

Model Identification Using Stochastic Differential Equation Grey-Box Models in Diabetes

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Abstract

Background:

The acceptance of virtual preclinical testing of control algorithms is growing and thus also the need for robust and reliable models. Models based on ordinary differential equations (ODEs) can rarely be validated with standard statistical tools. Stochastic differential equations (SDEs) offer the possibility of building models that can be validated statistically and that are capable of predicting not only a realistic trajectory, but also the uncertainty of the prediction. In an SDE, the prediction error is split into two noise terms. This separation ensures that the errors are uncorrelated and provides the possibility to pinpoint model deficiencies.

Methods:

An identifiable model of the glucoregulatory system in a type 1 diabetes mellitus (T1DM) patient is used as the basis for development of a stochastic-differential-equation-based grey-box model (SDE-GB). The parameters are estimated on clinical data from four T1DM patients. The optimal SDE-GB is determined from likelihood-ratio tests. Finally, parameter tracking is used to track the variation in the “time to peak of meal response” parameter.

Results:

We found that the transformation of the ODE model into an SDE-GB resulted in a significant improvement in the prediction and uncorrelated errors. Tracking of the “peak time of meal absorption” parameter showed that the absorption rate varied according to meal type.

Conclusion:

This study shows the potential of using SDE-GBs in diabetes modeling. Improved model predictions were obtained due to the separation of the prediction error. SDE-GBs offer a solid framework for using statistical tools for model validation and model development.

J Diabetes Sci Technol 2013;7(2):431–440

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Abbreviations: (ACF) autocorrelation function, (BG) blood glucose, (BW) body weight, (CHO) carbohydrate, (CSII) continuous subcutaneous insulin infusion, (IVP) Identifiable Virtual Patient, (ODE) ordinary differential equation, (PD) pharmacodynamic, (PK) pharmacokinetic, (SDE) stochastic differential equation, (SDE-GB) stochastic-differential-equation-based grey-box model, (T1DM) type 1 diabetes mellitus

Keywords: autocorrelation, blood glucose dynamics, statistical model building, stochastic differential equations, stochastic grey-box modeling, type 1 diabetes mellitus

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