Personalized Data-Driven Verification and Synthesis for Artificial Pancreas Controllers

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Background and Aims

People with T1D exhibit variability in physiological characteristics such as hormonal fluctuations, activity, and food, which affect their glucose-insulin physiology. At the same time, control algorithms for the artificial pancreas can be tuned using numerous parameters that affect the correctness and performance of the closed-loop system.

Currently, the process of tuning and re-tuning parameters is carried out by the patient and physician following guidelines that are often vague and result in what is essentially an educated guess-and-check approach. We aim to improve efficiency and guarantee safety of the tuning protocol utilizing a novel data-driven patient-specific modeling approach.

Patient Data

Data was obtained from an outpatient clinical trial of a predictive low-glucose pump shutoff involving CGM, finger prick, and insulin data for nearly 50 patients with 90 sessions/patient

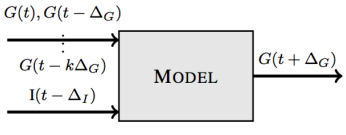
Table 1: Overall bio-demographic data

Characteristics:	range and median, unless noted
Number	49
Female (%)	53%
Age (yr)	15-46 (30)
BMI (kg/m^2)	17.9-34.6 (24.3)
Diabetes duration (yr)	2-42 (15)
HbA1C (%)	5.6-8 (6.9)
Total Daily Dose (U)	17.6-95 (42)

Modeling Methods

Whereas existing approaches use deterministic models, we propose non-deterministic relational models that predict a range of possible glucose values rather than a single point. [Fig 1.] In order to replicate nonlinearity, we combine 5 models which are learned over various look-back windows, Δ_G. [Fig. 2]

$$G(t+\Delta_G) \in a_0 G(t) + a_1 G(t-\Delta_G) + bI(t-\Delta_I) + [L, U]$$



Eqn. and Fig. 1: Overall model structure and base equation that predicts future glucose values from past glucose (G) and insulin (I) values. The bound $[L, U]$ gives 99% confidence interval range.

Fig. 2: Figure illustrating the prediction of a composite model, shown here with three combinations of (ΔG,ΔI). Predicted values are obtained as the intersection of the individual interval ranges predicted by each model.

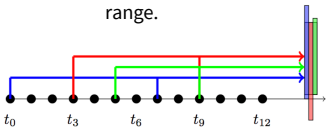
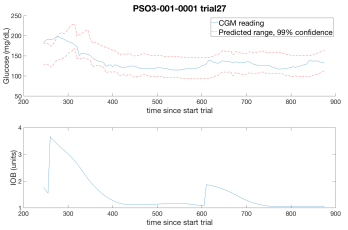


Fig. 3: Example of model predictions using our nondeterministic approach (dashed red) and actual patient blood glucose (solid blue) for patient ID 1.



These models capture important glucose trends as well as uncertainty in predictions arising from uncontrollable externalities such as CGM noise.

Results

Treating our patient model equations as constraints, and coupling them with a PID control scheme [2,3], we predict all possible behaviors of the closed-loop system over a time horizon using integer linear optimization solvers.

Under the standard tuning protocol for gain [2,3], 5% of patients are predicted to be *safe*, defined as 100% time in range. [Fig 4]

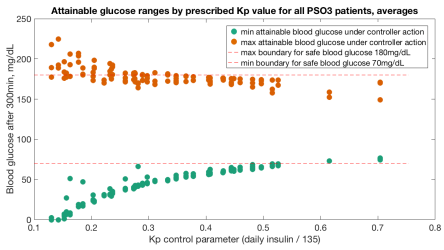
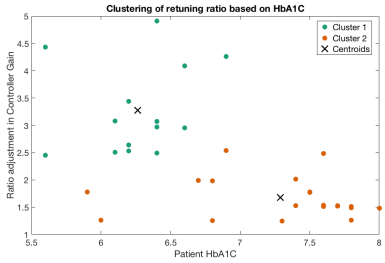


Fig. 4: Min and max attainable blood glucose levels after 6hrs for patients under closed-loop control using the tuning protocol from [2,3]

Through exhaustive search, we find ideal gain parameters for each patient. K-means clustering shows a strong correlation between amount of retuning required, and patient HbA1C levels [Fig 5]

Fig. 5: Ratio of best found gain parameter, K_p, to suggested parameter from [2,3] clustered by patient HbA1C.



Based on clustering analysis, we construct a patient-specific retuning law based on readily available patient demographic data:

$$K_p^r = \begin{cases} (0.52\text{HbA1c} + 0.036)\dfrac{\text{DailyInsulin}}{135} & \text{if HbA1c} \leq 7 \\ (-0.08\text{HbA1c} + 2.24)\dfrac{\text{DailyInsulin}}{135} & \text{otherwise} \end{cases}$$

Under this retuning strategy, we find improved control and safety for 82% of patients [Fig 6]

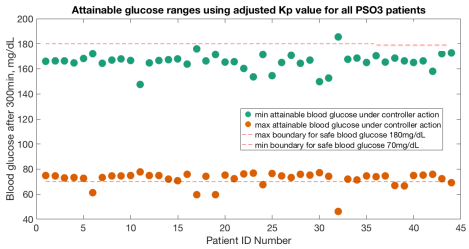


Fig. 6: Min and max attainable blood glucose levels after 6hrs for patients under closed-loop control using our improved tuning law

Conclusions

- We provide a data-driven, patient-specific re-tuning methodology which can potentially improve control for 82% of patients, based on the results of an exhaustive reachability analysis
- Our results demonstrate that simple nondeterministic models allow us to efficiently tune key controller parameters, thus paving the way for interesting clinical translational applications
- To our knowledge, the correlation of closed-loop controller efficacy with patient HbA1c levels has not yet been studied in medial trials and presents a novel consideration for future work

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References

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