Overnight glucose control in people with type 1 diabetes

This paper presents an individualized model predictive control (MPC) algorithm for overnight blood glucose stabilization in people with type 1 diabetes (T1D). The MPC formulation uses an asymmetric objective function that penalizes low glucose levels more heavily. We compute the model parameters in the MPC in a systematic way based on a priori available patient information. The model used by the MPC algorithm for filtering and prediction is an autoregressive integrated moving average with exogenous input (ARIMAX) model implemented as a linear state space model in innovation form. The control algorithm uses frequent glucose measurements from a continuous glucose monitor (CGM) and its decisions are implemented by a continuous subcutaneous insulin infusion (CSII) pump. We provide guidelines for tuning the control algorithm and computing the Kalman gain in the linear state space model in innovation form. We test the controller on a cohort of 100 randomly generated virtual patients with a representative inter-subject variability. We use the same control algorithm for a feasibility overnight study using 5 real patients. In this study, we compare the performance of this control algorithm with the patient’s usual pump setting. We discuss the results of the numerical simulations and the in vivo clinical study from a control engineering perspective. The results demonstrate that the proposed control strategy increases the time spent in euglycemia.
Adaptive control in an artificial pancreas for people with type 1 diabetes

In this paper, we discuss overnight blood glucose stabilization in patients with type 1 diabetes using a Model Predictive Controller (MPC). We compute the model parameters in the MPC using a simple and systematic method based on a priori available patient information. We describe and compare 3 different model structures. The first model structure is an autoregressive integrated moving average with exogenous input (ARIMAX) structure. The second model structure is an autoregressive moving average with exogenous input (ARMAX) model, i.e. a model without an integrator. The third model structure is an adaptive ARMAX model in which we use a recursive extended least squares (RELS) method to estimate parameters of the stochastic part. In addition, we describe some safety layers in the control algorithm that improve the controller robustness and reduce the risk of hypoglycemia. We test and compare our control strategies using a virtual clinic of 100 randomly generated patients with a representative inter-subject variability. This virtual clinic is based on the Hovorka model. We consider the case where only half of the meal bolus is administered at mealtime, and the case where the insulin sensitivity increases during the night. The numerical results suggest that the use of an integrator leads to higher occurrence of hypoglycemia than for the controllers without the integrator. Compared to other control strategies, the adaptive MPC reduces both the time spent in hypoglycemia and the time spent in hyperglycemia.

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An Adaptive Nonlinear Basal-Bolus Calculator for Patients With Type 1 Diabetes

Background: Bolus calculators help patients with type 1 diabetes to mitigate the effect of meals on their blood glucose by administering a large amount of insulin at mealtime. Intraindividual changes in patients physiology and nonlinearity in insulin-glucose dynamics pose a challenge to the accuracy of such calculators.

Method: We propose a method based on a continuous-discrete unscented Kalman filter to continuously track the postprandial glucose dynamics and the insulin sensitivity. We augment the Medtronic Virtual Patient (MVP) model to simulate noise-corrupted data from a continuous glucose monitor (CGM). The basal rate is determined by calculating the steady state of the model and is adjusted once a day before breakfast. The bolus size is determined by optimizing the postprandial glucose values based on an estimate of the insulin sensitivity and states, as well as the announced meal size. Following meal announcements, the meal compartment and the meal time constant are estimated, otherwise insulin sensitivity is estimated.

Results: We compare the performance of a conventional linear bolus calculator with the proposed bolus calculator. The
proposed basal-bolus calculator significantly improves the time spent in glucose target (P < .01) compared to the conventional bolus calculator.

**Conclusion:** An adaptive nonlinear basal-bolus calculator can efficiently compensate for physiological changes. Further clinical studies will be needed to validate the results.

**General information**

State: Published
Organisations: Department of Applied Mathematics and Computer Science, Scientific Computing, Dynamical Systems, Copenhagen University Hospital
Authors: Boiroux, D. (Intern), Aradóttir, T. B. (Intern), Nørgaard, K. (Ekstern), Poulsen, N. K. (Intern), Madsen, H. (Intern), Jørgensen, J. B. (Intern)
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.855 SNIP 0.897 CiteScore 1.99
BFI (2014): BFI-level 1
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Scopus rating (2012): SJR 0.69 SNIP 0.972 CiteScore 1.33
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Scopus rating (2011): SJR 0.687 SNIP 0.916 CiteScore 0.6
ISI indexed (2011): ISI indexed no
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Scopus rating (2010): SJR 0.452 SNIP 0.683
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Publication: Research - peer-review › Journal article – Annual report year: 2016
C code generation applied to nonlinear model predictive control for an artificial pancreas

This paper presents a method to generate C code from MATLAB code applied to a nonlinear model predictive control (NMPC) algorithm. The C code generation uses the MATLAB Coder Toolbox. It can drastically reduce the time required for development compared to a manual porting of code from MATLAB to C, while ensuring a reliable and fairly optimized code. We present an application of code generation to the numerical solution of nonlinear optimal control problems (OCP). The OCP uses a sequential quadratic programming algorithm with multiple shooting and sensitivity computation. We consider the problem of glucose regulation for people with type 1 diabetes as a case study. The average computation time when using generated C code is 0.21 s (MATLAB: 1.5 s), and the maximum computation time when using generated C code is 0.97 s (MATLAB: 5.7 s). Compared to the MATLAB implementation, generated C code can run in average more than 7 times faster.

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Organisations: Department of Applied Mathematics and Computer Science, Scientific Computing
Authors: Boiroux, D. (Intern), Jørgensen, J. B. (Intern)
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Model for Simulating Fasting Glucose in Type 2 Diabetes and the Effect of Adherence to Treatment.

The primary goal of this paper is to predict fasting glucose levels in type 2 diabetes (T2D) in long-acting insulin treatment. The paper presents a model for simulating insulin-glucose dynamics in T2D patients. The model combines a physiological model of type 1 diabetes (T1D) and an endogenous insulin production model in T2D. We include a review of sources of variance in fasting glucose values in long-acting insulin treatment, with respect to dose guidance algorithms. We use the model to simulate fasting glucose levels in T2D long-acting insulin treatment and compare the results with clinical trial results where a dose guidance algorithm was used. We investigate sources of variance and through simulations evaluate the contribution of adherence to variance and dose guidance quality. The results suggest that the model for simulation of T2D patients is sufficient for simulating fasting glucose levels during titration in a clinical trial. Adherence to insulin injections plays an important role considering variance in fasting glucose. For adherence levels 100%, 70% and 50%, the coefficient of variation of simulated fasting glucose levels were similar to observed variances in insulin treatment. The dose guidance algorithm suggested too large doses in 0.0%, 5.3% and 24.4% of cases, respectively. Adherence to treatment is an important source of variance in long-acting insulin titration.

General information
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Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, Scientific Computing, Novo Nordisk A/S
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An Efficient UD-Based Algorithm for the Computation of Maximum Likelihood Sensitivity of Continuous-Discrete Systems

This paper addresses maximum likelihood parameter estimation of continuous-time nonlinear systems with discrete-time measurements. We derive an efficient algorithm for the computation of the log-likelihood function and its gradient, which can be used in gradient-based optimization algorithms. This algorithm uses UD decomposition of symmetric matrices and the array algorithm for covariance update and gradient computation. We test our algorithm on the Lotka-Volterra equations. Compared to the maximum likelihood estimation based on finite difference gradient computation, we get a significant speedup without compromising the numerical accuracy.

General information
State: Published
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Publication: Research - peer-review › Conference article – Annual report year: 2017
Application of the Continuous-Discrete Extended Kalman Filter for Fault Detection in Continuous Glucose Monitors for Type 1 Diabetes

The purpose of this study is the online detection of faults and anomalies of a continuous glucose monitor (CGM). We simulated a type 1 diabetes patient using the Medtronic virtual patient model. The model is a system of stochastic differential equations and includes insulin pharmacokinetics, insulin-glucose interaction, and carbohydrate absorption. We simulated and detected two types of CGM faults, i.e., spike and drift. A fault was defined as a CGM value in any of the zones C, D, and E of the Clarke error grid analysis classification. Spike was modelled by a binomial distribution, and drift was modelled by a Gaussian random walk. We used a continuous-discrete extended Kalman filter for the fault detection, based on the statistical tests of the filter innovation and the 90-min prediction residuals of the sensor measurements. The spike detection had a sensitivity of 93% and a specificity of 100%. Also, the drift detection had a sensitivity of 80% and a specificity of 85%. Furthermore, with 100% sensitivity the proposed method was able to detect if the drift overestimates or underestimates the interstitial glucose concentration.

Comparison of Three Nonlinear Filters for Fault Detection in Continuous Glucose Monitors

The purpose of this study is to compare the performance of three nonlinear filters in online drift detection of continuous glucose monitors. The nonlinear filters are the extended Kalman filter (EKF), the unscented Kalman filter (UKF), and the particle filter (PF). They are all based on a nonlinear model of the glucose-insulin dynamics in people with type 1 diabetes. Drift is modelled by a Gaussian random walk and is detected based on the statistical tests of the 90-min prediction residuals of the filters. The unscented Kalman filter had the highest average F score of 85.9%, and the smallest average detection delay of 84.1%, with the average detection sensitivity of 82.6%, and average specificity of 91.0%.
Model Identification using Continuous Glucose Monitoring Data for Type 1 Diabetes

This paper addresses model identification of continuous-discrete nonlinear models for people with type 1 diabetes using sampled data from a continuous glucose monitor (CGM). We compare five identification techniques: least squares, weighted least squares, Huber regression, maximum likelihood with extended Kalman filter and maximum likelihood with unscented Kalman filter. We perform the identification on a 24-hour simulation of a stochastic differential equation (SDE) version of the Medtronic Virtual Patient (MVP) model including process and output noise. We compare the fits with the actual CGM signal, as well as the short- and long-term predictions for each identified model. The numerical results show that the maximum likelihood-based identification techniques offer the best performance in terms of fitting and prediction. Moreover, they have other advantages compared to ODE-based modeling, such as parameter tracking, population modeling and handling of outliers.
On the significance of the noise model for the performance of a linear MPC in closed-loop operation
This paper discusses the significance of the noise model for the performance of a Model Predictive Controller when operating in closed-loop. The process model is parametrized as a continuous-time (CT) model and the relevant sampled-data filtering and control algorithms are developed. Using CT models typically means less parameters to identify. Systematic tuning of such controllers is discussed. Simulation studies are conducted for linear time-invariant systems showing that choosing a noise model of low order is beneficial for closed-loop performance. (C) 2016, IFAC (International Federation of Automatic Control) Hosting by Elsevier Ltd. All rights reserved.

A Bolus Calculator Based on Continuous-Discrete Unscented Kalman Filtering for Type 1 Diabetics
In patients with type 1 diabetes, the effects of meals intake on blood glucose level are usually mitigated by administering a large amount of insulin (bolus) at mealtime or even slightly before. This strategy assumes, among other things, a prior knowledge of the meal size and the postprandial glucose dynamics. On the other hand, administering the meal bolus during or after mealtime could benefit from the information provided by the postprandial meal dynamics at the expense of a delayed meal bolus. The present paper investigates different bolus administration strategies (at mealtime, 15 minutes after or 30 minutes after the beginning of the meal). We implement a continuous-discrete unscented Kalman filter to estimate the states and insulin sensitivity. These estimates are used in a bolus calculator. The numerical results demonstrate that administering the meal bolus 15 minutes after mealtime both reduces the risk of hypoglycemia in case of an overestimated meal and the time spent in hyperglycemia if the meal size is underestimated. Faster insulin and the use of glucagon will have the potential to encourage postprandial meal bolus administration and hence will not require to accurately estimate the meal size.
A Continuous-Discrete Extended Kalman Filter for State and Parameter Estimation in People with Type 1 Diabetes
An artificial pancreas for automated blood glucose control in patients with Type 1 diabetes

Automated glucose control in patients with Type 1 diabetes is much-coveted by patients, relatives and healthcare professionals. It is the expectation that a system for automated control, also know as an artificial pancreas, will improve glucose control, reduce the risk of diabetes complications and markedly improve patient quality of life. An artificial pancreas consists of portable devices for glucose sensing and insulin delivery which are controlled by an algorithm residing on a computer. The technology is still under development and currently no artificial pancreas is commercially available. This review gives an introduction to recent progress, challenges and future prospects within the field of artificial pancreas research.

General information
State: Published
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Bi-hormonal Closed-loop Control of Blood Glucose for People With Type 1 Diabetes - the Diacon Project

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Comparison of Prediction Models for a Dual-Hormone Artificial Pancreas

In this paper we compare the performance of five different continuous time transfer function models used in closed-loop model predictive control (MPC). These models describe the glucose-insulin and glucose-glucagon dynamics. They are discretized into a state-space description and used as prediction models in the MPC algorithm. We simulate a scenario including meals and daily variations in the model parameters. The numerical results do not show significant changes in the glucose traces for any of the models, excepted for the first order model. From the present study, we can conclude that the second order model without delay should provide the best trade-off between sensitivity to uncertainties and practical usability for in vivo clinical studies.
Remarks on models for estimating the carbohydrate to insulin ratio and insulin sensitivity in T1DM

In this paper we estimate linear models for prediction of the interstitial glucose concentration in response to meals and bolus insulin. Parameters of these models can be directly used in simple bolus calculation rules. In contrast to models proposed in the literature, we present a model without an integrator. This model maintains the benefits of the existing empirical models and allows simulation of a longer time period than the post-prandial period, i.e. the couple of hours following a meal. Furthermore, the new model proposed in this paper does not require any re-initialization before meals.

General information
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Organisations: Department of Applied Mathematics and Computer Science, Scientific Computing, Slovak University of Technology
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Main Research Area: Technical/natural sciences
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Source-ID: 118977940
Publication: Research - peer-review › Article in proceedings – Annual report year: 2015

The contribution of glucagon in an Artificial Pancreas for people with type 1 diabetes

The risk of hypoglycemia is one of the main concerns in treatment of type 1 diabetes (T1D). In this paper we present a head-to-head comparison of a currently used insulin-only controller and a prospective bihormonal controller for blood glucose in people with T1D. The bihormonal strategy uses insulin to treat hyperglycemia as well as glucagon to ensure fast recovery from hypoglycemic episodes. Two separate model predictive controllers (MPC) based on patient-specific models handle insulin and glucagon infusion. In addition, the control algorithm consists of a Kalman filter and a meal time insulin bolus calculator. The feedback is obtained from a continuous glucose monitor (CGM). We implement a bihormonal simulation model with time-varying parameters available for 3 subjects to compare the strategies. We consider a protocol with 3 events - a correct mealtime insulin bolus, a missed bolus and a bolus overestimated by 60%. During normal operation both strategies provide similar results. The contribution of glucagon becomes evident after administration of the overestimated insulin bolus. In a 10h period following an overbolused meal, the bihormonal strategy reduces time spent in hypoglycemia in the most severe case by almost 15% (1.5h), outperforming the insulin-only control. Therefore, glucagon contributes to the safety of an Artificial Pancreas.

General information
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Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, Scientific Computing, Center for Energy Resources Engineering, Slovak University of Technology, Copenhagen University Hospital
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DOIs: 10.1109/ACC.2015.7172134
Publication: Research - peer-review › Article in proceedings – Annual report year: 2015

Assessment of Model Predictive and Adaptive Glucose Control Strategies for People with Type 1 Diabetes

This paper addresses overnight blood glucose stabilization in people with type 1 diabetes using a Model Predictive Controller (MPC). We use a control strategy based on an adaptive ARMAX model in which we use a Recursive Extended Least Squares (RELS) method to estimate parameters of the stochastic part. We compare this model structure with an
autoregressive integrated moving average with exogenous input (ARIMAX) structure, and with an autoregressive moving average with exogenous input (ARMAX) model, i.e. without an integrator. Additionally, safety layers improve the controller robustness and reduce the risk of hypoglycemia. We test our control strategies on a virtual clinic of 100 randomly generated patients with a representative inter-subject variability. This virtual clinic is based on the Hovorka model. We consider the case where only half of the meal bolus is administered at mealtime, and the case where the insulin sensitivity varies during the night. The simulation results demonstrate that the adaptive control strategy can reduce the risks of hypoglycemia and hyperglycemia during the night.

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Model-Based Closed-Loop Glucose Control in Type 1 Diabetes: The DiaCon Experience

Background:
To improve type 1 diabetes mellitus (T1DM) management, we developed a model predictive control (MPC) algorithm for closed-loop (CL) glucose control based on a linear second-order deterministic-stochastic model. The deterministic part of the model is specified by three patient-specific parameters: insulin sensitivity factor, insulin action time, and basal insulin infusion rate. The stochastic part is identical for all patients but identified from data from a single patient. Results of the first clinical feasibility test of the algorithm are presented.

Methods:
We conducted two randomized crossover studies. Study 1 compared CL with open-loop (OL) control. Study 2 compared glucose control after CL initiation in the euglycemic (CL-Eu) and hyperglycemic (CL-Hyper) ranges, respectively. Patients were studied from 22:00–07:00 on two separate nights.

Results:
Each study included six T1DM patients (hemoglobin A1c 7.2% ± 0.4%). In study 1, hypoglycemic events (plasma glucose < 54 mg/dl) occurred on two OL and one CL nights. Average glucose from 22:00–07:00 was 90 mg/dl [74–146 mg/dl; median (interquartile range)] during OL and 108 mg/dl (101–128 mg/dl) during CL (determined by continuous glucose monitoring). However, median time spent in the range 70–144 mg/dl was 67.9% (3.0–73.3%) during OL and 80.8% (70.5–89.7%) during CL. In study 2, there was one episode of hypoglycemia with plasma glucose <54 mg/dl in a CL-Eu night. Mean glucose from 22:00–07:00 and time spent in the range 70–144 mg/dl were 121 mg/dl (117–133 mg/dl) and 69.0% (30.7–77.9%) in CL-Eu and 149 mg/dl (140–193 mg/dl) and 48.2% (34.9–72.5%) in CL-Hyper, respectively.

Conclusions:
This study suggests that our novel MPC algorithm can safely and effectively control glucose overnight, also when CL control is initiated during hyperglycemia.

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Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, Center for Energy Resources Engineering, Scientific Computing, Copenhagen University Hospital
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Main Research Area: Technical/natural sciences

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Computational Methods for Model Predictive Control: New Opportunities for Computational Scientists

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Organisations: Center for Energy Resources Engineering, Department of Informatics and Mathematical Modeling, Scientific Computing, Automation and Control, Computer Science and Engineering, Mathematical Statistics, Technical University of Denmark
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Computational Methods for Model Predictive Control.pdf
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Source-ID: u::4982
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Control of Blood Glucose for People with Type 1 Diabetes: an in Vivo Study

Since continuous glucose monitoring (CGM) technology and insulin pumps have improved recent years, a strong interest in a closed-loop artificial pancreas for people with type 1 diabetes has arisen. Presently, a fully automated controller of blood glucose must face many challenges, such as daily variations of patient's physiology and lack of accuracy of glucose sensors. In this paper we design and discuss an algorithm for overnight closed-loop control of blood glucose in people with type 1 diabetes. The algorithm is based on Model Predictive Control (MPC). We use an offset-free autoregressive model with exogenous input and moving average (ARMAX) to model the patient. Observer design and a time-varying glucose reference signal improve robustness of the algorithm. We test the algorithm in two clinical studies conducted at Hvidovre Hospital. The first study took place overnight, and the second one took place during daytime. These trials demonstrate the importance of observer design in ARMAX models and show the possibility of stabilizing blood glucose during the night.

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Control of Blood Glucose for People with Type 1 Diabetes: an in Vivo Study

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Model Predictive Control Algorithms for Pen and Pump Insulin Administration

Despite recent developments within diabetes management such as rapidacting insulin, continuous glucose monitors (CGM) and insulin pumps, tight blood glucose control still remains a challenge. A fully automated closed-loop controller, also known as an artificial pancreas (AP), has the potential to ease the life and reduce the risk of acute and chronic
diabetic complications. However, the noise associated to CGMs, the long insulin action time for continuous subcutaneous infusion of insulin (CSII) pumps, and the high intra- and inter-patient variability significantly limits the performance of current closed-loop controllers.

In this thesis, we present different control strategies based on Model Predictive Control (MPC) for an artificial pancreas. We use Nonlinear Model Predictive Control (NMPC) in order to determine the optimal insulin and blood glucose profiles. The optimal control problem (OCP) is solved using a multiple-shooting based algorithm. We use an explicit Runge-Kutta method (DOPRI45) with an adaptive stepsize for numerical integration and sensitivity computation. The OCP is solved using a Quasi-Newton sequential quadratic programming (SQP) with a linesearch and a BFGS update for the Hessian of the Lagrangian. In addition, we apply a Continuous-Discrete Extended Kalman Filter (CDEKF) in order to simulate cases where the meal size is uncertain, or even unannounced.

We also propose a novel control strategy based on linear MPC for overnight stabilization of blood glucose. The model parameters are personalized using a priori available patient information. We consider an autoregressive integrated moving average with exogenous input (ARIMAX) model. We summarize and discuss the results of the overnight clinical studies conducted at Hvidovre Hospital. Based on these results, we propose improvements for the stochastic part of our controller model. We compare three different stochastic model structures. The first one is the ARIMAX structure that has been used for the clinical studies. The second one is an autoregressive moving average with exogenous input (ARMAX) model. The third one is an adaptive ARMAX model in which we estimate the parameters of the stochastic part using a Recursive Least Square (RLS) method. We test the controller in a virtual clinic of 100 patients. This virtual clinic is based on the Hovorka model. We consider the case where only half of the bolus is administrated at mealtime, and the case where the insulin sensitivity increases during the night.

This thesis consists of a summary report, glucose and insulin profiles of the clinical studies and research papers submitted, peer-reviewed and/or published in the period September 2009 - September 2012.
Tuning of Controller for Type 1 Diabetes Treatment with Stochastic Differential Equations

People with type 1 diabetes need several insulin injections every day to keep their blood glucose level in the normal range and thereby avoiding the acute and long term complications of diabetes. One of the recent treatments consists of a pump injecting insulin into the subcutaneous layer combined with a continuous glucose monitor (CGM) frequently observing the glucose level. Automatic control of the insulin pump based on CGM observations would ease the burden of constant diabetes treatment and management. We have developed a controller designed to keep the blood glucose level in the normal range by adjusting the size of insulin infusions from the pump based on model predictive control (MPC). A clinical pilot study to test the performance of the MPC controller overnight was performed. The conclusion was that the controller relied too much on the local trend of the blood glucose level which is a problem due to the noise corrupted observations from the CGM. In this paper we present a method to estimate the optimal Kalman gain in the controller based on stochastic differential equation modeling. With this model type we could estimate the process noise and observation noise separately based on data from the first clinical pilot study. In doing so we obtained a more robust control algorithm which is less sensitive to fluctuations in the CGM observations and rely more on the global physiological trend of the blood glucose level. Finally, we present the promising results from the second pilot study testing the improved controller.
Insulin Administration for People with Type 1 diabetes

In this paper, we apply model predictive control (MPC) for control of blood glucose in people with type 1 diabetes. The two first control strategies are based on nonlinear model predictive control (NMPC). The first control strategy is based on meal announcement in advance, while the second one considers meal announcement at mealtimes only. They give a quantitative upper bound on the achievable control performance. The third control strategy is a feedforward-feedback control strategy. This strategy uses a time-varying setpoint to reduce the risk of hypoglycemia. The feedback controller computes the optimal basal insulin infusion rate. The feedforward controller consists of a bolus calculator. It computes the optimal bolus, along with the time-varying glucose setpoint. We test these three strategies on a virtual patient with type 1 diabetes. The numerical results demonstrate the robustness of the last control strategy with respect to changes in the model parameters and incorrect meal announcement.

Strategies for glucose control in people with type 1 diabetes

In this paper we apply a robust feedforward-feedback control strategy to people with type 1 diabetes. The feedforward controller consists of a bolus calculator which compensates the disturbance coming from meals. The feedback controller is based on a linearized description of the model describing the patient. We minimize the risk of hypoglycemia by introducing a time-varying glucose setpoint based on the announced meal size and the physiological model of the patient. The simulation results are based on a virtual patient simulated by the Hovorka model. They include the cases where the insulin sensitivity changes, and mismatches in meal estimation. They demonstrate that the designed controller is able to achieve offset-free control when the insulin sensitivity change, and that having a time-varying reference signal enables more robust control of blood glucose in the cases where the meal size is known, but also when the ingested meal does not match the announced one.
ARX MPC for People with Type 1 Diabetes

Type 1 diabetes is a chronic disease characterized by a lack of production of pancreatic insulin, consequently leading to high blood glucose concentrations (hyperglycemia). Hyperglycemia has negative health effects in the long term such as eye, nerve, and kidney disease. Exogenous insulin must be injected to keep the blood glucose in the normoglycemic range (approximately 60 – 140 mg/dL, or 3.3 – 8 mmol/L). However, the dosing of exogenous insulin must be done carefully, because low blood glucose concentrations (hypoglycemia) can have immediate and severe consequences like insulin shock, coma, or even death. Currently, insulin administration is performed by the subject with type 1 diabetes based on infrequent glucose measurements (in the form of finger-sticks), often resulting in an unsatisfactory blood glucose control. An artificial pancreas is a medical device that injects exogenous insulin automatically in order to regulate the glucose concentration. Blood glucose measurements are obtained from a continuous glucose monitor (CGM). Insulin is administrated either continuously through an insulin pump, or at discrete times using an insulin pen. A control algorithm uses previous glucose measurements and insulin injection information to compute the optimal insulin administration for the current conditions. We use model predictive control (MPC) to compute the optimal insulin administration for 20 virtual type 1 diabetes subjects. The system (i.e., subject) has one manipulated input (insulin infusion rate), one disturbance input (carbohydrate meals), and one measured output (blood glucose concentration). The subject is represented by a system of nonlinear differential equations describing the dynamic effects of insulin and meals on blood glucose. Twenty parameter sets are used in the study, each representing a different virtual subject. The model used in the MPC is a low order autoregressive exogenous-input (ARX) model. Due to both the linearity and relative parsimony of the ARX model, there is a significant amount of subject/model mismatch in the model predictions, reflecting real-world conditions. In general, a simple ARX MPC cannot reject a step disturbance without a resulting offset; thus, the state vector is reformulated using an extended ΔARX description (E-ΔARX). The reference signal is time-varying, and is based on the optimal open-loop glucose profile. Insulin-on-board constraints are implemented to avoid overdosing insulin. State estimation is based on a Kalman filter using the noise model to simulate a realistic CGM. We present the MPC results for simulations of the 20 virtual subjects with type 1 diabetes. In particular, we investigate the effects of the prediction horizon length on the control quality of blood glucose and the robustness of the solution.
Meal Estimation in Nonlinear Model Predictive Control for Type 1 Diabetes

General information
State: Published
Organisations: Center for Energy Resources Engineering, Department of Informatics and Mathematical Modeling, Scientific Computing, Mathematical Statistics
Pages: 1052-1057
Publication date: 2010

Nonlinear Model Predictive Control for an Artificial Beta-Cell

General information
State: E-pub ahead of print
Organisations: Scientific Computing, Department of Informatics and Mathematical Modeling, Mathematical Statistics, Center for Energy Resources Engineering
Pages: 299-308
Publication date: 2010

Optimal Insulin Administration for People with Type 1 Diabetes

General information
State: Published
Organisations: Scientific Computing, Department of Informatics and Mathematical Modeling, Mathematical Statistics, Center for Energy Resources Engineering
Publication date: 2010

DiaCon: an interdisciplinary approach to diabetes control

General information
State: Published
Organisations: Scientific Computing, Department of Informatics and Mathematical Modeling, Mathematical Statistics, Center for Systems Microbiology, Department of Systems Biology
Publication date: 2009
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 257648
Publication: Research - peer-review › Poster – Annual report year: 2009

Projects:

A bi-hormonal Artificial Pancreas based on an Ensemble Nonlinear Model Predictive Control Algorithm
Department of Applied Mathematics and Computer Science
Scientific Computing
Period: 01/08/2014 → 31/07/2017
Number of participants: 1
Project participant:
Boiroux, Dimitri (Intern)
Project

Model Predictive Control algorithms for pen and pump insulin administration
Department of Informatics and Mathematical Modeling
Period: 01/09/2009 → 22/11/2012
Number of participants: 7
Phd Student:
Boiroux, Dimitri (Intern)
Supervisor:
Madsen, Henrik (Intern)
Poulsen, Niels Kjølstad (Intern)
Main Supervisor:
Jørgensen, John Bagterp (Intern)
Examiner:
Sørensen, Mads Peter (Intern)
Knudsen, Jørgen K. H. (Ekstern)
del Re, Luigi (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering
Project: PhD

Activities:

Mathematical modeling of neurons: Perspectives for the treatment of epilepsy
Period: 13 Dec 2017
Dimitri Boiroux (Guest lecturer)
Department of Applied Mathematics and Computer Science
10th International Conference on Advanced Technologies and Treatments for Diabetes
Period: 15 Feb 2017 → 18 Feb 2017
Dimitri Boiroux (Participant)
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Degree of recognition: International

University of Virginia
Period: 1 Oct 2016 → 10 Dec 2016
Dimitri Boiroux (Visiting researcher)
Department of Applied Mathematics and Computer Science
Scientific Computing
Activity: Visiting an external institution › Visiting another research institution

19th Nordic Process Control Workshop
Period: 16 Jan 2015
Dimitri Boiroux (Speaker)
Department of Applied Mathematics and Computer Science
Scientific Computing
Documents:
NPCW 2015 abstract

18th Nordic Process Control Workshop
13/01/2015 → 16/01/2015
Trondheim, Norway
Activity: Talks and presentations › Conference presentations