

Preface

Standard diabetes insulin therapy for type 1 diabetes and late stages of type 2 is based on the expected development of blood glucose (BG) both as a consequence of the metabolic glucose consumption as well as of meals and exogenous insulin intake. Traditionally, this is not done explicitly, but the insulin amount is chosen using factors that account for this expectation.

The increasing availability of more accurate continuous blood glucose measurement (CGM) systems is attracting much interest to the possibilities of explicit prediction of future BG values. Against this background, in 2014 a two-day workshop on the design, use and evaluation of prediction methods for blood glucose concentration was held at the Johannes Kepler University Linz, Austria. One intention of the workshop was to bring together experts working in various fields on the same topic, in order to shed light from different angles on the underlying problem of modeling the glucose insulin dynamics of type 1 diabetes patients. Among the international participants were continuous glucose monitoring developers, diabetologists, mathematicians and control engineers, both, from academia and industry. In total 18 talks were given followed by panel discussions which allowed to receive direct feedback from the point of view of different disciplines.

This book is based on the contributions of that workshop and is intended to convey an overview of the different aspects involved in the prediction. The individual chapters are based on the presentations given by the authors at the workshop but were written afterward which allowed to include the findings and conclusions of the various discussions and of course updates.

The chapter “[Alternative Frameworks for Personalized Insulin–Glucose Models](#)” by Harald Kirchsteiger et al. asks the question whether more and more detailed physiological descriptions of the glucose metabolism with an ever-increasing degree of sophistication and number of modeled phenomena are really what is needed for pushing the boundaries in glucose prediction for control. As an alternative, the chapter introduces two data-based approaches that focus not on the prediction of exact future blood glucose values, but rather on the prediction of changes in the patients’ blood glucose range.

The chapter “[Accuracy of BG Meters and CGM Systems: Possible Influence Factors for the Glucose Prediction Based on Tissue Glucose Concentrations](#)” by Guido Freckmann et al. discusses performance metrics used to characterize the accuracy of continuous glucose measurement devices. This topic is highly relevant for prediction models since many of them rely on the data given by the continuous sensors which are previously calibrated with blood glucose meter measurements which are also subject to measurement errors. Inaccurate measurements will directly affect the performance of the corresponding predictions.

The chapter “[CGM—How Good Is Good Enough?](#)” by Michael Schoemaker and Christopher G. Parkin also tackles the problem of continuous glucose monitor performance evaluation. Several performance metrics used in different published studies are compared and their individual characteristics analyzed. The chapter reveals why the comparison of a sensor evaluated in two different clinical studies is not always straightforward.

The chapter “[Can We Use Measurements to Classify Patients Suffering from Type 1 Diabetes into Subcategories and Does It Make Sense?](#)” by Florian Reiterer et al. makes use of continuous time prediction models to describe the interaction between ingested carbohydrates, subcutaneously injected insulin, and continuously measured glucose concentration. The identified model parameters of 12 subjects were analyzed and statistically significant correlations between the parameters and patient characteristics such as weight and age could be found.

The chapter “[Prevention of Severe Hypoglycemia by Continuous EEG Monitoring](#)” by Claus Borg Juhl et al. shows how to use EEG signals to predict upcoming hypoglycemic situations in real-time by employing artificial neural networks. The results of a 30-day long clinical study with the implanted device and the developed algorithm are presented.

The chapter “[Meta-Learning Based Blood Glucose Predictor for Diabetic Smartphone App](#)” by Valeriya Naumova et al. demonstrates how a highly sophisticated glucose prediction model can be ported from a development language running on a PC to a format such that it can be used conveniently by the patients. A unique feature of the algorithm is its independence of any user input other than historic CGM data which is automatically transmitted from a CGM device. No parameter estimation nor prediction model individualization is required.

The chapter “[Predicting Glycemia in Type 1 Diabetes Mellitus with Subspace-Based Linear Multistep Predictors](#)” by Marzia Cescon et al. uses data-based methods to develop individualized prediction models. The model can be considered as a combination of physiological models to precompute the rate of appearance of injected insulin and ingested carbohydrates in the bloodstream and of data-based models to combine this information and compute predictions up to 120 min in the future. The results show the performance on data from 14 type 1 diabetes patients in a clinical trial.

The chapter “[Empirical Representation of Blood Glucose Variability in a Compartmental Model](#)” by Stephen D. Patek et al. shows a modeling technique designed to extract the information on the net effect of meals on the blood glucose concentration. By assuming that all major unexplained glycemic excursions can be

attributed to oral glucose ingestion, a meal vector is estimated which significantly improves the mathematical model. Results are shown on three patients during a clinical trial and on virtual patients where it is shown how the method can be used for adjustments of the basal insulin rate.

The chapter “[Physiology-Based Interval Models: A Framework for Glucose Prediction Under Intra-patient Variability](#)” by Jorge Bondia and Josep Vehi tries to cope with the large intrasubject variability by using the concept of interval predictions. Instead of predicting a single blood glucose value in the future, a whole solution envelope is determined. With the presented theory it can be guaranteed that the real value is always inside of the envelope and moreover the envelope is not conservative. The method is evaluated on a physiological diabetes model.

The chapter “[Modeling and Prediction Using Stochastic Differential Equations](#)” by Rune Juhl et al. considers uncertainty in the dynamics between different patients as well as within a patient by making use of stochastic differential equations. It is shown how the mixed effects modeling methodology can be applied such that the underlying information of several datasets from different patients is extracted to form the model.

The chapter “[Uncertainties and Modeling Errors of Type 1 Diabetes Models](#)” by Levente Kovács and Péter Szalay analyzes the effect of prediction model uncertainties on the control system during a design procedure involving the steps model reduction by elimination of state variables, state estimation using extended Kalman Filters and Sigma Point filters and linear parameter-varying control synthesis.

The chapter “[Recent Results on Glucose–Insulin Predictions by Means of a State Observer for Time-Delay Systems](#)” by Pasquale Palumbo et al. introduces a prediction model which in real time predicts the insulin concentration in blood which in turn is used in a control system. The method is tested in simulation on a time-delay system representing the glucose–insulin system.

The chapter “[Performance Assessment of Model-Based Artificial Pancreas Control Systems](#)” by Jianyuan Feng et al. makes use of prediction models to compute treatment advices. The novelty of the proposed algorithm consists in explicitly considering (among others) the model prediction error and model error elimination speed. A retuning of the advisory system is done in case the prediction model does not perform well. Results on 30 virtual patients show the performance of the control system.

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