Non-invasive Glucose Measurement using Radio-Frequency Spectroscopy and Machine Learning

Alishba Fatmi[1], Subhash Nerella[1], Dominic Klyve[2], Parisa Rashidi[1], Adam Khalifa[3]
[1]Department of Biomedical Engineering, University of Florida, Gainesville, Fl, 32608
[2]KnowLabs, Inc. Seattle, WA, USA, 98101
[3]Department of Electrical and Computer Engineering, University of Florida, Gainesville, Fl, 32608

Abstract. **Continuous glucose monitoring (CGM) devices provide critical real-time data but remain minimally invasive and require frequent replacement. This study presents a novel, personalized machine learning approach for non-invasive glucose monitoring using radiofrequency (RF) spectroscopy to address these limitations. To simulate real-world usage and ensure clinical relevance, we developed a model for a single individual using data collected during standardized meals. The model was trained and tested on data collected on separate days, ensuring that the training and test sets are drawn from distinct, non-overlapping time periods. A comprehensive machine learning pipeline was validated using 3,101 spectral features (400–3500 MHz) combined with contextual data to predict glucose levels. Our best-performing model, multi-layer perception regressor (MLP), achieved a Mean Absolute Relative Difference (MARD) of 11.6%. These findings demonstrate that a personalized machine learning model holds potential to predict glucose non-invasively. This highlights a promising path toward a more user-friendly and sustainable solution for continuous glucose management**

Keywords—Continuous Glucose Monitoring, machine learning, non-invasive

I. Introduction

Diabetes affects over 11% of the U.S. population, and this prevalence continues to rise due to factors such as aging, obesity, and sedentary lifestyles [1]. Current glucose monitoring methods, primarily invasive finger-stick tests and subcutaneous continuous glucose monitors (CGMs), pose significant challenges to patient compliance. The pain, cost, and inconvenience of these technologies underscore the urgent need for a reliable, non-invasive alternative.

Radiofrequency (RF) spectroscopy presents a promising solution by exploiting the principle that fluctuations in blood glucose levels induce measurable changes in the dielectric properties of human blood [2]. These changes can be detected by analyzing how RF signals are altered as they propagate through the body. Although prior studies have demonstrated the potential of RF spectroscopy for glucose sensing [3] [4] [5], achieving clinical-grade accuracy remains challenging due to issues of sensitivity and specificity [6]. The subtle dielectric shifts associated with glucose are often masked by the stronger and variable dielectric properties of surrounding tissues such as skin, fat, and muscle.

This study addresses these limitations through three key innovations: (1) personalized model calibration tailored to individual physiological signatures; (2) a robust, temporally separated validation strategy to better simulate real-world use; and (3) the use of standardized meal protocols to induce realistic glucose fluctuations in physiologically complex conditions.

II. Related Work

NIR spectroscopy operates by measuring glucose-dependent absorption in specific near-infrared wavelength bands (typically 700–2500 nm) [7]. Techniques using NIR light have been evaluated in both transmission and reflection modes across tissue sites such as the fingertip, earlobe, and forearm. While several studies have reported moderate correlation with reference glucose values, performance is often confounded by physiological and environmental factors, including skin thickness, temperature, and hydration. Despite advances in instrumentation and signal processing, NIR-based approaches have also struggled to meet the accuracy standards required for clinical deployment [7]. Another promising technique for noninvasive blood glucose monitoring is RF and microwave-based sensing. This method exploits the fact that glucose concentration alters the dielectric properties of blood, thereby affecting the interaction of microwave electromagnetic fields with biological tissue. Most prior studies have employed single-frequency systems operating in the 1–10 GHz range [8] [9], although some have explored broader frequency sweeps. While these studies have shown the potential of RF-based glucose sensing, achieving clinical-grade accuracy remains a significant challenge.

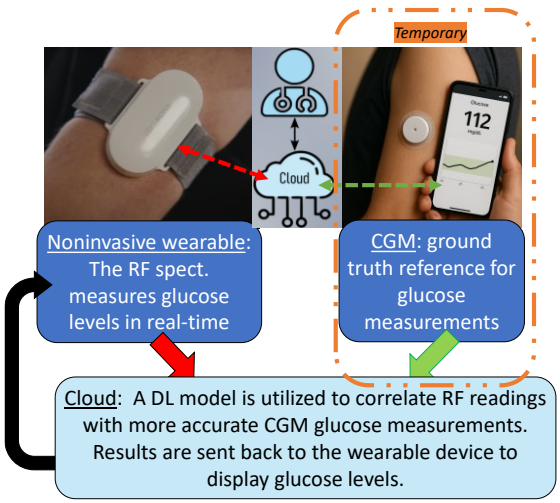

Fig. 1. Conceptual drawing of the proposed platform.

III. Concept Overview

Our proposed system (**Fig. 1**) utilizes a wearable, non-invasive device to monitor glucose levels. Initially, the device needs to be used alongside a CGM, which provides ground truth data to train a cloud-based neural network model. The wearable transmits RF spectral data to the cloud, where the model performs inference and returns predicted glucose values to the device. In this configuration, the wearable functions as a sensor and display unit, while computation is handled in the cloud. As more data is collected, the model is refined, and its accuracy improves. Once sufficient agreement with CGM readings is observed over time, users may discontinue CGM use and rely solely on the RF device. Periodic calibration using CGM use may be employed to maintain accuracy.

IV. Materials and Methods

A. RF Device

We used a proprietary device developed by Know Labs, Inc. designed for non-invasive glucose monitoring via RF spectroscopy. The sensor scans a wide spectral range (400–3500 MHz), capturing 3,101 voltage measurements per sweep that reflect tissue dielectric properties correlated with blood glucose levels. As illustrated in **Fig. 2**, the system architecture includes a microcontroller unit (MCU) that coordinates a signal generator and transmit amplifier (TX Amp) to drive a multi-element antenna array. The emitted RF signals propagate through tissue and are modulated by its dielectric characteristics. These altered signals are received, amplified by a low-noise amplifier (LNA), and converted to digital voltage values using a power detection circuit and an analog-to-digital converter (ADC). Each sweep provides the spectral features used as input to the machine learning model. Onboard temperature sensors offer additional contextual data to improve prediction robustness.

B. Data Acquisition

Data were collected from three adult participants (Subjects 1–3) under an identical standardized meal protocol with two physiological states per session (pre-prandial baseline and post-prandial) and the RF sensor placed on the forearm while seated and still, consistent with the setup illustrated in **Fig. 3**. Data was collected over multiple days, and was labeled as corresponding to breakfast, lunch, or dinner. Each session followed a standardized meal protocol and included two physiological states: pre-prandial (baseline) and post-prandial (after meal). Glucose levels were continuously recorded every 5 minutes using the Dexcom G7 CGM as a reference standard.

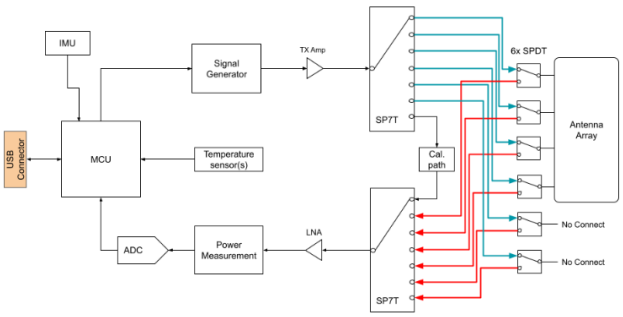

Fig. 2. Engineering diagram of the sensor.

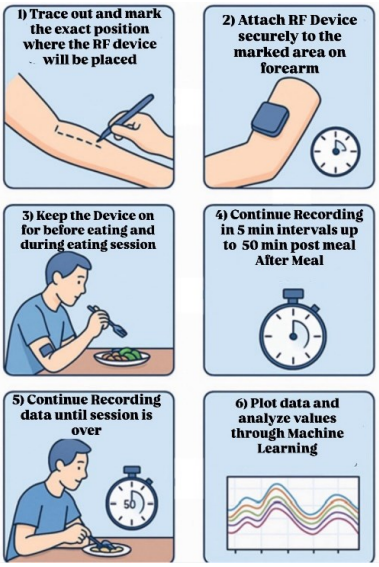

Fig. 3. Overview of the design protocol.

Simultaneously, RF spectral sweeps were acquired using the wearable device, with each sweep capturing 3,101 frequency features. To ensure data quality, RF measurements were recorded for 15 minutes before meal consumption and for 50 minutes afterward. Data acquisition was paused during the 10–20 minute eating period to minimize motion artifacts. Each session lasted approximately 70–80 minutes.

C. Feature Engineering and Machine Learning Pipeline

Spectral Features: Each RF sweep captured 3,101 voltage measurements representing the dielectric response across the frequency range. These features formed the primary input into the machine learning pipeline.

Contextual Features: Meal type (breakfast, lunch, dinner), metabolic state (pre/post-prandial), and temperature measurements from onboard sensors were included to account for physiological and environmental variations

Model Selection: A total of eight models were evaluated, including Lasso, Ridge, ElasticNet, Support Vector Regression, k-Nearest Neighbors, Multi-Layer Perceptron (MLP), LightGBM, XGBoost. Each model leverages distinct algorithmic principles, offering a broad comparison of linear, non-linear, and ensemble-based approaches.

Training Strategy: We implemented a temporal data splitting strategy, assigning earlier timepoints exclusively to the training set and reserving later timepoints for the test set. To prevent data leakage, we ensured that no samples collected on the same day appeared in both the training and test sets. This methodology more accurately reflects real-world deployment scenarios, where future data is predicted based on past observations.

V. Results

A. RF Signature Validation

This project is based on the premise that everyone exhibits a unique RF spectral signature. To investigate this, an identical data collection protocol was applied to three participants—Subject 1, Subject 2, and Subject 3, the latter of whom has a clinical diagnosis of diabetes. Their spectral responses at baseline glucose levels are compared in **Fig. 4**. The results

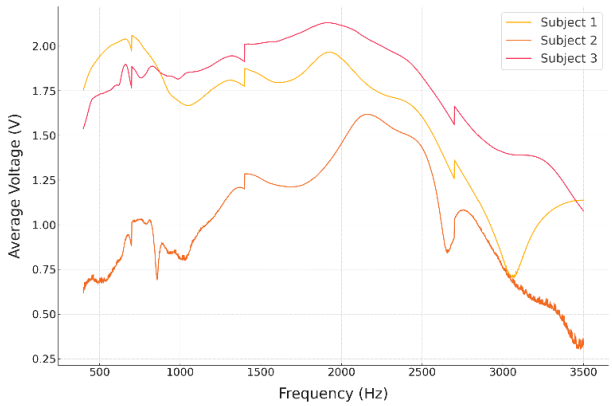

Fig. 4. RF signatures of Subject 1, Subject 2, and Subject 3. The results highlight subject-specific spectral patterns, demonstrating that each individual exhibits a distinct RF signature.

demonstrate clear and consistent differences in RF signatures between the subjects, supporting that individuals have distinct physiological profiles. Previous studies have also established that RF signatures vary with glucose levels, particularly when comparing pre- and post-meal states [10].

B. Model Performance and Glucose Prediction Trends

To assess model performance, we employed three standard regression metrics: Mean Absolute Relative Difference (MARD), Mean Absolute Error (MAE), and Root Mean Squared Error (RMSE), shown in the following equations:

$$MARD = \left(\frac{1}{n}\right)\sum_{i=1}^{n}\left|\frac{\hat{y}_i - y_i}{y_i}\right| \times 100$$

$$MAE = \left(\frac{1}{n}\right)\sum_{i=1}^{n}|\hat{y}_i - y_i|$$

$$RMSE = \sqrt{\left(\frac{1}{n}\right)\sum_{i=1}^{n}(\hat{y}_i - y_i)^2}$$

The dataset consists of 10,356 sweeps obtained from the participant using the KnowLabs RFID device. The data is split into train and test splits, consisting of 9169 and 1187 sweeps, respectively. Among all evaluated machine learning models, the MLP regressor achieved the best clinical performance on the test dataset with a MARD of 11.66%, satisfying the threshold (MARD < 15%) and outperforming all other models (see **Table I**). The MLP regressor model has two hidden layers with a squared error loss function.

Table I: Performance Comparison of Regression Models for Glucose Prediction Using RF Spectral Features

Model	RMSE (mg/dL)	MAE (mg/dL)	MARD (%)
Ridge	18.62	15.36	14.33
Lasso	16.93	14.29	13.77
ElasticNet	17.33	15.03	14.5
SVR	19.55	15.2	14.9
KNN	22.89	16.85	16.26
MLP	**16.65**	**12.59**	**11.66**
LightGBM	16.99	13.66	12.95
XGBoost	18.32	14.41	13.71

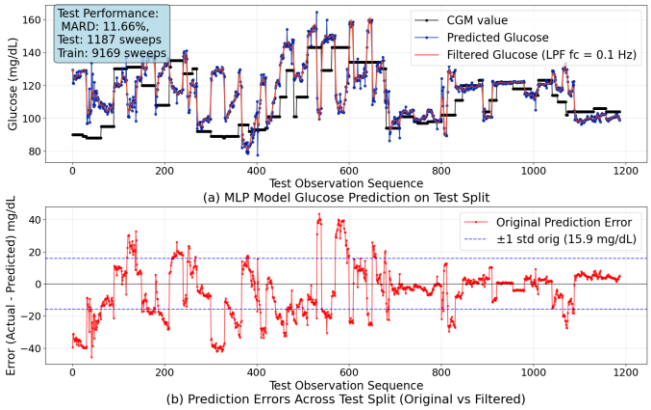

Fig. 5. (a) Predicted glucose levels from the MLP model (blue line) overlaid with a low-pass filtered (LPF) version of the predictions (orange line), compared to reference CGM measurements (black line) on the test dataset. (b) Prediction error (red line) computed as the difference between MLP-predicted values and CGM ground truth readings.

The MLP regression model demonstrated strong alignment with actual glucose measurements from the CGM device, as shown in **Fig. 5a**. The model generally follows the overall trends observed in the CGM data, capturing many of the rises and falls in glucose levels. A second-order low-pass filter with a cutoff frequency of 0.1 Hz was applied to smooth the predicted glucose values, reducing high-frequency noise and making the model's output easier to interpret. Most prediction errors remain within one standard deviation, highlighting the model's consistency and reliability (**Fig. 5b**).

To assess model interpretability, a SHAP (SHapley Additive exPlanations) summary plot was generated for theMLP model [10] (**Fig. 6**). The analysis identified several key features that significantly influenced glucose predictions:

- Meal type and metabolic state (pre-/post-prandial): These contextual features aligned with expected physiological glucose fluctuations surrounding food intake.
- Spectral features: Specific RF frequencies, including 2985 MHz, 3394 MHz, 1598 MHz, 769 MHz, and 462 MHz, were among the most predictive. These correspond to distinct dielectric responses of biological tissue.
- Temperature sensor readings: Environmental and physiological temperature variations contributed to prediction refinement by providing additional contextual information. Our SHAP analysis revealed that contextual features such as meal type and pre-/post-prandial state contributed substantially to model performance. This reliance highlights the challenge of extracting glucose-specific signatures from RF signals alone, as glucose-induced dielectric shifts are subtle and often masked by stronger tissue and environmental effects.

VI. Discussion

The results from this study indicate that non-invasive glucose monitoring using RF signals in combination with machine learning shows promising potential. The MLP regressor model performed best, achieving a MARD of 11.66%, meeting the clinical standard (MARD < 15%). while remaining simple and efficient. We show that the model captured the overall trends

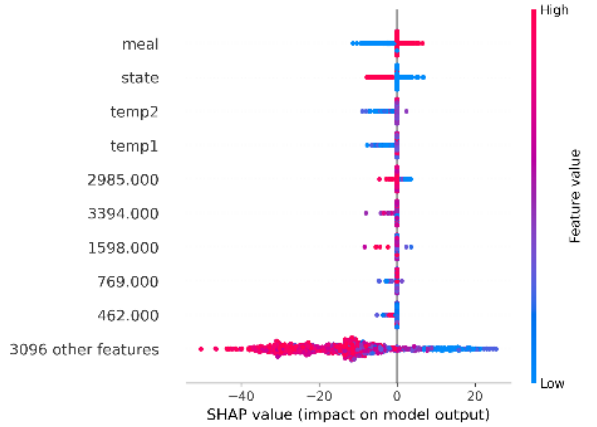

Fig. 6. SHAP (SHapley Additive exPlanations) summary plot for the MLP model, showing the relative impact and importance of individual features on glucose prediction. Key contributors include meal type, metabolic state, selected RF spectral frequencies, and temperature readings.

and fluctuations in glucose dynamics, although some deviations remain, particularly during rapid changes. The error analysis further highlights the model's strengths and limitations. Most prediction errors fall within ±1 standard deviation (15.9 mg/dL), indicating consistent performance across most of the test set. However, there are periods where error spikes often coincide with abrupt changes in glucose levels. This suggests that while the model performs well under stable conditions, it may struggle with glucose transitions. Overall, the results support RF spectroscopy as a potential alternative to traditional glucose monitoring methods, offering a needle-free and user-friendly solution for continuous glucose tracking.

In our machine learning framework, we incorporated over 3,000 input features. To gain deeper insight into how these features influence model predictions, we employed SHAP analysis (**Fig. 6**). The SHAP results reveal that features such as "meal," "state," "temp1," and "temp2" possess the highest SHAP values, underscoring their dominant impact on model output. Notably, the majority of the remaining features exhibit SHAP values clustered near zero, indicating minimal contribution to the model's predictions. This observation suggests that, despite the extensive feature set, only a select few features substantially drive model performance. These findings emphasize valuable opportunities for future work, including targeted feature selection and dimensionality reduction. We view contextual data integration as a pragmatic strategy to improve robustness in early-stage non-invasive sensing systems. By streamlining the model to focus on the most impactful features, we can enhance computational efficiency and improve interpretability, both of which are critical for practical deployment and clinical acceptance

While the results are promising, further work is needed to strengthen the system's clinical readiness. The current study is limited to one adult participant. In the future, we plan to recruit participants with diabetes and a wider range of glucose levels, especially in the hypoglycemic range, where data is limited. Longer monitoring periods and diverse real-world conditions will also help evaluate the system's reliability over time. A formal time series analysis was not performed in the current study. Future work will incorporate time series modeling approaches to better capture temporal dynamics and improve predictive accuracy. Expanded studies across participants with diverse demographics and glycemic ranges, including hypoglycemia, will be essential to assess generalizability and clinical applicability. Additionally, efforts should be made to miniaturize and integrate the RF device into a wearable form for continuous use. Regulatory validation, usability testing, and comparisons to commercial CGMs are also essential steps before clinical deployment.

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