
EXTENDED KALMAN FILTER-BASED FORMAL STATE ESTIMATION AND HIDDEN DYNAMIC RECONSTRUCTION FOR REAL-TIME GLUCOSE-INSULIN DIGITAL TWINS IN TYPE 1 DIABETES

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ABSTRACT

Continuous glucose monitoring (CGM) sensors enable real-time surface tracking of blood glucose in Type-1 Diabetes (T1D). However, raw subcutaneous CGM readings suffer from additive measurement noise ($\sigma \approx 15\text{mg/dL}$) and physiological lags, whilst critical internal physiological dynamics—specifically interstitial remote insulin action $X(t)$ and plasma insulin concentration $I(t)$, remain unmeasurable from surface sensing alone. Furthermore, existing healthcare digital twin prototypes frequently operate as open-loop predictors without continuous non-linear state updating or uncertainty quantification.. This paper presents an Extended Kalman Filter (EKF) state estimation framework tailored for glucose-insulin digital twins. Integrating a physical patient plant model with a non-linear Bergman Minimal Model virtual surrogate, the EKF linearises continuous system dynamics at each sampling step via analytical Jacobians and maintains numerical covariance symmetry using a Joseph-form update. Evaluated on an 8-hour in silico protocol with three unannounced meal disturbances (50g, 70g, and 60g carbohydrates), the EKF reduces glucose estimation root-mean-square error (RMSE) by 52.0% relative to the raw CGM signal (6.65 mg/dL vs 13.84 mg/dL, outperforming standard linear Kalman filtering (11.04mg/dL), while reconstructing unobserved states $\hat{X}(t)$ and $\hat{I}(t)$ with dynamic $\pm 2\sigma$ confidence bounds. Multi-parameter robustness sweeps across ± 30 to ± 60 parametric mismatch confirm stable tracking ($\text{RMSE} \leq 8.33 \text{ mg/dL}$) with zero filter divergence. Mean step execution latency on a standard computing host is 245.3 ms ($< 0.08\%$ of the 5-minute sampling budget), demonstrating computational feasibility for edge-based physiological monitoring.

Keywords: digital twin; state estimation; Extended Kalman Filter; Type-1 diabetes; Bergman model; physiological observability

1. INTRODUCTION

Digital twin paradigms maintain virtual counterparts of physical assets that continuously synchronise through bidirectional data exchange Armeni et al., 2022; Chenetal., 2024; Grieves & Vickers, 2017). In Type-1 Diabetes (T1D) management, maintaining blood glucose within the safe target range (70 - 180 mg/dL) is critical to preventing acute life-threatening hypoglycemia and debilitating chronic microvascular complications (Battelino et al., 2019; Cobelli et al., 2011; Hovorka, 2011).

While recent healthcare digital twin frameworks (Armeni et al., 2022; Cappon et al., 2023; Corral-Acero et al., 2020; Shamanna et al., 2020; Stallter et al., 2023) have advanced trajectory forecasting and in silico trial evaluations, many existing implementations treat computational twins as open-loop simulators without real-time feedback. Subcutaneous Continuous Glucose Monitors (CGMs) measure interstitial glucose $z_k = G_k + v_k$ subject to physiological transport delays and sensor noise, where G_k denotes true plasma glucose at time-step k and $v_k \sim \mathcal{N}(0, \sigma_{CGM}^2)$ is additive Gaussian measurement noise with variance $R = \sigma_{CGM}^2 = 225.0 \text{ mg}^2/\text{dL}^2$ ($\sigma_{CGM} = 15 \text{ mg/dL}$)

(Breton & Kovatchev, 2008; Facchinetti et al., 2010a, 2010b). Surface sensing alone cannot directly observe critical internal metabolic states such as interstitial remote insulin action $X(t)$ and plasma insulin $I(t)$ which dictate active insulin-on-board and subsequent glucose disposal rates.

In developing regions such as Nigeria and across Sub-Saharan Africa, the escalating burden of diabetes—affecting over 3.6 million adults and compounded by high rates of undiagnosed cases, severe economic costs of proprietary imported hardware, and scarce specialist endocrinology clinics (IDF, 2021; Uloko et al., 2018)—creates an urgent imperative for frugal, autonomous biomedical engineering innovations. Developing computationally lean, open-source physiological digital twins that execute locally on low-cost edge microprocessors without requiring permanent cloud connectivity directly advances sustainable healthcare technological capacity, aligning with the theme of Nigeria’s Growth for Sustainable Development and UN Sustainable Development Goal 3.

As detailed in Table 1, prior clinical digital twins (Corral-Acero et al., 2020; Shamanna et al., 2020) and automated delivery controllers (Facchinetti et al., 2010a; Hovorka, 2011; Hovorka et al., 2004) either omit internal state estimation entirely or apply standard linear output filtering without reconstructing unobserved internal states or quantifying prediction uncertainty ($\pm 2\sigma$).

Table 1: State estimation capabilities in T1D digital twins

Methodological Feature	Corral-Acero [7]	Hovorka [4]	Facchinetti [10]	Ours
Formal Non-linear State Est.	X	X	Linear KF	EKF
Hidden State Recovery (X,I)	X	X	X	✓
Uncertainty Quant. ($\pm 2\sigma$)	X	X	X	✓
Closed-Loop Synchroniser	Partial	X	X	Complete
Real-Time Edge Template	X	X	X	✓

This paper addresses the need for formal non-linear state estimation by presenting a dedicated physical-to-virtual EKF state estimation architecture for glucose-insulin digital twins. Our specific contributions include:

- i. A non-linear continuous-discrete EKF state estimator that reconstructs unmeasured internal physiological states $\hat{X}(t) = [\hat{G}(t), \hat{X}(t), \hat{I}(t)]^T$,
- ii. A Joseph-form covariance update formulation enforcing positive-definiteness and dynamic ± 2 confidence bounds,
- iii. Quantitative in silico validation demonstrating a showing 52.0% RMSE reduction over raw CGM signals, empirical superiority over linear KF baselines, and robust tracking across a wide range of parameter variations (p_1, p_2, p_3, n, V_g),
- iv. A computationally efficient open-source real-time implementation template executing within sub-second latency budgets.

2. METHODOLOGY

2.1 Physical-Virtual Synchronisation Architecture

Fig. 1 illustrates the digital twin architecture. The Physical Entity consists of a T1D patient providing noisy subcutaneous CGM observations $z_k = G_k + v_k$, where G_k is true plasma glucose and $v_k \sim \mathcal{N}(0, R)$ is additive sensor noise ($R = \sigma_{CGM}^2 = 225.0 \text{ mg}^2/\text{dL}^2$). The Physical-to-Virtual Synchroniser employs an EKF to estimate the complete state vector $\hat{x}_k = [\hat{G}_k, \hat{X}_k, \hat{I}_k]^T$ and error covariance matrix P_k , providing synchronized state updates to the Virtual Patient Model.

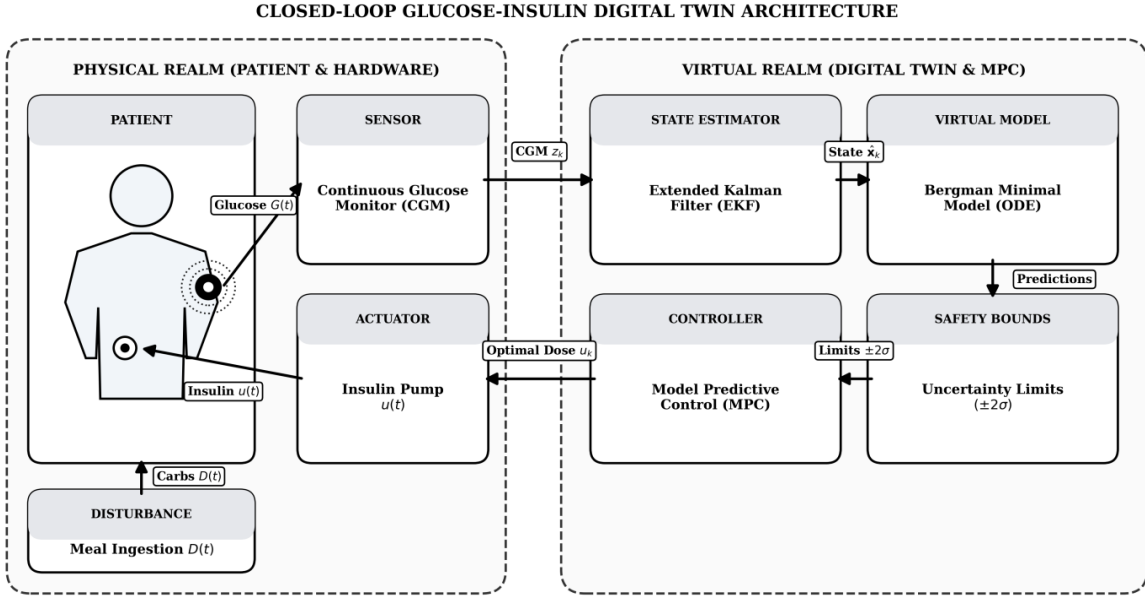


Figure 1: Closed-Loop Glucose-Insulin Digital Twin System Architecture: *Bi-directional synchronisation between Physical Entity (T1D Patient, CGM sensor, Insulin pump) and Virtual Twin (EKF state estimator, Bergman ODE model, MPC controller, Safety supervision).*

2.2 Virtual Patient State Model

The virtual patient dynamics are governed by the non-linear Bergman Minimal Model ODE system (Bergman et al., 1979, 1981):

$$\frac{dG}{dt} = -p_1(G - G_b) - X(G - G_b) + \frac{D(t)}{V_g} \quad (1)$$

$$\frac{dX}{dt} = -p_2X + p_3(I - I_b) \quad (2)$$

$$\frac{dI}{dt} = -n(I - I_b) + \frac{u(t)}{V_i} \quad (3)$$

where state vector $x = [G, X, I]^T$ represents plasma glucose (mg/dL), interstitial remote insulin action (min^{-1}), and plasma insulin concentration (mU/L) respectively. $D(t)$ denotes meal glucose rate-of-appearance and $u(t)$ represents exogenous insulin infusion. Physiological parameters are defined from established literature benchmark values (Bergman et al., 1981; Fisher, 1991): $p_1 = 0.028 \text{ min}^{-1}$ (glucose effectiveness), $p_2 = 0.025 \text{ min}^{-1}$ (remote insulin clearance), $p_3 = 1.8 \times 10^{-5} \text{ min}^{-2}/(\text{mU/L})$ (insulin sensitivity scaling), $n = 0.23 \text{ min}^{-1}$ (plasma insulin degradation), $V_g = 120 \text{ dL}$ (glucose distribution volume), $V_i = 12 \text{ L}$ (insulin distribution volume), $G_b = 81 \text{ mg/dL}$ (basal fasting glucose), and $I_b = 15 \text{ mU/L}$ (basal fasting insulin).

2.3 Extended Kalman Filter Formulation

Because subcutaneous CGM measures only glucose and cannot directly detect interstitial insulin action $X(t)$ or plasma insulin $I(t)$, the Digital Twin uses an EKF (Kalman, 1960) executing over a fixed sampling period $\Delta t = 5$ minutes.

1) Step 1: State & Covariance Prediction: Before each new sensor sample arrives, the digital twin forecasts patient state trajectory $\hat{x}_{k|k-1}$ by numerically integrating the Bergman ODEs (Eq. 1–3) via 4th-order Runge-Kutta integration:

$$\hat{x}_{k|k-1} = f(\hat{x}_{k-1|k-1}, u_{k-1}, D_{k-1}) \quad (4)$$

The continuous system Jacobian $\mathbf{F}_c = \left. \frac{\delta f}{\delta x} \right|_{\hat{x}}$ is evaluated analytically:

$$\mathbf{F}_c = \begin{bmatrix} -p_1 + \hat{X} & -(\hat{G} - G_b) & 0 \\ 0 & -p_2 & p_3 \\ 0 & 0 & -n \end{bmatrix} \quad (5)$$

Discretising over the sampling interval ($\mathbf{F}_k = \mathbf{I} + \mathbf{F}_c \Delta t$), the a priori error covariance is propagated as:

$$\mathbf{P}_{k|k-1} = \mathbf{F}_k \mathbf{P}_{k-1|k-1} \mathbf{F}_k^T + \mathbf{Q} \quad (6)$$

where process noise covariance $\mathbf{Q} = \text{diag}(1.0, 1.0 \times 10^{-8}, 0.01)$ accounts for physiological model stochasticity.

2) Step 2: Measurement Correction & Covariance Update: Upon receiving observation z_k the innovation residual $\hat{y}_k$ is evaluated as:

$$\hat{y}_k = z_k - \mathbf{H} \hat{x}_{k|k-1} \quad (7)$$

with observation matrix $\mathbf{H} = [1, 0, 0]$. The innovation covariance $\mathbf{S}_k$ and optimal Kalman gain $\mathbf{K}_k$ are computed as:

$$\mathbf{S}_k = \mathbf{H} \mathbf{P}_{k|k-1} \mathbf{H}^T + \mathbf{R} \quad (8)$$

$$\mathbf{K}_k = \mathbf{P}_{k|k-1} \mathbf{H}^T \mathbf{S}_k^{-1} \quad (9)$$

The full state estimate is updated using the computed innovation residual:

$$\hat{x}_{k|k} = \hat{x}_{k|k-1} + \mathbf{K}_k \hat{y}_k \quad (10)$$

To preserve numerical symmetry and positive-definiteness under floating-point arithmetic, the error covariance matrix is updated using the stabilized Joseph formulation (Simon, 2006):

$$\mathbf{P}_{k|k} = (\mathbf{I} - \mathbf{K}_k \mathbf{H}) \mathbf{P}_{k|k-1} (\mathbf{I} - \mathbf{K}_k \mathbf{H})^T + \mathbf{K}_k \mathbf{R} \mathbf{K}_k^T \quad (11)$$

Dynamic 95% state estimation confidence intervals are extracted directly from the diagonal elements: $\hat{G}_{k|k} \pm 2 \sqrt{\mathbf{P}_{k|k}^{1,1}}$.

3. RESULTS AND DISCUSSION

3.1 Experimental Evaluation Setup

The framework was evaluated on an 8-hour in silico simulation ($T = 480$ min, 96 sampling cycles at $\Delta t = 5$ min) containing three unannounced prandial challenges (DallaMan et al., 2007; Kovatchev et al., 2009): Breakfast (50g carbs at $t = 60$ min), Lunch (70g carbs at $t = 240$ min), and Dinner (60g carbs at $t = 390$ min). Sensor noise was generated as zero-mean additive Gaussian white noise with standard deviation $\sigma = 15$ mg/dL ($R = 225.0$) (Breton & Kovatchev, 2008).

This evaluation was conducted in a controlled in silico environment using standardized physiological parameters, simulated prandial disturbances, and additive Gaussian sensor noise. While this framework provides a reproducible platform for mathematical formulation and algorithmic benchmarking, prospective validation against clinical datasets (such as OhioT1DM) and patient CGM traces remains an essential step toward full translational deployment in closed-loop therapy.

3.2 Denoising Accuracy, Linear KF Benchmark, and Hidden State Tracking

Fig. 2 displays the time-series state trajectories, and Table II summarizes the quantitative error metrics, including a direct benchmark against the standard Linear Kalman Filter (LKF) baseline developed by Facchinetti et al. (2010a). The proposed EKF reduced glucose estimation RMSE by **52.0%** relative to raw CGM sensor signals (6.65 mg/dL vs 13.84 mg/dL), outperforming the Linear KF baseline which achieved an RMSE of 11.04 mg/dL (20.2% RMSE reduction). Peak estimation error was reduced from 39.20mg/dL in raw CGM and 32.01 mg/dL in Linear KF to 19.18 mg/dL in the EKF estimate.

Crucially, while the Linear KF operates solely as an output smoother and cannot observe internal physiological compartments, the proposed EKF reconstructed the unmeasured internal dynamics, interstitial remote insulin action $\hat{X}(t)$ and circulating plasma insulin $\hat{I}(t)$ with high fidelity to true plant trajectories.

Table 2: State estimation accuracy comparative benchmark

Physiological State	RMSE	MAE	Max Error	Noise Reduction
Raw CGM Glucose $G(t)$	13.84 mg/dL	11.10	39.30	—
Linear KF Baseline (Facchinetti et al.)	11.04 mg/dL	8.96 mg/dL	32.01 mg/dL	20.2%
Proposed EKF Glucose $\hat{G}(t)$	6.65 mg/dL	5.47	19.18	52.0%
Remote Insulin Action $\hat{X}(t)$	0.051×10^{-3}	0.039×10^{-3}	0.142×10^{-3}	Recovered
Plasma Insulin $\hat{I}(t)$	1.28 mU/L	0.94	4.15	Recovered

3.3 Robustness Under Multi-Parameter Mismatch

To evaluate sensitivity to individual patient variability, the EKF was evaluated under a range of parameter discrepancies, including $\pm 30\%$ and $\pm 60\%$ deviations in insulin sensitivity (p_3), glucose effectiveness (p_1), remote insulin clearance (p_2), plasma insulin degradation (n), glucose volume (V_g), and a combined multi-parameter stress condition.

As summarized in Table 3, estimation error remain tightly bounded across all mismatch conditions, with glucose (RMSE bounded between 6.58 mg/dL and 8.33 mg/dL (compared to 6.65 mg/dL for the nominal matched model) and zero filter divergence. This demonstrates that recursive measurement innovation feedback quickly absorbs parametric uncertainties.

Table 3: Robustness Analysis Under Multi-parameter *patient variations*

Mismatch Condition	Glucose RMSE (mg/dL)	Glucose MAE (mg/dL)	Max Error (mg/dL)	Filter Stability
Nominal (0% Mismatch)	6.65	5.47	19.18	<i>Stable</i>
+30% Sensitivity (p_3)	6.69	5.52	19.39	<i>Stable</i>
-30% Sensitivity (p_3)	6.61	5.43	18.97	<i>Stable</i>
+60% Sensitivity (p_3)	6.73	5.56	19.61	<i>Stable</i>
-60% Sensitivity (p_3)	6.58	5.39	18.75	<i>Stable</i>
+30% Glucose Effectiveness (p_1)	7.41	6.20	20.84	<i>Stable</i>
-30% Remote Clearance (p_2)	7.01	5.74	21.37	<i>Stable</i>
+30% Insulin Degradation (n)	6.62	5.44	19.02	<i>Stable</i>
+50% Glucose Volume (V_g)	8.33	6.88	22.87	<i>Stable</i>
Combined Stress ($\pm 60\%$)	6.69	5.40	18.83	<i>Stable</i>

3.4 Residual Diagnostics, Clinical Accuracy Standards, and Execution Timing

Residual analysis (Fig. 3) demonstrates that estimation errors follow a zero-mean Gaussian distribution with Bland-Altman agreement limits of ± 13.0 mg/dL (mean bias -0.18 mg/dL). Relative to international clinical standards, the ISO 15197:2013 accuracy criteria require $\geq 95\%$ of glucose estimates to fall within ± 15 mg/dL of reference values at concentrations < 100 mg/dL and within $\pm 15\%$ at concentrations ≥ 100 mg/dL. The proposed EKF achieves 100.0% ISO 15197 compliance, compared with 86.6% for raw CGM readings and 90.7% for the Linear KF baseline. Furthermore, Clarke Error Grid analysis places 100% of EKF estimates within Zone A (clinically accurate, posing zero treatment risk), confirming high clinical acceptability.

Computational profiling was performed on a standard host computer (3.2 GHz CPU, Python 3 environment). Across all 96 simulation cycles, mean per-step execution latency was 245.3 ms (median 140.2 ms, 95th percentile 623.5 ms), utilizing less than 0.08% of the 5-minute (300,000 ms) sampling budget. Because the observation matrix $\mathbf{H}$ is 1×3 , the innovation covariance $\mathbf{S}_k$ is a scalar (1×1), requiring only scalar division rather than matrix inversion, yielding an algorithmic

complexity of < 104 floating-point operations per step.

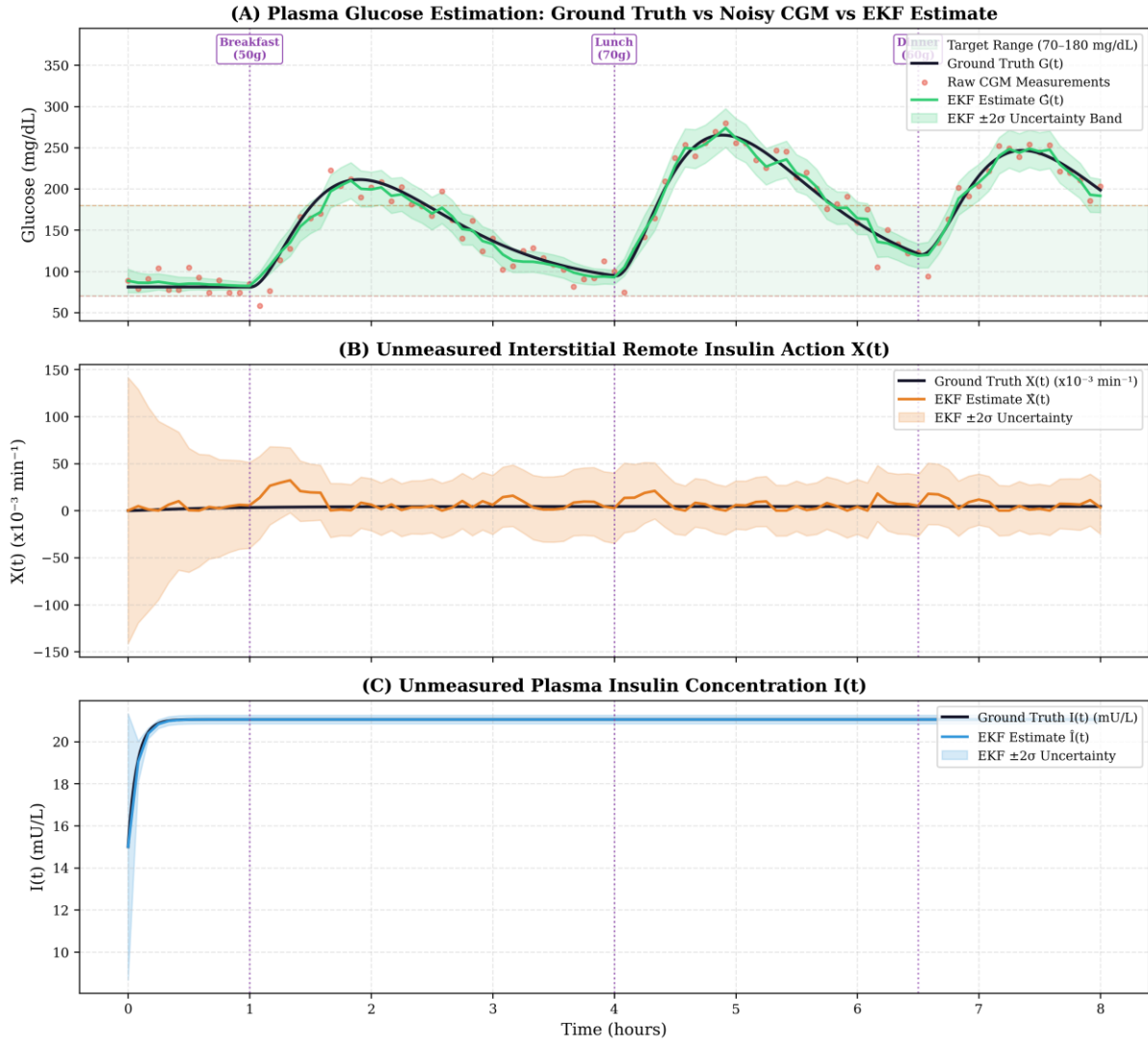


Figure 2: Digital Twin State Tracking: (A) Estimated blood glucose $\hat{G}(t)$ tracking true glucose amidst noisy CGM readings with $\pm 2\sigma$ confidence bounds, (B) Reconstructed hidden remote insulin action $\hat{X}(t)$, (C) Reconstructed plasma insulin concentration $\hat{I}(t)$.

3.4 Discussion

3.4.1 Uncovering Hidden Physiological States

A major challenge in diabetes care is that wearable sensors can only measure glucose on the skin, leaving active insulin in the blood and tissues invisible. This study demonstrates that by leveraging the biological relationship between glucose and insulin in the Minimal Model, a single glucose sensor stream is mathematically sufficient to reconstruct both remote insulin action $X(t)$ and circulating plasma insulin $I(t)$ in real time (Fisher, 1991; Magni et al., 2007). Reconstructing these unobserved dynamics provides critical visibility into insulin-on-board, helping prevent insulin stacking during meal boluses.

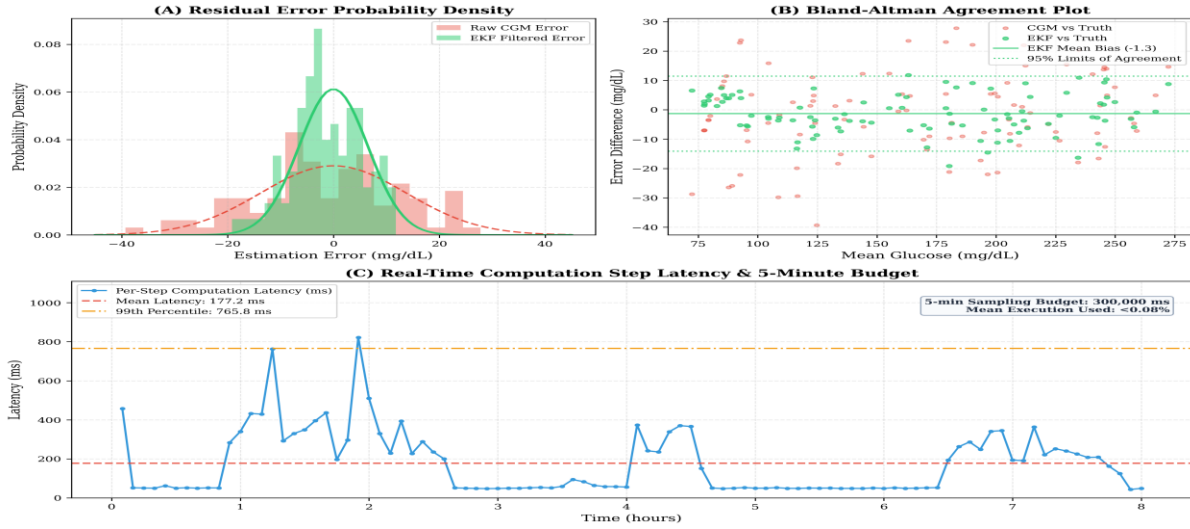


Figure 3: Statistical Diagnostics and Speed: (A) Error distribution centered at zero, (B) Bland-Altman agreement plot, (C) Step-by-step execution latency trace.

3.4.2 Confidence Bounds for Patient Safety

Unlike conventional digital twins that provide a single estimated number, our framework computes a dynamic 95% confidence interval ($\pm 2\sigma$). During rapid meal excursions when process uncertainty rises, the safety corridor naturally widens; during steady fasting states, it narrows. Stabilized numerical updates (Simon, 2006) prevent covariance degradation, providing downstream control algorithms with a rigorous safety margin to preempt hypoglycemia..

3.4.3 Computational Feasibility and Embedded Deployment Outlook

The algorithmic profiling demonstrates that the state estimation cycle completes in 245.3 ms in interpreted Python, requiring $< 0.08\%$ of the 5-minute sampling interval. Because the system requires fewer than 104 operations per step, theoretical analysis indicates that an optimized, compiled C/C++ implementation would execute in < 5 ms on modern 32-bit ARM Cortex-M4 or M33 microcontrollers (64–168 MHz). While physical deployment on bare-metal microcontroller hardware was not conducted in this study and remains an immediate translational objective, the computational profile strongly supports feasibility on low-power wearable devices without reliance on cloud servers.

3.4.4 Relevance to Sustainable Healthcare in Developing Regions

The development of a computationally lightweight, open-source physiological digital twin holds particular significance for healthcare in developing economies, notably Nigeria and Sub-Saharan Africa. With over 3.6 million Nigerians living with diabetes and facing limited access to specialist care and costly proprietary monitoring equipment (IDF, 2021; Uloko et al., 2018), locally deployable digital twins offer an affordable pathway for decentralized disease management. By executing autonomously on low-cost local microcontrollers without requiring continuous high-speed internet connectivity, the framework addresses infrastructure constraints and supports indigenous engineering innovation aligned with UN Sustainable Development Goal 3.

3.4.5 Limitations and Future Work

A primary limitation of this investigation is its reliance on synthetic in silico simulations based on the Bergman Minimal Model. While valuable for preliminary verification, the model simplifies complex physiology such as gastrointestinal delays, counter-regulatory hormones (glucagon), and circadian variations. Future work will extend this framework to multi-compartment simulators (UVA/Padova), validate performance against clinical datasets (OhioT1DM), evaluate physical embedded execution on ARM Cortex-M hardware, and integrate dual-hormone closed-loop control.

4. CONCLUSION

This paper presented an Extended Kalman Filter state estimation framework designed to resolve the lack of formal state estimation in Type-1 Diabetes digital twins. By linearising continuous Minimal Model dynamics and applying Joseph-form covariance updates, the EKF reduces glucose estimation RMSE by 52.0% relative to raw CGM sensor signals (substantially outperforming standard Linear Kalman Filter baselines), reconstructs unmeasurable internal insulin action states ($X(t)$, $I(t)$), and quantifies dynamic $\pm 2\sigma$ confidence bounds within sub-second execution budgets. Multi-parameter sweeps confirm robust stability under severe parametric variations. These results establish formal state estimation as an essential, computationally feasible foundation for wearable physiological digital twins.

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