Clinical Data Validation of an Improved, Physiologically Relevant Critical Care Glycaemic Control Model

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1 Background

Stress induced hyperglycaemia is prevalent in critical care. Tight glycaemic control can significantly improve clinical outcomes. Model-based and model-derived methods, such as SPRINT in Christchurch, have shown significant mortality reductions. This research uses prediction validation on an improved metabolic control model for real-time glycaemic control.

A stochastic insulin sensitivity variability model is derived to capture patient dynamics hour to hour. The BG distribution resulting from a given intervention can thus be derived, enabling better control and safety.

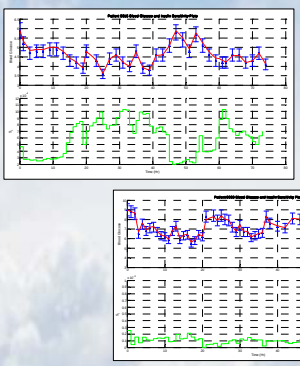

Figure 1. Fitted and actual BG with modelled S_I

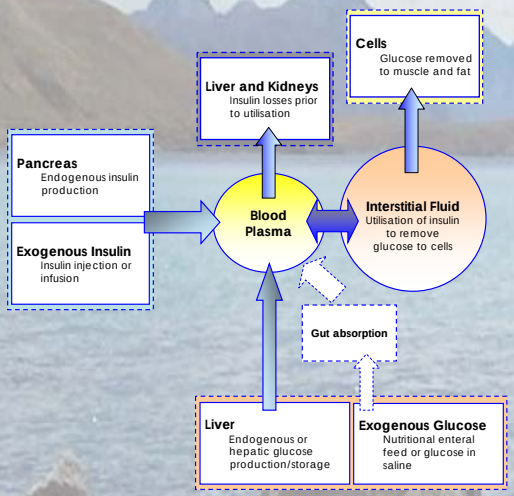

Figure 2. Compartmental Glucose-Insulin model

Glucose-Insulin Model

$$\dot{G} = -p_G G - S_I G \frac{Q}{1+\alpha_G Q} + \frac{P(t) + EGP - CNS}{V_G(t)}$$

$$\dot{Q} = -kQ + kI$$

$$\dot{I} = -\frac{I}{1+\alpha_I I} + \frac{u_{ex}(t)}{V_I} + e^{-k_I u_{ex}(t)} I_B$$

$$P(t) = \min(d_2 P_2, P_{\max})$$

$$\dot{P}_2 = -\min(d_2 P_2, P_{\max}) + d_1 P_1$$

$$\dot{P}_1 = -d_1 P_1 + D(t)$$

3 Results

Parameter identification:
The p_G and EGP values found agreed well with literature. Patient specific values resulted in no performance improvement.

p_G = 0.006 min-1
EGP = 1.16 mmol.min-1

Model Validation:
Fitting and prediction errors (median, IQR, 90% CI) are:

	FITTING			PREDICTION		
	Median	IQR	90% CI	Median	IQR	90% CI
New Model	1.21%	[0.53-1.99%]	[0-3.82%]	5.49%	[2.37-10.83%]	[0.43-23.16%]
Old Model	1.01%	[0.38-1.96%]	[0-4.76%]	5.75%	[2.51-10.95%]	[0.46-23.27%]

All errors are well within the measurement error of 7-12%. Predictions outside measurement error are primarily due to outlying measurement errors or sensor failures.

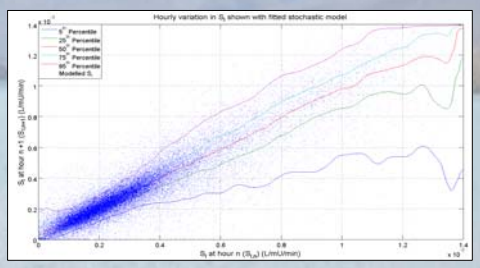

Figure 3. Hourly variation in S_I with fitted stochastic model.

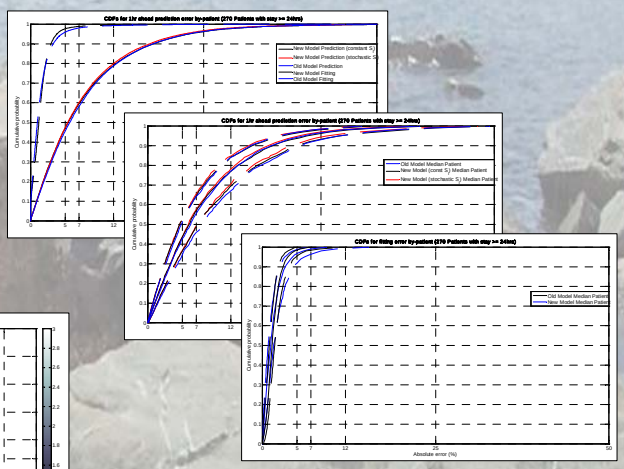

Figure 4. Prediction and fitting error results comparison

2 Models & Methods

Data: N = 270 patients (≥ 24 hour stay) and 47,126 hours from patients on SPRINT at Christchurch Hospital

Population Parameters:

α_G = 0.0154 l.mU^{-1}	α_I = 0.0017 l.mU^{-1}
V_G = 13.3 l	V_I = 3.15 l
k = 0.0198 min^{-1}	n = 0.16 min^{-1}
d_1 = 0.0347 min^{-1}	d_2 = 0.0069 min^{-1}

Time-Varying Parameters: Insulin Sensitivity (S_I)

Cohort-Specific Parameters: EGP and p_G identified using a grid search based on minimal prediction and fitting errors, while held constant over the entire cohort.

ID Method: An Integral-based method is used to identify time-varying insulin sensitivity for virtual patient trials.

Virtual Patients: are created by identifying time-varying $S_I(t)$ profiles for each patient to be used with different interventions. Prediction errors are the error using the known intervention.

Stochastic Model: The 44,386 hourly $S_I(t)$ values are used to evaluate the hour to hour change $\Delta S_I(t)$. A 2D kernel density estimation method is used to construct the model. Given a current identified $S_I(t)$ value, the glucose levels can be calculated over the next hour for a given intervention.

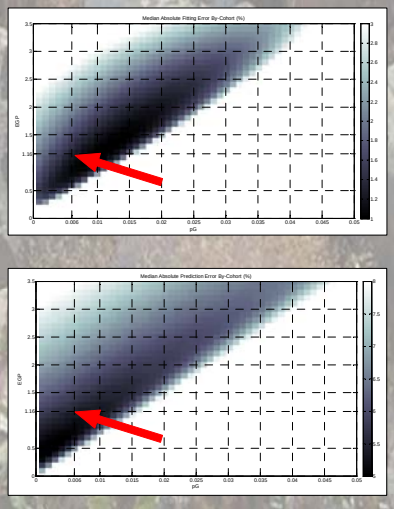

Figure 5. Error surfaces used for parameter identification

4 Conclusions

Model-based tight glycaemic control is primarily a function of model quality. A new, more physiologically relevant control model is presented and validated over a 270 patient data set. Prediction and fitting errors lie within measurement error, indicating a suitability for clinical use.
A stochastic model is developed and shows the same trends expected in the dynamic, critically ill patient who gets well slowly, can decline quite rapidly in some (more rare) cases.
The combination of these models is suitable for use in acute and critical care settings
This deterministic + stochastic model combination has already been applied successfully in 24-hour NICU trials.

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