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Parameter identification of a model describing the blood glucose metabolism using clinical data

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Abstract: Models of the blood glucose metabolism in critically ill patients allow an enhanced understanding of the underlying pathology. Especially for the development of assisted insulin therapy the knowledge of the glucose dynamic is relevant. In modeling of blood glucose dynamic, identification of model parameters is a crucial step, also regarding personalized health care. Therefore, we present a workflow of parameter identification to obtain patient-specific model parameter and estimation of insulin sensitivity.

I. Introduction

Patients in the intensive care unit (ICU) can suffer from stress-induced hyperglycemia exceeding 180 [mg/dL] and high glycemic variability. The change in insulin sensitivity which describes the effectiveness of insulin, plays a central role in this dynamic. Insulin therapy is a common treatment used to lower blood glucose (BG) level [1]. Critically ill patients showed an improved recovery in the ICU using intensive insulin therapy, which requires tight monitoring of the BG level to avoid hypoglycemia [2]. Assisted insulin therapy based on continuous glucose measurement can assist clinical staff and improve therapy [3, 4]. The development of such systems requires adequate models describing the BG metabolism. However, identification of model parameters based on clinical data is crucial. In the following, we present the optimization of parameters for a given model of the BG metabolism using novel clinical data. The variance in identified parameters allows to estimate their uncertainty, which is useful for a robust control design. In addition, parameter identification facilitates personalized models to improve insulin therapy.

II. Material and methods

I.I. Clinical Dataset

The clinical data were acquired at University Hospital Aachen in context of a retrospective study based on 100 patients over a time of 30h in the ICU. The data were postprocessed in MATLAB to extract BG measurements, insulin infusion and nutrition data.

I.II. Modeling Critically Ill Patients

The BG metabolism in critically ill patients is described using the so-called ICING Model [5]. The model describes the interaction between plasma glucose, BG, and plasma insulin, I. The remote insulin compartment, Q, accounts for the insulin being utilized in the interstitium (see fig. 1).

The model inputs are intravenous exogenous insulin, U_{ex}, enteral nutrition, D, and parenteral nutrition, PN.

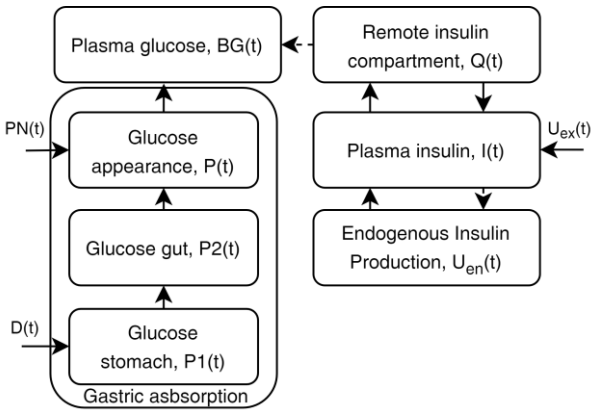

Figure 1: ICING model with its inputs. Solid arrows describe direct mass flows, dashed arrows represent a direct influence.

The effect of interstitial insulin on the plasma glucose is influenced by the insulin sensitivity, S_I, which is as a time variant parameter. High insulin sensitivity leads to a strong influence of interstitial insulin on blood glucose. For a detailed description of the model, the reader is referred to [5]. The model is implemented in MATLAB Simulink, the workflow of simulation is given in fig. 2.

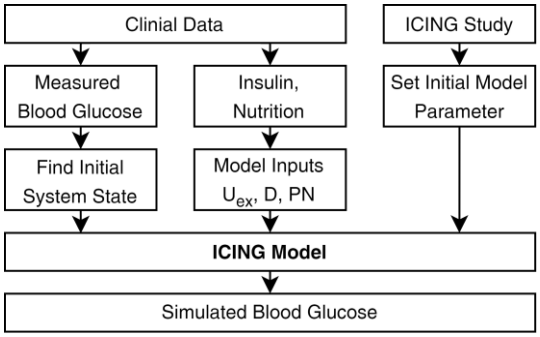

Figure 2: Flow chart of simulation in MATLAB Simulink.

I.III. Parameter Optimization

The model parameters are optimized for each patient as in [5-7]. Here, we use a combination of particle swarm and nonlinear optimization. Thereby, the insulin sensitivity is treated as time variant parameter. Thus, the optimization procedure is performed in two phases. In the first phase, the constant model parameters are optimized:

- Define vector with parameters as in [5]: $\vec{p} = \vec{p}_0$
- Define boundary constraints for optimization, $\vec{p}_{min} < \vec{p} < \vec{p}_{max}$
- Apply particle swarm optimization and further local nonlinear optimization to obtain optimal local solution, $\vec{p} = \vec{p}_{opt}$

In the second phase, the previously constant insulin sensitivity is adjusted over time. Therefore, the change $S_I(t)/S_{I,0}$ is identified each hour. The resulting parameter vector $\vec{x} = \left[S_I(t_0)/S_{I,0}, \dots, S_I(t_N)/S_{I,0}\right]^T$ is optimized as following:

- Define boundary constraints for optimization, to restrict variations: $\vec{x}_{min} < \vec{x} < \vec{x}_{max}$
- Define auxiliary constraint with approximation of first derivative of $\vec{x}$ to avoid high fluctuations and overfitting of insulin sensitivity: $A \cdot \vec{x} < \vec{b}$
- Local nonlinear optimization to obtain optimal solution, $\vec{x} = \vec{x}_{opt}$

For the optimization, the MATLAB nonlinear optimization solvers *fmincon* and *particleswarm* are used. The functions' objective is the minimization of the error between the simulated and the measured data set (see fig. 3).

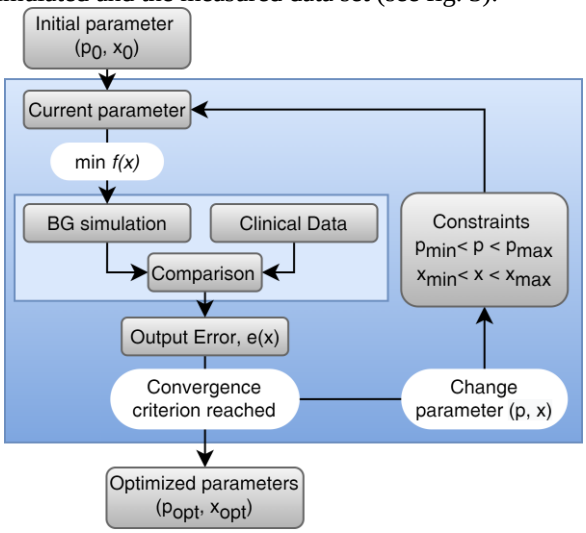

Figure 3: Optimization procedure of system parameter and time variant insulin sensitivity.

III. Results and discussion

In fig. 4 BG, insulin infusion and nutrition of a single patient are given. The blood glucose values comprise the simulated BG using the optimized parameter set and the measured data from the clinical data set. Furthermore, the scaled change in insulin sensitivity is plotted. The simulation shows a good convergence of the identification procedure. The algorithm identifies parameter without converging towards the constraint boundaries.

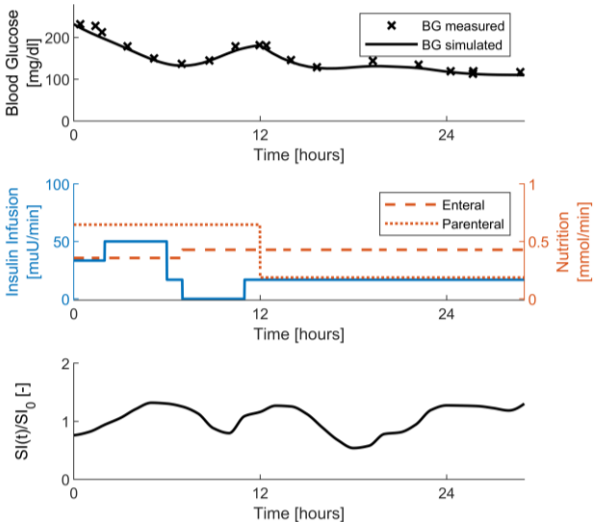

Figure 4: Simulation of a single patient after optimization. The top plot shows the simulated and measured BG. The plot in the middle shows the external inputs. The plot at the bottom shows the estimated change in insulin sensitivity.

The parameters are within the range as provided in [5]. However, in patients with only few measurement values, naturally, the solver identifying the insulin sensitivity can overfit the data. A possible solution would be to scale the number of data points for the insulin sensitivity depending on the frequency of BG measurements.

IV. Conclusions

The proposed workflow allows an effective way to optimize model parameters to a new clinical data set. The combined particle swarm and local nonlinear optimization allows fast convergence. Deviation in individual parameters enhances an estimation of parameter uncertainty for robust controller synthesis. Finally, trained parameter sets allow a personalized, optimal insulin therapy.

Author's Statement

The Authors state no conflicts of interest. The clinical study was approved by the Ethics Committee of the Medical Faculty, RWTH Aachen University (approval. no. EK 275/20) and complies with the Declaration of Helsinki.

References

[1] K. Stoudt and S. Chawla, "Don't Sugar Coat It: Glycemic Control in the Intensive Care Unit," J. Intensive Care Med., vol. 34, no. 11–12, pp. 889–896, 2019.

[2] G. Van Den Berghe et al., "Intensive Insulin Therapy in Critically Ill Patients," N. Engl. J. Med., vol. 345, no. 19, pp. 1359–1367, 2001.

[3] S. Finfer et al., "Clinical review: Consensus recommendations on measurement of blood glucose and reporting glycemic control in critically ill adults," Crit. Care, vol. 17, no. 3, 2013.

[4] J. G. Chase et al., "Next-generation, personalised, model-based critical care medicine: A state-of-the art review of in silico virtual patient models, methods, and cohorts, and how to validation them," Biomed. Eng. Online, vol. 17, no. 1, pp. 1–29, 2018.

[5] J. Lin et al., "A physiological Intensive Control Insulin-Nutrition-Glucose (ICING) model validated in critically ill patients," Comput. Methods Programs Biomed., vol. 102, no. 2, pp. 192–205, 2011.

[6] T. D. Knab, G. Clermont, and R. S. Parker, "A 'Virtual Patient' Cohort and Mathematical Model of Glucose Dynamics in Critical Care," IFAC-PapersOnLine, vol. 49, no. 26, pp. 1–7, 2016.

[7] M. van den Boorn et al., "The development of a glucose prediction model in critically ill patients," *Comput. Methods Programs Biomed.*, vol. 206, p. 106105, 2021.