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Hybrid Physiological and Neural ODE Model with Probabilistic Outputs for Personalized Glucose Dynamics in T2DM

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INTRODUCTION & AIM

- Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder with insulin resistance and impaired secretion.
- Glucose–insulin dynamics are nonlinear and patient-specific.
- Mathematical models are essential for understanding disease and enabling personalized treatment.
- Physiological models are interpretable but less flexible, while data-driven models are flexible but less interpretable.

Aim:

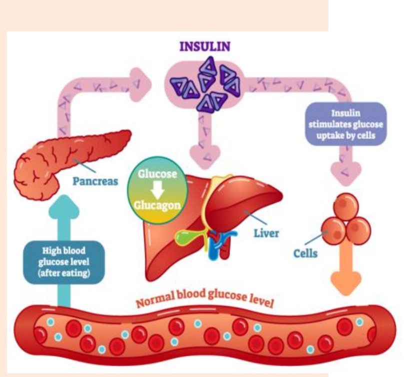
Develop a hybrid model combining:
- Physiological ODE model
- Residual learning using Neural ODEs
- Gaussian Mixture Model (GMM) outputs

Enable **personalized glucose trajectory prediction** in **T2DM patients**

METHOD

Physiological ODE Model

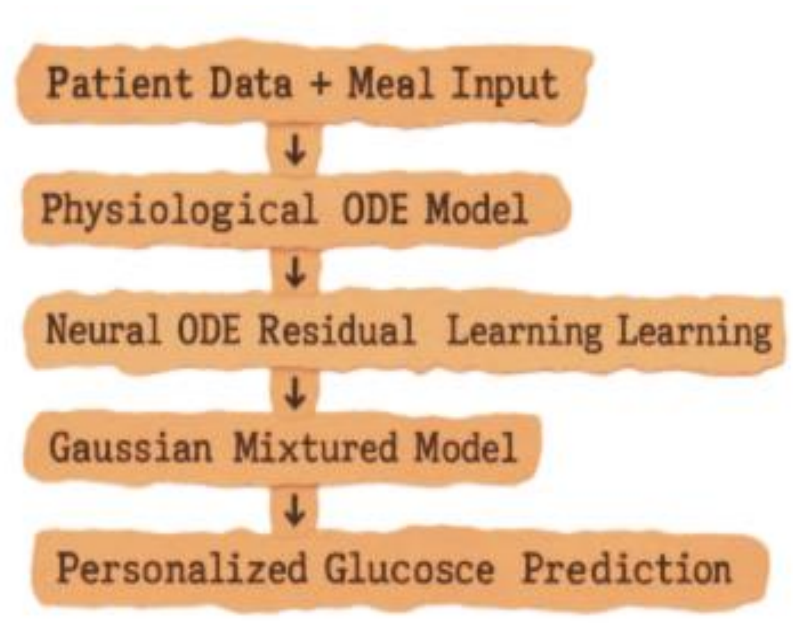
Key Components:
- Gastric glucose dynamics
- Intestinal absorption
- Plasma glucose regulation
- Insulin secretion and action



State Variables
- $G(t)$:Plasma glucose
- $I(t)$:Plasma insulin
- $X(t)$:Insulin action
- $Q_{sto}(t)$:Gastric glucose
- $Q_{gut}(t)$:Intestinal glucose

Equations:
- Gastric emptying:
$$\frac{dQ_{sto}}{dt} = -k_{ge}Q_{sto}$$
- Gut absorption:
$$\frac{dQ_{gut}}{dt} = k_{ge}Q_{sto} - k_{abs}Q_{gut}$$
- Plasma glucose &
$$\frac{dG}{dt} = (s_G + X)G + k_{abs}Q_{gut} - \frac{HGO_b}{1+\alpha_I X}$$
- insulin dynamics:
$$\frac{dX}{dt} = -p_2X + p_3(I - I_b)$$
$$\frac{dI}{dt} = -k_I I + \beta_F(G - G_b)^+$$

Key Idea:
- Provides **biological interpretability**
- Ensures **physiological consistency**



Residual learning

Purpose:
- Captures **patient-specific nonlinear dynamics**
- Learns **missing physiological mechanisms** from data

Hybrid Model

Model Equation
$$\frac{dx}{dt} = f_{phys}(x, u, \theta) + f_{NODE}(x, t, \phi)$$

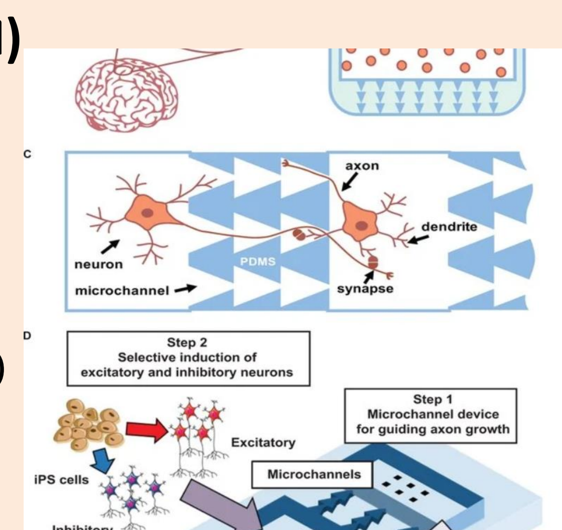
Advantages:
- Continuous-time learning
- Personalized modeling
- Data-driven correction of physiological model

Probabilistic Output (GMM)

Purpose
- Models **uncertainty in glucose prediction**
- Captures **multiple possible outcomes**

Model Equation
$$p(y \mid x) = \sum_{k=1}^{K} \pi_k \, \mathcal{N}(y \mid \mu_k \Sigma_k)$$

Benefits
- Uncertainty quantification
- Multimodal prediction
- Robust personalized forecasting



RESULTS & DISCUSSION

Results
- Developed a **hybrid physiological and Neural ODE framework** for glucose dynamics modeling in T2DM.
- Incorporated a **Gaussian Mixture Model (GMM)** layer for **probabilistic glucose prediction**.
- The physiological component captures **glucose–insulin interactions** and **fasting equilibrium behavior**.
- Neural ODE residual learning improves modeling of **patient-specific nonlinear dynamics**. The framework enables **uncertainty-aware and personalized glucose trajectory prediction**.

Discussion
- Combines **mechanistic interpretability** with **data-driven adaptability**
- **Physiological ODEs** preserve biological meaning
- **Neural ODEs** enhance model flexibility
- **GMM outputs** capture prediction uncertainty
- Supports **personalized glucose monitoring** and **precision medicine**

Figure 3: Probabilistic Glucose Prediction Distribution

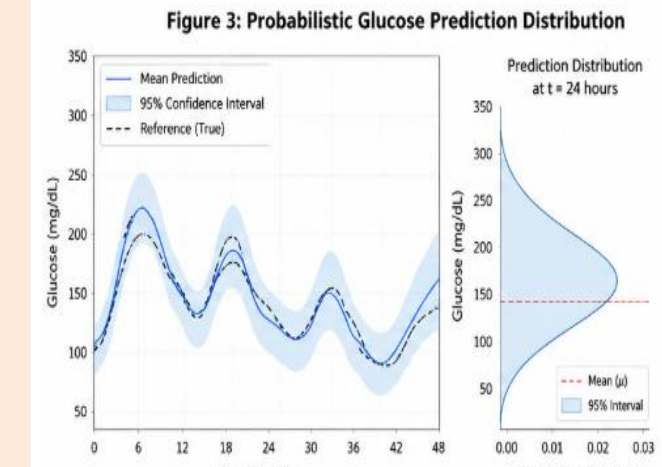
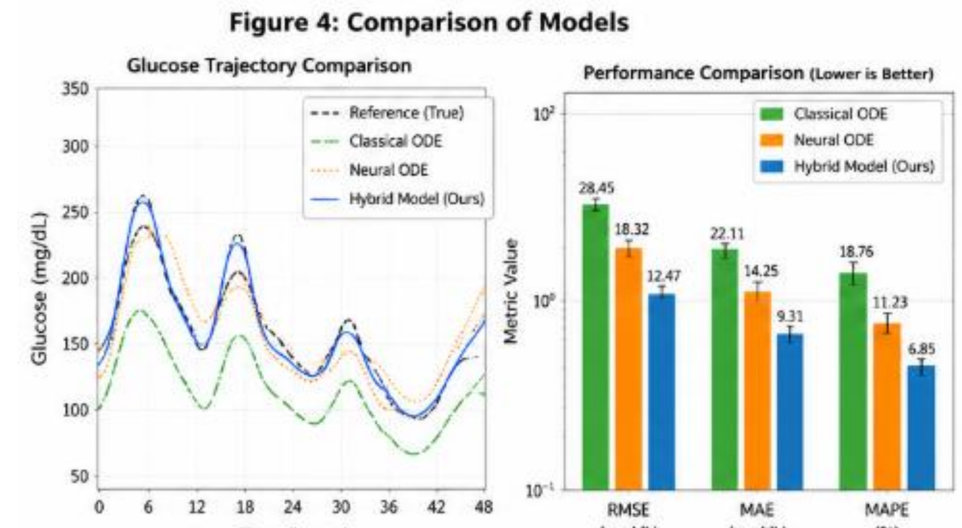
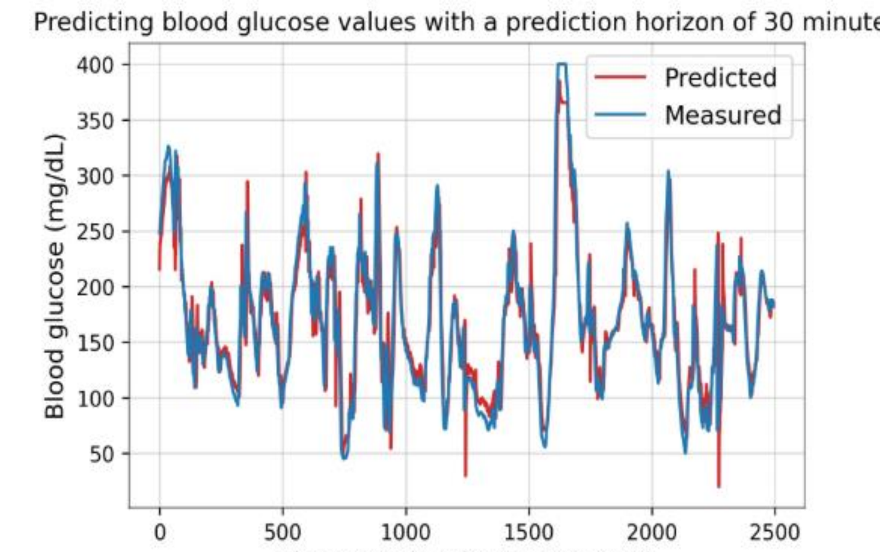


Figure 4: Comparison of Models



Predicting blood glucose values with a prediction horizon of 30 minutes



CONCLUSION

- A **novel hybrid framework** combining **physiological ODEs**, **Neural ODE residual learning**, and **Gaussian Mixture Model (GMM) outputs** was developed for **personalized glucose dynamics modeling in T2DM**.
- The model integrates **biological interpretability** with **data-driven adaptability** in a unified framework.
- A key novelty is the **probabilistic GMM output layer**, enabling **uncertainty-aware glucose prediction**.
- The framework shows strong potential for **personalized diabetes monitoring** and **precision medicine**.

FUTURE WORK / REFERENCES

Future work
- Clinical validation using patient datasets
- Integration with continuous glucose monitoring data
- Personalized parameter estimation
- Development of real-time glucose prediction systems

References

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