Model Predictive Control Algorithms for Pen and Pump Insulin Administration

Despite recent developments within diabetes management such as rapid-acting 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 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 state and 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.