Risk and reward trade-off of glycaemic control in intensive care units

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Stress-induced hyperglycaemia is a frequent glycaemic complication in critically ill patients. The resulting elevated blood sugar levels are associated with increased mortality and morbidity in intensive care units. Glycaemic control (GC) has been used to regulate stress-induced hyperglycaemia and is mostly achieved through insulinotherapy. The Stochastic TARgeted (STAR) protocol is a model-based GC protocol modulating both insulin and nutrition minimising risk for the BG levels to be outside a pre-set target range.

STAR has been clinically validated and provides safe and effective control for nearly all patients. However, one of the main identified drawback from the implementation of STAR in clinical environment is the possible increased workload compared to some intensive care units (ICU) local practice. This work aims at investigating solutions to reduce this workload and the insulin dosing variability also affecting nurse's compliance to the protocol. The solutions are studied by means of virtual trials on virtual patients allowing to assess and validate likely outcomes prior potential clinical trial, ultimately saving clinical time and costs.

The first solution investigated aims at increasing measurement intervals in STAR from 1-3 hourly to 1-6 hourly. New stochastic models are built to forecast insulin sensitivity variability over 1-6 hours intervals. These models are first validated using five-fold cross-validation, then used in virtual trials to validate their impact on simulated BG outcomes. Results obtained show a risk and reward trade-off with, as expected, a reduced workload for longer time intervals at the cost of reduced safety. However, both performance and safety remains very high confirming the results obtained for a virtual trial performed on an older version of the stochastic models. These results should be further confirmed by conducting clinical trials.

To further reduce workload, new treatment selection processes are considered in the STAR framework. Different modifications are implemented on the current version allowing longer treatment intervals and reducing insulin dosage variations between interventions. Results obtained from the different virtual trials performed with these modifications once again highlight risk and reward trade-offs with reduced workload and median insulin variations at the expense of respectively reduced safety and nutrition, and increased workload. Their combination results in a safe and effective control, but should be clinically validated after some further optimisations.

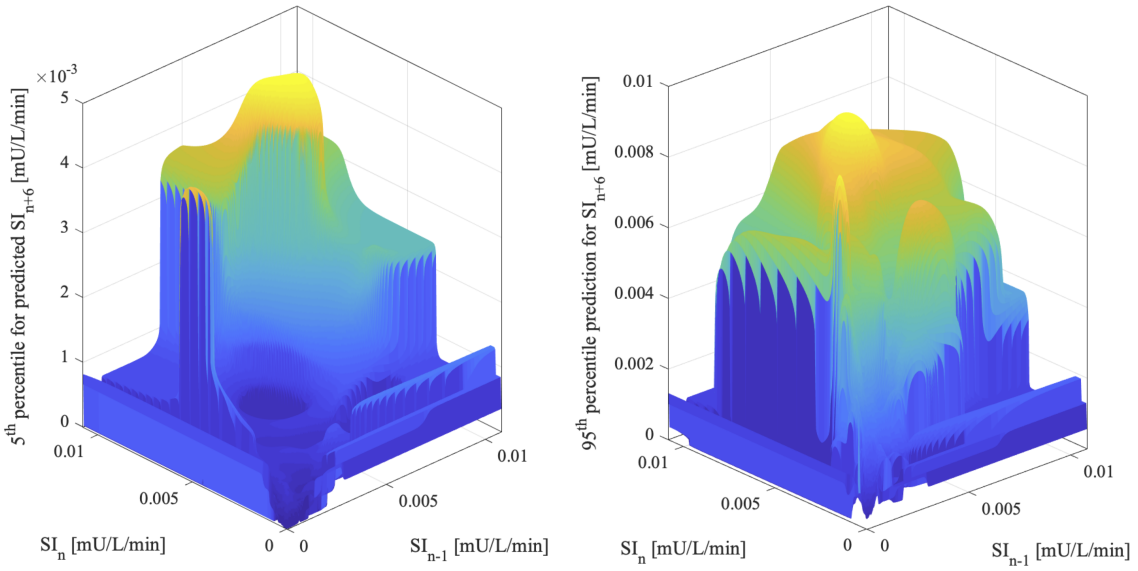

Figure 1: Example of 5$^{\text{th}}$(left) and 95$^{\text{th}}$(right) percentile prediction for 6-hourly 3D stochastic model.

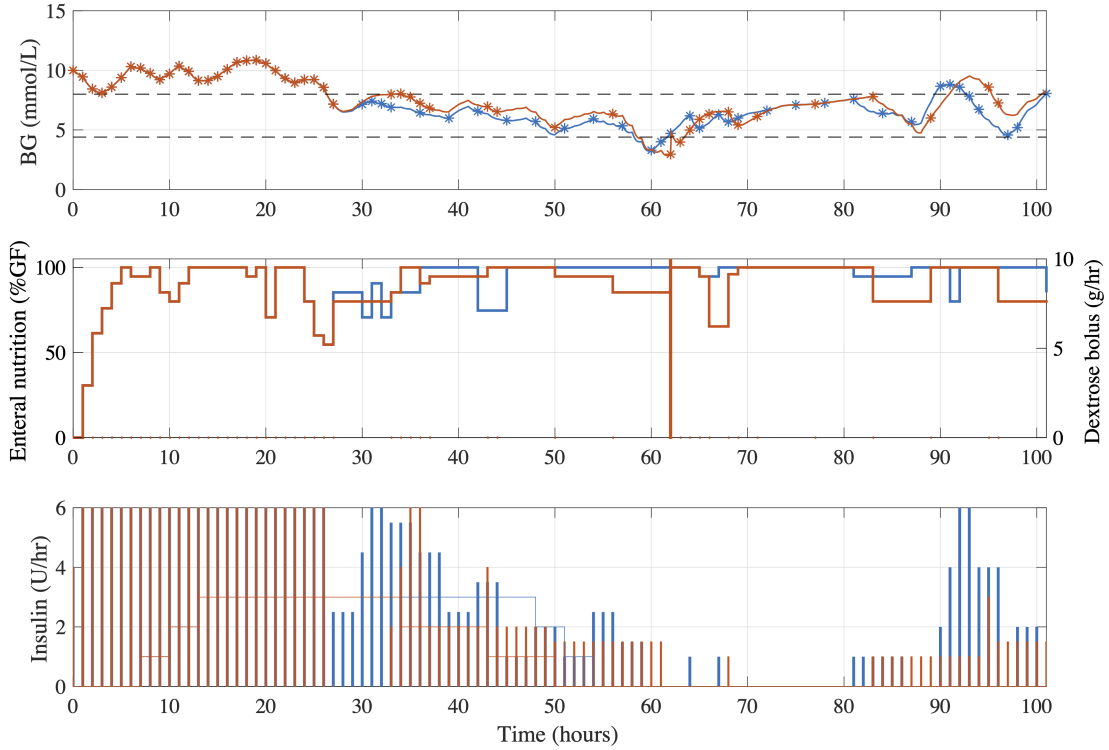

Figure 2: Representation of the virtual trial results for one patient with the BG level (top), the nutrition rates and dextrose bolus (middle), the insulin bolus and infusion rates (bottom). Results are compared between 1-3 hourly (blue) and 1-6 hourly (red) time intervals.

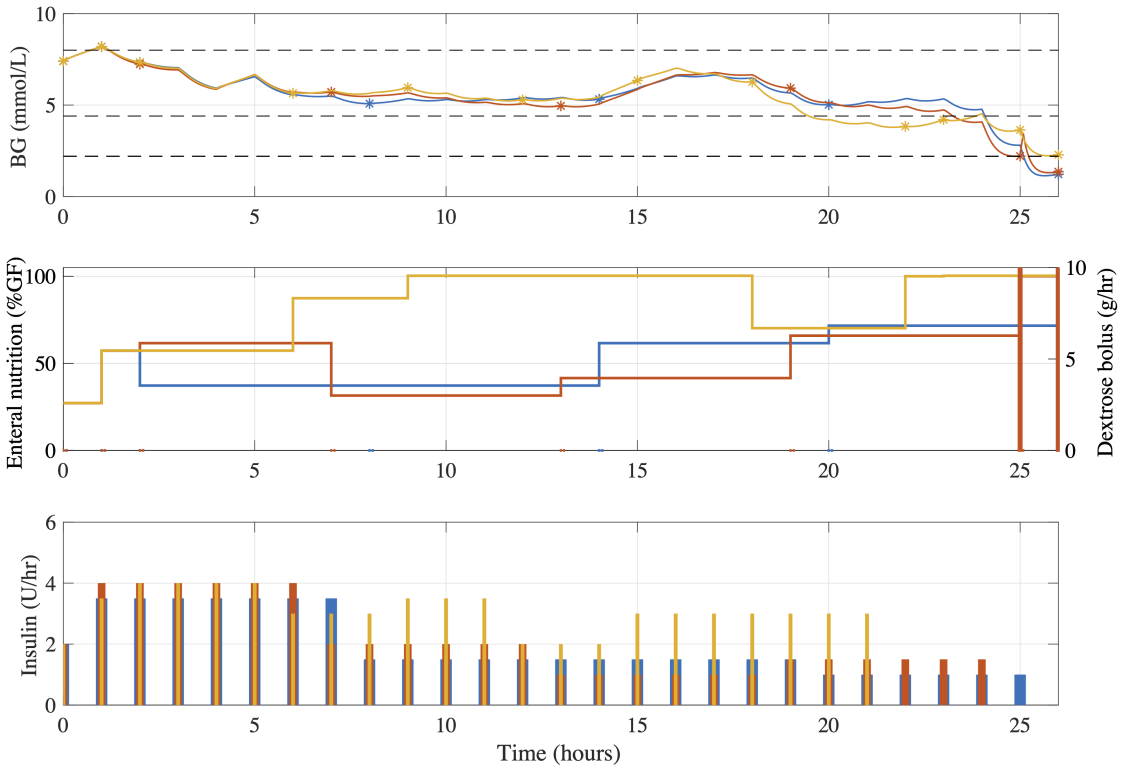

Figure 3: Representation of the virtual results for one patient. The BG level (top), the nutrition rates and dextrose bolus (middle), the insulin bolus and infusion (bottom) are shown. Results are compared for 6-hourly time intervals between time interval maximisation (red), insulin dosing variations minimisation (yellow) and combination (blue).