# Mid-Term Blood Glucose Prediction: A Hybrid Approach using Grammatical Evolution and Physiological Models

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## Background

Personalization of blood Glucose (BG) prediction models and improving the Prediction Horizon (PH) without compromising a safe level of accuracy is an important challenge to tackle in the artificial pancreas.

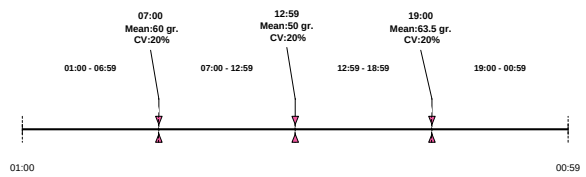
## Aim

Proposal of personalized hybrid models using Grammatical Evolution (GE) and physiological models for mid-term blood glucose predictions.

PH=120 minutes

## DATA

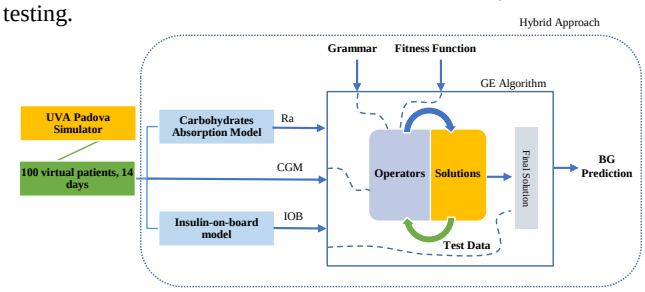
The data set correspond to 100 *in-silico* patients simulated using the UVA-Padova simulator[1]: 14-day time series of BG readings collected by CGM sensor, carbohydrate (CHO) intake and insulin delivery via insulin pump. The CHO intake (gr) includes three meals per day sampled from Gaussian distributions with a mean of 50, 60 and 63.5 gr. for breakfast, lunch and dinner, respectively, and a coefficient of variation equal to 20% [2].




## METHODS

Insulin-on-Board and glucose rate of appearance models were included into a hybrid predictive model that uses symbolic regression through grammatical evolution[3]. Four personalized models per patient were developed, corresponding to 6-hour periods of the day.

A fitness function based on a glucose-specific root mean squared function[4] (gRMSE) that penalizes the deviations according to their clinical harmfulness was used. Four additional days were used for testing.




$$G(t) = \sum_{i=0}^{i=n} [Preop(G^{\alpha}_{t-\beta})\ Op\ \delta]$$

$$R_a(t) = \sum_{i=0}^{i=n} [Preop(R^{\alpha}_{at-\beta})\ Op\ \delta]$$

$$I_{OB}(t) = \sum_{i=0}^{i=n} [Preop(IOB^{\alpha}_{t-\beta})\ Op\ \delta]$$

$$Circadian(t) = A\cos(\omega t + \phi)$$

***Op*** {+,-,*,/ }
***Preop*** {sqrt(*x*),log(*x*),$x^{-1}$,$x^{y}$,sin(*x*)}
***α*** and ***β*** are parameters adjusted by the evolutionary process.

The ***grammar*** plays a crucial role in the generated models. It constraints the search space of solutions using a set of rules.

## RESULTS

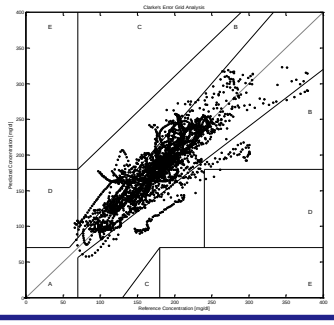
The results are displayed for training and testing of each one of the models designated for 4 different segments of the day, in terms of the mean RMSE, MAD,MARD and their corresponding glucose-specific metrics gRMSE, gMAD and gMARD for all of the patients:

| Segment | | RMSE (mg/dl) | gRMSE (mg/dl) | MAD (mg/dl) | gMAD (mg/dl) | MARD (%) | gMARD (%) |
|---|---|---|---|---|---|---|---|
| 1 am-7am | Training | 10.89 | 11.36 | 8.24 | 8.83 | 7.01 | 7.62 |
| | Testing | 11.8 | 12.19 | 9.1 | 9.68 | 7.62 | 8.25 |
| 7am-1pm | Training | 19.9 | 21.99 | 15.62 | 18.71 | 10.25 | 12.13 |
| | Testing | 22.09 | 24.6 | 17.39 | 21.11 | 11.5 | 13.78 |
| 1pm-7pm | Training | 18.74 | 20.37 | 14.69 | 16.86 | 11.32 | 13.23 |
| | Testing | 21.43 | 23.61 | 16.83 | 19.9 | 12.67 | 15.16 |
| 7pm-1am | Training | 25.14 | 28.16 | 19.38 | 23.4 | 14.24 | 17.18 |
| | Testing | 29 | 33 | 22.8 | 27.9 | 16 | 19.8 |

The table below shows the mean percentages in the Clarke Error Grid zones, indicating the level of clinical harmfulness of the deviation of the predictions made in both the training and testing phase for all the patients:

| Segment | ZONE A (%) | | ZONE C (%) | ZONE D (%) | ZONE E (%) | ZONE E (%) |
|---|---|---|---|---|---|---|
| 1 am-7am | Training | 91.93 | 7.54 | 0 | 0.53 | 0 |
| | Test | 90.53 | 8.84 | 0 | 0.63 | 0 |
| 7am-1pm | Training | 87.3 | 11.5 | 0 | 1.16 | 0 |
| | Test | 83.38 | 15.3 | 0 | 1.26 | 0 |
| 1pm-7pm | Training | 84.50 | 14.23 | 0 | 1.67 | 0 |
| | Test | 80.75 | 17.18 | 0.02 | 2.03 | 0.003 |
| 7pm-1am | Training | 75.53 | 21.88 | 0.04 | 2.52 | 0 |
| | Test | 70.66 | 26.5 | 0.22 | 2.65 | 0.01 |

Example of the Clarke Error Grid for 10 patients, corresponding to the test results for the model from 7am to 1 pm.



## CONCLUSIONS

- It is feasible to predict mid-term BG profiles using grammatical evolution with a reasonable deviation and safety metrics for the virtual cohort chosen in this study.
- The selection and customization of the grammar plays a key role in the accuracy of the prediction. Additionally, the use of a glucose-specific metric as a fitness function for the optimization process led to clinically safer models.

## FUTURE WORK

- Personalization of BG prediction models using real patient data.
- The risk of hyper/hypo-glycemia events can be incorporated in the fitness function to increase the safety of the algorithm.
- Exploring alternative grammar architectures in order to make the patient model more accurate.

## REFERENCES

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