Diabetes: Cybernetic point of view

Matúš Rebro, Marián Tárník, Eva Miklovičová, Ján Murgaš
Institute of Robotics and Cybernetics
Faculty of Electrical Engineering and Information Technology
Slovak University of Technology in Bratislava, Slovak Republic

Cybernetic modeling and simulation find more and more use in non-technical areas like medicine. The aim of this paper is to summarize and present some of the applications of cybernetics for diabetes. One of the applications comes from control systems theory in the form of algorithm for automated insulin administration for type 1 diabetes patients while mathematical models of insulin-glucose system can be used for verification of this algorithm via simulations. Another use of the mathematical modeling can be found in prediction of glycemia evolution on the basis of data from continous glucose monitoring for both type 1 and type 2 patients.
Keywords: diabetes mellitus, glycemia, dynamical model, simulation, prediction

Diabetes z pohľadu kybernetiky
Kybernetické modely a ich simulácia nachádzajú čoraz väčšie uplatnenie v netechnických oblastiach ako medicína. Cieľom tohto článku je zhrnutie a prezentácia niektorých aplikácií kybernetiky pre diabetes. Jedna z aplikácií pochádza z teórie riadenia vo forme algoritmu pre automatické dávkovanie inzulínu pre pacientov s diabetom prvého typu, zatiaľ čo matematické modely inzulínovo-glukózového systému môžu byť použité na verifikáciu takéhoto algoritmu pomocou simulácií. Ďalšie uplatnenie matematického modelovania možno nájsť pri predikcii priebehu glykémie na základe dát z kontinuálneho merania glukózy pre diabetikov prvého aj druhého typu.
Kľúčové slová: diabetes mellitus, glykémia, dynamický model, simulácia, predikcia

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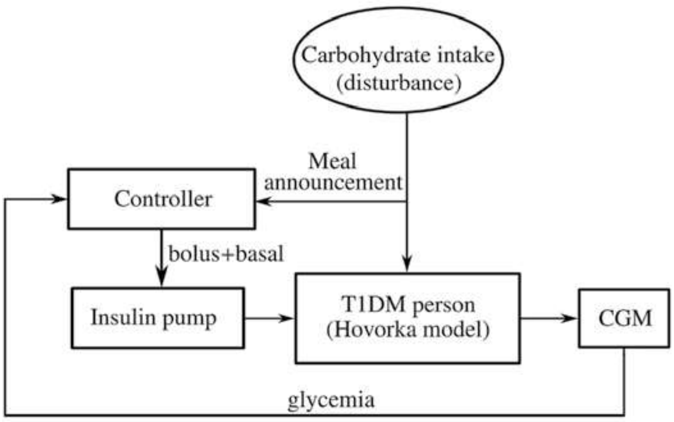
Introduction

Diabetes mellitus can be described as a group of metabolic diseases, which if unchecked can cause chronic hyperglycemia. Two most common types of this disease are type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). The first one is caused by absolute insulin deficiency and thus the patients are dependent on external insulin administration and regular checks of blood glucose concentration. The second one is caused by relative insulin deficiency and/or insulin resistance, whereas in this case, therapy consists of lifestyle changes and in late stages oral antidiabetics and insulin therapy.

In both T1DM and T2DM, the dynamics of glucose and insulin concentrations is modeled. In case of T1DM such models can be used together with continuous glucose monitoring (CGM) device and insulin pump to predict the future glycemia and/or to design control algorithm for insulin administration. Connection of glycemia measurement system (CGM) and insulin pump with control algorithm (which can be implemented in the insulin pump device itself) creates closed loop control system where controlled output is the glycemia and system input is the insulin administration, see ***Figure 1***. Carbohydrate intake can be viewed as a disturbance which is measurable (it can be estimated how much carbohydrates is in the meal) and thus can serve as an additional input to the control algorithm which can further improve glycemia regulation. Connection of the CGM device with insulin pump and control algorithm is often called artificial pancreas[1] because of the its goal to mimic the pancreas in healthy man.

Figure 1. *Automated insulin administration scheme*

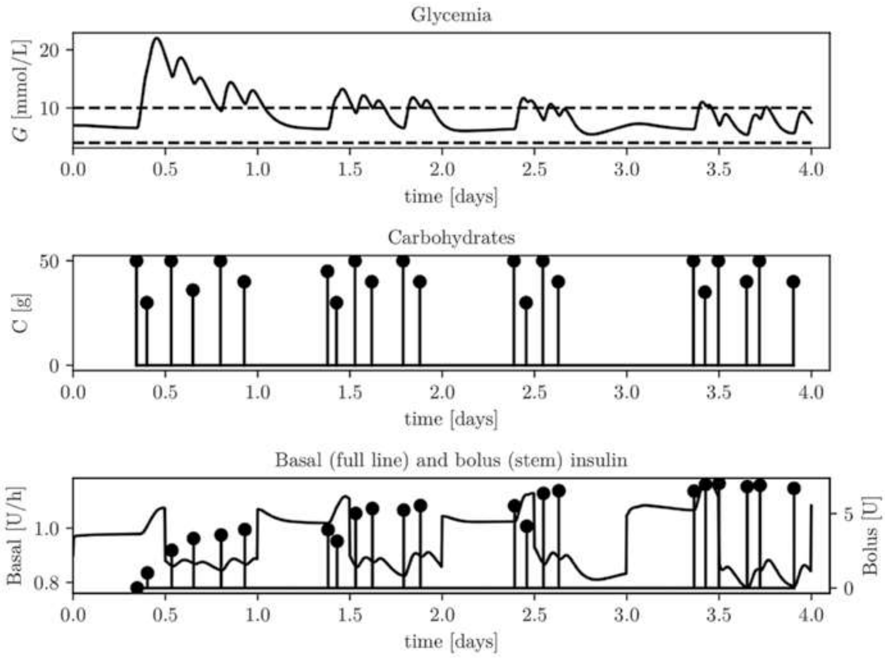


Generally, the control algorithm is designed via simpler linear models, which can only approximate behavior of insulin-glucose system for only small deviations from basal (steady) state. These models, although not so accurate in prediction, can be directly used in wide range of control design approaches. More complex, physiological models are used for evaluation and verification of these algorithms via simulations.

Adaptive control in T1DM

Insulin-glucose system in T1DM subject can be viewed in control systems theory as dynamical system with one output (glycemia) and one input (insulin administration).

Figure 2. Simulation of adaptive control of glycemia in T1DM subject



The carbohydrate intake from food can be then viewed as disturbance input. The goal of the control system design is to keep the glycemia in some healthy range. This glycemia range is often chosen to be around 4-10 mmol/L or in other words, between hypoglycemia and hyperglycemia with more emphasis on avoiding the hypoglycemic state.

Since it is reasonable to assume that the insulin-glucose system can vary from person to person and also change its behavior over time, the adaptive control is considered as a control algorithm for glycemia(2). In control systems theory this means that we assume that the parameters of model of the controlled system are unknown and are prone to change.

The control design can be divided into two steps(3,4). The first step is to design the control in the absence of disturbances. This means we design the algorithm to keep glycemia in basal state or in its close proximity via continuous basal insulin administration. The second step is to design the algorithm for bolus insulin administration, which should compensate the postprandial glycemia rise. This algorithm also uses the information about carbohydrate intake from patient to calculate the bolus dosage and can adapt over time even when the carbohydrate amounts are not exactly known.

For performance assessment the simulations of nonlinear dynamical model such as for example Hovorka model(5) can be used. Results of such simulation can be seen in ***Figure 2*** (note the obvious increase in bolus dosage as a result of adaptation process). Parameters of this model are identified on CGM data of T1DM subjects. This way we have glycemia response simulator for one specific subject. We can artificially create simulators of more subjects by altering the model parameters via small random changes and thus creating so called virtual subjects(4). Control algorithm can be then further tested for its robustness via simulations of multiple virtual subjects. These results can be further evaluated by the means of control variability grid analysis(6).

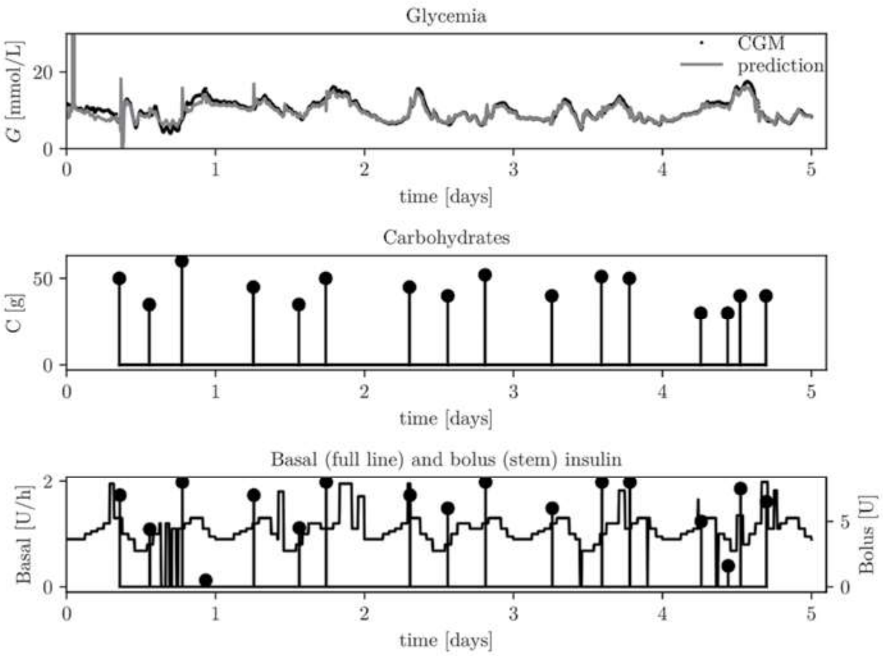
Short-term glycemia prediction

Another use of simpler models of insulin-glucose dynamics can be found in short-term glycemia prediction on the basis of CGM data. Motivation behind the glycemia prediction is to set up algorithm for early hypoglycemic or hyperglycemic event warning for T1DM patient and also possibly for T2DM patient(7). If we want to use simple linear models for prediction of glycemia, we have to take into consideration some unmodeled dynamics either of exogenous (physical activity) or endogenous (effects of other hormones) nature. Since we would possibly find many different sets of model parameters for different patients, which could also vary in time, it would be also good to incorporate some adaptation mechanism into prediction algorithm. Stochastic linear models such as ARX (Autoregressive with exogenous inputs) and ARMAX (Autoregressive moving average with exogenous inputs) together with recursive least squares algorithm are able to predict glycemia with prediction horizon of up to 1 hour. Prediction accuracy and performance metric is more detailly described in(8). Prediction algorithm uses present and past measured glycemia data and data about carbohydrate intake and insulin administration and is able to learn or adapt model parameters in approximately 1 day ***(see Figure 3)***.

Conclusion

Cybernetic dynamical models can be used in diabetes modeling for simulation, prediction and control design. Simple linear models, although not that accurate, can be used to design control algorithms for artificial pancreas while more complex models are used to verify the functionality of these algorithms via simulation experiments. Using the continuous glucose measurements and self-monitoring data can be also used together with simple linear stochastic models for accurate short-term glycemia prediction with online parameter identification algorithm, which can adapt the model parameters for specific patient.

Figure 3. 1-hour glycemia prediction for T1DM using ARMAX model with online parameter identification and CGM data



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Ing. Matúš Rebro
Institute of Robotics and Cybernetics
Faculty of Electrical Engineering and Information Technology
Slovak University of Technology in Bratislava
Ilkovičova 3, 812 19 Bratislava, Slovak Republic
e-mail: matus.rebro@stuba.sk