The University of Virginia/Padova Type 1 Diabetes Simulator Goes Single Day

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BACKGROUND AND AIM

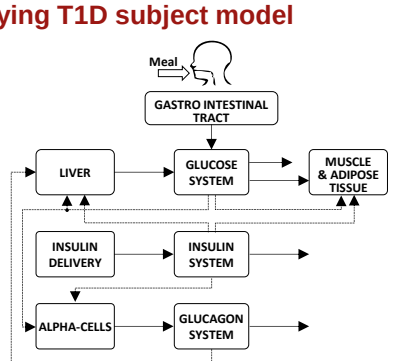
Since its acceptance by the U.S. Food and Drug Administration in 2008, the UVA/Padova Type 1 Diabetes (T1D) Simulator has been extensively used for in silico testing of several diabetes treatments, such as Artificial Pancreas controllers, novel insulin compounds and continuous glucose monitoring sensors.

A new version of the simulator has been recently developed in order to mimic diurnal glucose variability of T1D subjects, and to be up-to-date with the latest technological advances in insulin delivery and glucose measuring systems.

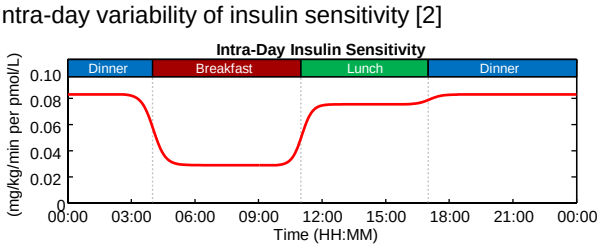
Here we present the new features with respect to the previous simulator version (release. 2013 [1]).

T1D SIMULATOR

Time-varying T1D subject model



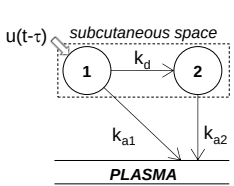
- Intra-day variability of insulin sensitivity [2]



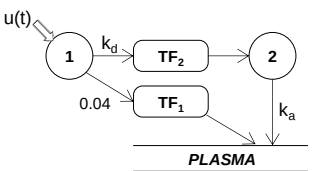
- "Dawn" phenomenon, based on clinical findings in T1D subjects [3]

Insulin delivery models

- Updated subcutaneous insulin kinetics [4] using data of 112 T1D subjects, to reproduce the commercially available fast-acting insulin analogs

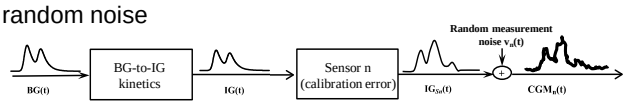


- New model of intra-dermal insulin delivery [5], characterized by serial-compartmental diffusion blocks and built on data of 10 healthy subjects



CGM & SMBG models

- CGM error model [6] (tuned against Dexcom G4® Platinum), described as a combination of calibration error and a random noise



- SMBG error model [7-9] (tuned on published meter data) describing most of the commercially available meters

In silico population

The new T1D simulator is equipped with a population of 300 in silico subjects (100 adults, 100 adolescents and 100 children, respectively).

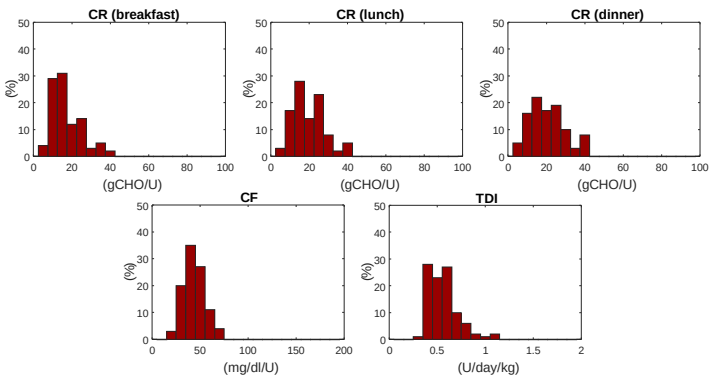
In silico subjects have been generated by randomly extracting different realizations of the parameter vector from appropriate joint parameter distributions, and using the same criteria described in [1].

Each in silico subject is equipped with parameters defining diabetic therapy:

- daily pattern of time-varying basal insulin rate, to compensate subject's intra-day variability of insulin sensitivity and dawn phenomenon
- daily pattern of time-varying carbohydrate-to-insulin ratio (CR), to compensate subject's insulin sensitivity pattern
- total daily insulin (TDI) and correction factor (CF), determined as in [1]

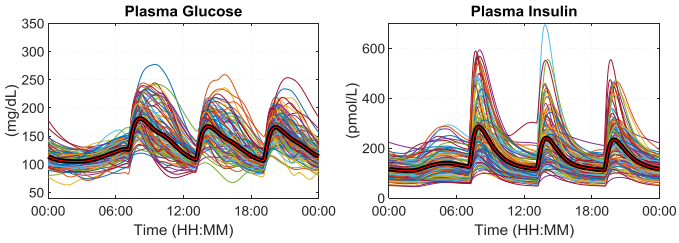
RESULTS

Diabetes therapy parameters

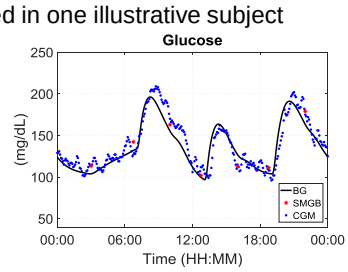


Simulated glucose & insulin time courses

One hundred in silico adults undergoing 1-day simulation, receiving 60g of carbs at 7.00 AM, 1.00 PM, 7.00PM and optimal insulin basal&bolus (according to subject CRs and CF).



- Plasma glucose time course with CGM and SMBG data superimposed in one illustrative subject



CONCLUSION

The new version of the UVA/Padova T1D simulator extends the domain of validity of the simulator from "single-meal" to "single-day multiple-meal" scenarios.

Such a tool, capable to well resemble T1D subjects in real life, provides a valid framework for the in silico testing of several novel diabetes treatments, e.g. adaptive artificial pancreas prototypes, smart sensors, and new insulin molecules.

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ACKNOWLEDGMENTS:

This work has been partially funded by University of Padova, "Progetto di Ateneo 2014".

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ATTD Advanced Technologies & Treatments for Diabetes