Addressing Intra-Subject Variability in Insulin Sensitivity Using the Hovorka Glucose Prediction Model

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Introduction

Type 1 Diabetes Mellitus (T1DM) is a chronic condition with no cure. Individuals with T1DM do not produce insulin, a hormone to regulate the blood glucose level (BGL), which causes severe short- and long-term consequences. Artificial Pancreas (AP) is the most advanced treatment to achieve good glucose control. This system is based on a hybrid closed-loop algorithm, which contains a sensor to measure BGL, an insulin pump to infuse insulin, and a control algorithm that decides how much insulin to infuse into the subject. An implemented control algorithm uses a phenomenological glucose prediction model to estimate future glucose trends. Due to the high inter-subject variability, the individualization of this model is crucial. Intra-subject variability has not yet been included in phenomenological models. Here we present two methods to make parameters dependent on the time of day and thus introduce intra-subject variability into the model.

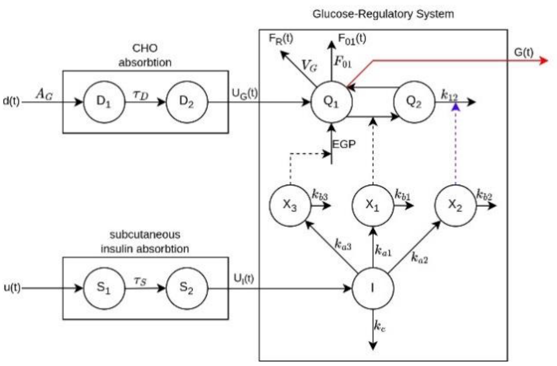

Fig. 1 Hovorka glucose prediction model. Continuous arrows show the flow, dashed arrows show the influence on the velocity of the flow. The red arrow shows the measured BGL. Our method creates a time varying impact on the glucose prediction at the purple arrow.

Materials and Methods

We simulated 30-days of glucose trends of 100 subjects from the UVA/PADOVA simulator, with random meal intakes and time of the day dependent insulin sensitivity variation. Knowing that insulin sensitivity in UVA/PADOVA is the only parameter that depends on time, we propose two methods to estimate a daily profile of the insulin sensitivity parameter (SI_2) in the Hovorka model with 7 days of training data:

Firstly, in a grid search, an SI_2 value is found for each full hour that minimizes the prediction error for that hour. The SI_2 values obtained for the same hour on each day are then averaged.
Secondly, the SI_2 profile is obtained with a physics-informed neural network (PINN), a neural network architecture which ensures to comply with the physical knowledge and with measured data.
Finally, we cluster the obtained SI_2-daily-profile to investigate the relationship between subjects, and to test the connection to the insulin sensitivity profiles from the UVA/PADOVA simulator.

Results

Compared to a fixed SI_2, applying the daily profile of SI_2 obtained with the first and second method reduced the error in the test data by 22% and 10%, respectively. Figure 2 shows the prediction over two test days with a fixed (yellow) and time-dependent (red) SI_2 parameter of the first method.
Clustering of the SI_2 profiles revealed five patterns, one with a constant SI_2 parameter during the day, another with a higher SI_2 parameter in the morning, one with a higher SI_2 parameter at night, and two with higher SI_2 in the afternoon.

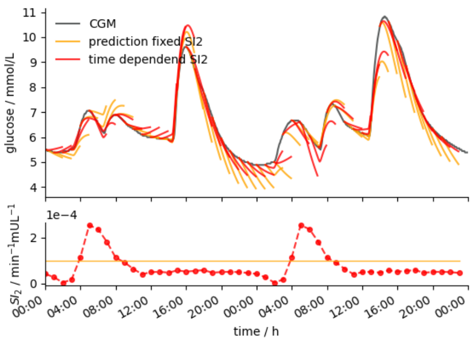

Fig. 2 Top: Prediction of glucose trends in one subject for 2 days. Each prediction is 2 hours long. Bottom: SI_2 trend fix and time dependent.

Discussion

We demonstrated that making insulin sensitivity time-dependent significantly reduces the RMSE in glucose prediction, proving that SI_2 is a significant parameter for glucose prediction. Additionally, we demonstrated that the obtained insulin sensitivity trends can be clustered into groups, revealing associations between subjects.