How Much Do We Gain From Greater Personalisation?

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Background

Stress-hyperglycaemia is a common complication in the ICU. Glycaemic control (GC) can improve outcomes, but has been difficult to achieve safely, increasing hypoglycaemic risk.

STAR is model-based GC with proven safety and performance. It uses a cohort-based **2D stochastic model** of patient-specific **insulin sensitivity (SI)** to predict future SI distributions to **dose insulin and nutrition based on specified risk of hypoglycaemia** (**Figure 1**).

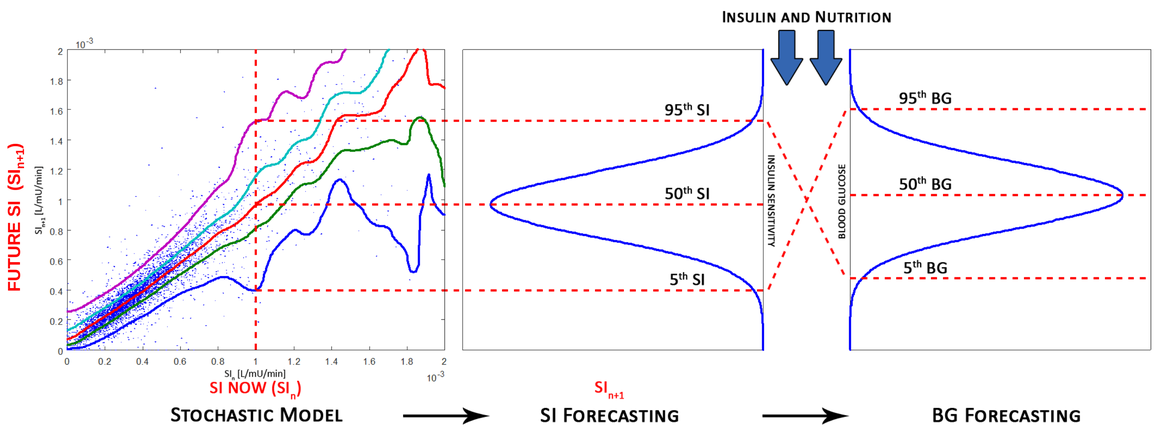

Figure 1 – Future insulin sensitivity (SI) is forecast from current SI. The distribution of future SI is used to predict likely BG outcomes for a given insulin-nutrition treatment intervention.

Objectives

- **Metabolic (SI) variability is makes GC hard to achieve safely.**
  → A new **3D stochastic model** is constructed to improve future SI forecasting based on **current and previous** SI values.
- **What is the impact of greater personalisation?**
  → Virtual trial on validated patients assesses performance, safety and workload.

Methods

Metabolic data from 3 clinical ICU cohorts (819 episodes and 68629 hours of treatment) are used in this study (**Table 1**).

Table 1 – Summary of patient demographics for three cohorts. Results are given as median [IQR] where relevant.

	SPRINT Christchurch	STAR Christchurch	STAR Gyula
# episodes	442	330	47
# hours	39838	22523	6268
% male	62.7	65.5	61.7
Age (years)	63 [48, 73]	65 [55, 72]	66 [58, 71]
APACHE II	19.0 [15.0,24.5]	21.0 [16.0,25.0]	32.0 [28.0,36.0]
LOS - ICU (days)	6.2 [2.7,13.0]	5.7 [2.5,13.4]	14.0 [8.0,20.5]

- SI is identified hourly from clinical data
- Bi-variate and tri-variate Gaussian kernel density methods estimate conditional probability estimation of future SI.
- Cross validation is uses data from 411 (70%) episodes to build new **2D** and **3D** stochastic models, and tested on the other 176 (30%).
- Process is repeated 3 times, resulting in 528 simulated episodes.

Results

Model comparison:

- The **2D** model is **over-conservative for 74% of hours** mainly where SI is **within an absolute 25% change** (**Figure 3**).
  → **Indicates patients are stable more than 74% of the time.**
  → **Stable patients tend to remain stable.**
- The 90% CI width in this region is **reduced by 22%** (**Figure 2**).
  → **More aggressive dosing allowed for these patients.**

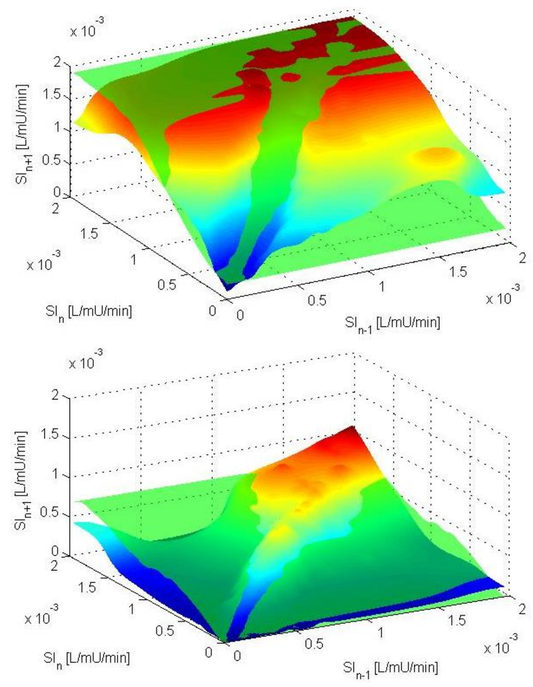

Figure 2 – Comparison between the 3D model (colour) and the original 2D model (green) for the 5th (a) and 95th (b) percentiles.

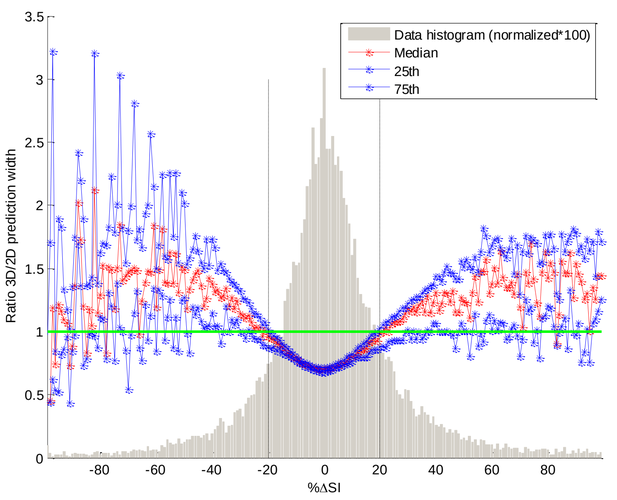

Figure 3 – Ratio of the 5th-95th percentile range between 3D and 2D models. Prediction range is reduced mainly when the absolute hour-to-hour SI variation is within 20%.

Virtual trial simulation results: **Table 2** and **Figure 4**

- **Median BG is lower** using the 3D model (6.0 vs. 6.3 mmol/L) for similar **high performance** (90% in target band). However, tighter for the 3D model (65% vs. 58% in 4.4-6.5 mmol/L).
- Slightly **higher incidence of moderate hypoglycaemia** for the 3D model (3% vs. 2% < 4.4 mmol/L). **No severe hypoglycaemia**.
- **Higher nutrition** rates achieved with the 3D model (99 vs. 92 %GF).

Table 2 – Simulation results of STAR using the 2D or 3D stochastic model. Results reported as median [IQR] where appropriate.

	2D	**3D**
# patients	528	528
Total hours of control	60246	60267
Workload (#measurements/day)	11.6	11.6
Median BG (mmol/L)	6.3 [5.7 6.9]	6.0 [5.5 6.7]
Insulin rate (U/h)	2.5 [1.5 4.0]	3.0 [1.5 5.0]
Nutrition (dextrose) rate (%GF)	92 [70 100]	99 [70 100]
%BG within 4.4-8.0 mmol/L (80-145 mg/dL)	90	90
%BG within 4.4-6.5 mmol/L (80-120 mg/dL)	58	65
%BG > 10.0 mmol/L (180 mg/dL)	2	2
%BG <4.4 mmol/L (80 mg/dL)	2	3
%BG <2.2 mmol/L (72 mg/dL)	0	0

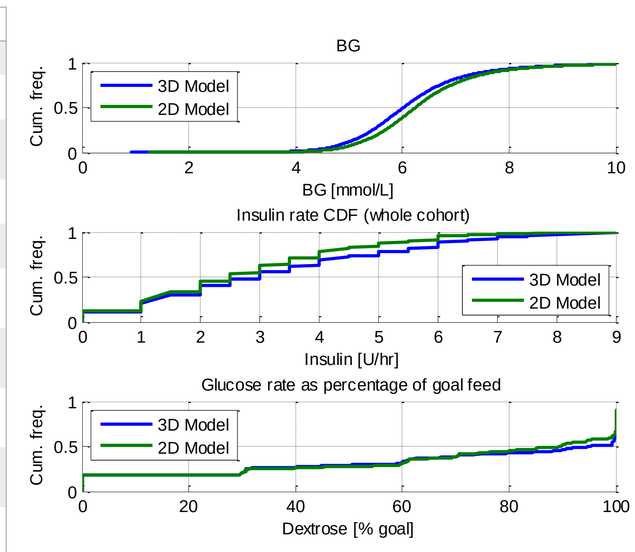

Figure 4 – BG level, Insulin rate , and glucose rate cdfs comparison.

Conclusions

- The new, more personalised 3D stochastic model provides moderately improved performance and similar safety for similar workload.
- The 3D model **better characterises patient-specific response to insulin, allowing more optimal dosing** while ensuring safety.
- These results justify potential clinical implementation to assess its impact on clinical outcomes.

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