

## SUPPLEMENTARY DATA

### Kalman Filter-Based Technique for the Real-Time Tracking of Insulin Sensitivity

The proposed smart bolus calculator leverages a technique for the real-time tracking of insulin sensitivity from glucose sensor and insulin pump data. The algorithm is presented and validated elsewhere.

Briefly, the technique relies on three compartmental models to describe the interaction of glucose and insulin in presence of meals and subcutaneous insulin infusion. Two models are linear and are designed to map ingested carbohydrates and administered insulin respectively into glucose rate of appearance into plasma and plasma insulin concentration. The outputs of these models serve as inputs to the third model describing the core glucose-insulin dynamics; this model is nonlinear and was derived as a variation of the oral minimal model of glucose kinetics [1], here augmented with an insulin sensitivity state

$$\begin{aligned}\dot{G}(t) &= -S_G(G(t) - G_b) - S_I(t) \cdot X(t) \cdot G(t) + R_a(t) \\ \dot{X}(t) &= -p_2 \cdot X(t) + p_2(I(t) - I_b) \\ \dot{S}_I(t) &= -p_{S_I}(S_I(t) - S_{I,b})\end{aligned}.$$

In the equations,  $G$  is plasma glucose concentration and  $G_b$  its basal value [mg/dl],  $X$  is insulin action [mU/l],  $S_I$  is insulin sensitivity and  $S_{I,b}$  its basal value [1/min per mU/l],  $R_a$  is plasma glucose rate of appearance [mg/dl/min],  $I$  is plasma insulin concentration and  $I_b$  its basal value [mU/l],  $S_G$  is glucose effect on its own variation (glucose effectiveness) [1/min],  $p_2$  is the delay between plasma insulin concentration and its action on glucose rate of change [1/min], and  $p_{S_I}$  is the time constant of the insulin sensitivity equation [1/min].

To allow a real-time tracking of insulin sensitivity, the model is linearized around an individualized operating point reflecting subject-specific metabolic features, and a Kalman filter is then used to obtain estimates of the  $S_I$  state every five minutes. To optimize the filter performance, some relevant model parameters are previously identified on the available data using a Bayesian estimator exploiting *a priori* second-order statistical information. The parameters that are not identified are either fixed to population values determined from *ad hoc* experiments generated using a type 1 diabetes simulation platform [2] or individualized based on previously published formulas relating metabolic parameters to anthropometric variables 0.

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### References

- [1] Cobelli C, Dalla Man C, Toffolo G, Basu R, Vella A, Rizza R. The Oral Minimal Model Method. *Diabetes*. 2014;63(4):1203-13.
- [2] Visentin R, Campos-Nanez E, Schiavon M, Lv D, Vettoretti M, Breton M, Kovatchev BP, Dalla Man C, Cobelli C. The UVA/Padova Type 1 Diabetes Simulator Goes from Single Meal to Single Day. *J Diabetes Sci Technol*. 2018;12(2):273-81.
- Campioni M, Toffolo G, Basu R, Rizza RA, Cobelli C. Minimal Model Assessment of Hepatic Insulin Extraction During an Oral Test from Standard Insulin Kinetic Parameters. *Am J Physiol Endocrinol Metab*. 2009;297(4):E941-8.