Learned Electrochemical Sensor Devices (LeSD) for Glucose Predictions: A Mini Review and Meta-Analytic Synthesis

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***Abstract*— The integration of machine learning (ML) with advanced electrochemical sensors (LeSD) is creating a paradigm shift in disease diagnosis, by enabling minimally invasive to non-invasive biomarker predictions, with high prediction accuracies, robustness to environmental variabilities. Such LeSDs provide easy to access, portable, miniaturized, wearable platforms for biomarker detection and its level quantification. This mini-review synthesizes recent studies employing diverse ML algorithms across enzymatic, non-enzymatic, wearable, and neuromorphic sensor types, specifically for predicting glucose and thus, diabetic diagnosis. The review follows a meta-analysis perspective, evaluating pooled accuracy effects and highlights the sources of heterogeneity. In addition, challenges and future research directions for effective clinical translation of advancements in LeSDs are discussed. With its in-depth coverage of recent advancements in LeSD realizations, this review could serve as a valuable information resource for both clinicians and researchers.**

Keywords*— *diabetic diagnosis, electrochemical sensors, glucose prediction, machine learning, meta-analysis.

I. Introduction

Continuous Glucose Monitoring (CGM), non-invasive glucose sensing, effective glucose sensing from low concentration biofluids are the demanding requirements, that drive research and developments in diabetic management worldwide. And electrochemical glucose sensors are the primary components used for sensing glucose from various biofluids. Recent developments in nano biosensor have enabled sensor miniaturization, minimally invasive to non-invasive sensing, low-analyte sensing, as well as multiplexed sensing feasible. Notable electrochemical sensing techniques include, enzymatic, non-enzymatic, wearable, and neuromorphic sensor [1]. However, sensing elements are often affected by noise signals, environmental fluctuations, electrode fouling that limits specificity in complex biological matrix [2]. These effects are difficult to be rectified (considering the effect of a live biological environment-in which the sensors are used) with conventional methods that rely on changing/optimizing sensor material/characteristics alone for betterment of results. Meanwhile, introduction of machine learning (ML) algorithms to enhance sensor data analysis, were proven to improve detection limits, provide reliable, adaptable, robust solutions, and enable continuous analyte monitoring capabilities [3]. These learning based methods are broadly classified into, (i) supervised learning – where an algorithm is trained from input samples along with known output predictions, then the learned knowledge is used for making predictions on unknown inputs, (ii) unsupervised learning – where an algorithm will classify/group the given input dataset by recognizing inherent patterns present in them. Further, a machine learning framework often relies on a separate feature extractor, feature selector and a final classifier while a deep learning based model uses deep neural networks for effective feature extraction, followed by a classification layer for achieving the desired task. Ensemble learning methods, Support Vector Machines (SVM) are among the notable methods in ML algorithms, while transfer learning based pre-trained models are efficient ones among the DL algorithms [4]. Inherent to the importance of ML-tuned electrochemical sensing based CGM relies a necessity to study the merits and demerits of the existing methods in order to advance future research in this field. This necessitated a review of potential researches in ML assisted electrochemical sensing based CGM systems. With the significance of glucose sensing, advancements in electrochemical glucose sensors and various classification of ML methods, the objectives of this mini-review include,

- To presents a focused mini-review on literatures that illustrate synergistic application of advanced materials and ML models in glucose sensing. Particularly, six representative studies from 2022 to 2024 are chosen and evaluated through a random-effects meta-analysis.
- To present a quantitative synthesis, in order to interpret performance variabilities across the studies.
- To present a qualitative synthesis, to understand practical implications and future prospects.

With this brief introduction, the rest of the manuscript is organized as follows: section 2 details the sensors and ML algorithms used/studied in the representative literatures considered for the present study. Section 3 presents the meta-analysis strategy adapted for the analysis and synthesis. Section 4 presents the results and inferences made from the conducted meta-analysis and section 5 details the significance, limitations and future scope and section 6 conclude the review.

II. LITERATURE SURVEY

Advancements in biosensor technologies are propelled by the integration of advanced materials and machine learning techniques. Specific material advancements include carbon nanotubes, molybdenum disulfide (MoS2), and organic polymers, that enable sensor sensitivity and specificity [5][6]. While, ML and DL algorithms provide powerful analytical tools capable of deciphering complex, noisy datasets generated by these sensors, facilitating more accurate biomarker detection and quantification [7][8]. The six representative studies considered for this meta-analysis are discussed below and the quantitative results obtained from each literature is shown in table I.

ML methods were used for enabling highly accurate glucose predictions from biofluids like sweat with extremely low concentration of glucose biomarker. Concentration regression analysis was carried out effectively for quantifying the correlation and determining optimal reactant addition in electrochemical detection. ML methods like, (i) Multiple Linear Regression (MLR), (ii) Decision Trees (DT), (iii) Artificial Neural Networks (ANN), (iv) Random Forest (RF), and (v) Extreme Gradient Boosting (XGBoost) are used for the analysis. Experimental results revealed that XGBoost method made the most accurate predictions with the highest correlation depicting an R2 value of 0.928 and a least mean absolute error (MAE) of 13.93 μmol/L. And random forest achieved the second place with an R2 of 0.842 and MAE of 17.76 μmol/L [9]. Even non-enzymatic sensing materials like MoS2 on paper substrates were developed for effective glucose predictions. Such a sensor was integrated with a robust ML-driven (SVM) standalone application GluQuantify for predicting glucose concentration from serum samples. This sensor had a sensing resolution of up to 0.01 μM and was able to predict glucose levels with 99% accuracy [10]. Similarly, ZnO sensing element functionalized with capture probes were integrated with wearable devices were demonstrated to predict glucose from eccrine sweat in real-time continuously. Complex impedances Zmod, Zphase, skin temperature and sweat RH% were obtained and their correlation with glucose values are found by employing various ML methods. Specifically, linear regression, decision tree, and ensemble algorithms were verified across the R2 and RMSE values. Experimental results in terms of R2 and RMSE for, (i) decision tree is 0.93 and 0.1, (ii) ensemble method is 0.94 and 0.15 respectively. This device performance was experimentally verified against blood glucose values collected using a glucometer [11]. In another experiment, neuromorphic organic polymer based electronic devices were integrated with ML methods in order predict glucose from minimally invasive sensing devices. The primary experimental motive of energy efficiency, biocompatibility along with improved prediction accuracy were demonstrated in the experiment [12]. Further, a strip type glucose sensor is fabricated using carbon nanotubes (CNTs)-cellulose nanofibers (CNFs), Prussian blue electrodeposition and glucose oxidase (GOx) immobilization and chitosan coating. Electrochemical results from this sensor, nanomaterial content, Prussian blue deposition cycles, used by an ML method to quantify the correlation between measured signals and glucose levels. This ML analytics is integrated with a smartphone read-out and the device was demonstrated to have a detection limit of 0.1mM which is well within the required limits to distinguish a diabetic from non-diabetic [13]. Commercial CGM devices necessitate periodical calibrations (manually) to circumvent the sensor degradation and biofouling effects. In addition, mathematical modelling based sensor sensitivity estimates are often misguiding. Thus, ML methods integrated with electrochemical impedance spectroscopy (EIS) are employed for the determining sensor sensitivity. Such an ML based method predicted sensor sensitivity including both reduction in GOx enzyme activity and degradation due to biofouling. Random forest based ML method was demonstrated to predict sensor sensitivity with a MAE of 1.50 nA/mM. Such an example demonstrates the use of ML to tackle sensor degradations [14].

In summary, ML methods based on Support Vector Machines, Random Forests, Gradient Boosting, and Neural Networks employed together with advanced electrochemical sensors were able to make accurate glucose predictions from low concentration biofluids [9][10]. In addition, such ML-powered biosensing when integrated with wearable devices were able to make continuous, real-time monitoring of glucose [11]. Further, the use of organic polymer based electronics and neuromorphic sensors with ML methods enable flexible and biocompatible glucose monitoring solutions [12] and use of ML could detect sensor degradations, biofouling and make effective glucose predictions [14]. These works highlight the prospects for creating more adaptive, interpretable and efficient glucose sensing systems by integrating ML and electrochemical sensors. However, challenges remain in harmonizing sensor outputs, standardizing report metrics and constructing robust training datasets reflective of clinical diversity [13]. Metric comparison and details of the six representative studies were presented in table I below

TABLE I. SUMMARY OF THE REPRESENTATIVE LESDS

Ref. No. Year	Study Focus	Sensor Type & Material	ML Model & Metrics
[9] 2024	ML-aided differential pulse voltammetry (DPV) glucose sensor	Carbon working electrode (WE), PBS, for use with sweat medium	XGBoost; R2=0.928, RMSE = 31.03 μmol/L
[14] 2023	Predicting sensitivity of CGM-like glucose sensor against biofouling & reduction in Gox	Gold-coated medical grade lancet needles, amperometry + EIS	Random Forest (RF); MAE = 1.50 nA mm^{-1}
[10] 2024	Non-enzymatic glucose sensor with MoS_2 modification	MoS_2 on chromatography paper, serum	SVM; accuracy = 99.64%
[11] 2022	Continuous glucose monitoring in sweat	Wearable EIS sensor, sweat	DT, R2=0.93, RMSE = 0.1 mg/dL
[12] 2024	Minimally invasive glucose sensing with flexible and biocompatible sensors	Organic polymer-based electronics, neuromorphic sensor, blood glucose	FCNN; Accuracy 84.85%, RMSE 23.19–24.02 mg/dL
[13] 2024	Sensor optimization for real-time glucose detection	CNT-CNF composite electrode, Sweat	XGBoost; R2=0.86, RMSE = 0.177 μA

III. MATERIALS AND METHODS

This review is based on details collected from six recent, high-impact studies related to the subject field of ML integrated electrochemical glucose sensors. Details related to sensor material, the biofluid platform used, ML methods studied, the primary research question addressed, accuracy of predictions achieved (in terms of accuracy, R2) and error measures (in terms of RMSE, MAE) are obtained from the literatures and the same is presented in table I.

With these details, three different analysis were carried which includes, (i) manual descriptive meta-analysis – comparing the sensitivity range, materials used for sensing, ML methods employed for prediction and the results achieved there-off, (ii) Normalization of error and accuracy parameters – for a fair comparison between the various methods and to identify gaps that exist, (iii) random-effects meta-analysis was conducted employing the DerSimonian-Laird method. Each of this analysis presented both merits and demerits as well as enabled significant inferences which are presented in the results section.

IV. Results and Discussion

This section summaries the results obtained from three different meta-analysis method adapted and each of them is arranged in individual sub-sections. The first section 4.1 presents the details obtained from the manual descriptive analysis.

A. *Summary of the descriptive meta-analysis*

- These studies cover both enzymatic and non-enzymatic glucose sensing. It used variety of advanced materials as electrodes which included, carbon electrodes, gold-coated lancets, MoS_2, and composite nanomaterials.
- The ML models used in these studies included XGBoost, Random Forest, Support Vector Regression, Decision Trees, and Neural Networks. These ML methods are chosen based on specific sensor modalities and data types.
- These sensors have demonstrated excellent prediction performance (in terms of their corresponding target variable), with accuracies above 84% and R2 values ranging between 0.86 and 0.93. This reveals reliability of model predictions.
- Neuromorphic sensors with organic polymeric flexible electronics and ML methods were recommended for biocompatible, glucose predictions.
- Most of the continuous monitoring devices relied on using sweat as the biofluid for making glucose predictions and employed ML methods to compensate for the variability introduced by environmental and temporal changes in sensor response.
- ML methods are reliably used for sensor optimisations thus, demonstrated their potential in sensor design in addition to offering reliable predictions

B. *Sensor sensitivity benchmarking – conversion to standard error unit, Normalized accuracy, Normalized Error value*

In order to make a fair comparison, similar error and performance parameters should be compared. As various measures are used across the studies, measures to obtain a common benchmark units were introduced. This included two methods, (i) conversion of units in µmol/L to mg/dL (where ever possible) – this conversion is carried out by using biochemical conversion factor (1 mg/dL = 55.5 micromol/L), (ii) Errors and accuracy were normalized to MAE and R2 values. The converted and normalized metrics are given in table II.

TABLE II. Metric Standardization by conversion and Normalization

Ref. No.	Error metric	Original value	Converted to mg/dL	Normalized Error (RMSE/ MAE)	Normalized Accuracy/R2
[9]	RMSE	31.03 µmol/L	(~0.56 mg/dL) [a]	0.0	0.54
[10]	None	NA	NA	NA	1.0
[11]	RMSE	0.1 mg/dL	0.1 mg/dL	1.0	0.55
[12]	RMSE	23.19 mg/dL	23.19 mg/dL	0.25	0.0
[13]	RMSE	0.177 µA	NA[b]	1.0	0.08
[14]	MAE	1.5 nA/mm	NA[b]	0.95	NA

a. (Converted using 55.5 µmol/L per mg/dL)

b. NA - No direct conversion feasible from current measurements

RMSE values converted to mg/dL equivalents highlight the influence of sensor design and ML model choice on quantitative precision. However, RMSE values could be directly compared (in terms of mg/dL) only in three cases [9][11][12] as other measurements are based on measured current values which demand additional conversions. Thus, normalized error and normalized accuracy parameters are devised to enable a fair comparison. A bar plot of the normalized parameters across the six cases is presented in fig. 1 below. And the inferences obtained from these two unit conversions were detailed in the below discussion.

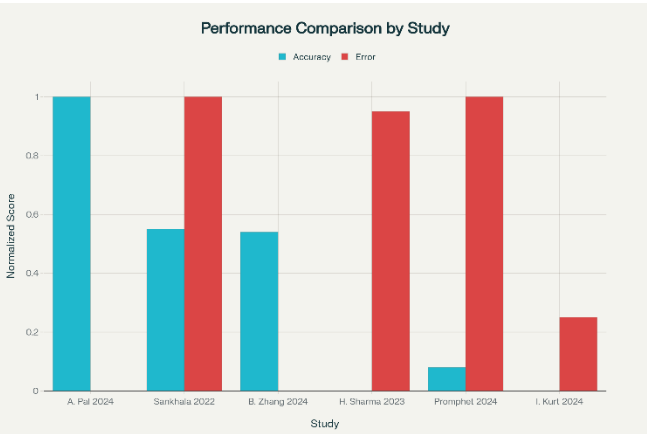

Fig. 1. Bar chart of Normalized accuracy and Normalized error obtained across the representative studies.

- Highest normalized accuracy (effect size) of 99.64% (1.0) is obtained in the case of MoS_2 based non-enzymatic sensor - SVM based predictions. But error metric was not reported in this study [10].
- Second high normalized accuracy of 0.55 is obtained with EIS sensor-Decision tree based wearable sensor device. This device registered a normalised error of 1.0 and the lowest RMSE of 0.1 mg/dL [11].

- Similar accuracy (0.54) was achieved in the case of DPV sensor – XGBoost based glucose predictions. However, the model presented the worst normalised error score of 0.0 which is reflected in RMSE as 31.03 μmol/L [9].
- EIS sensor – Random forest method achieved the good normalized error score of 0.95 resulting from MAE = 1.5 nA/mm. But accuracy of the method is not reported [14].
- CNT-CNF – XGBoost demonstrated the least normalised accuracy of 0.08 (relative to the other methods compared), but demonstrated good normalised error of 1.00 in comparison to other methods [13].
- Neuromorphic sensors – FCNN had registered the least accuracy and intermediate error 0.25 when compared to the other methods [12].

A major drawback found with the analysis is unavailability of error as well as accuracy parameters across the various studies. Though normalization enables a fair comparison, unavailability of data limits the possibilities of a complete and fair comparison in most cases.

C. *Random-effect meta-analysis - DerSimonian-Laird method*

Random effects meta-analysis was conducted employing the DerSimonian-Laird method. This enables understanding the heterogeneity arising from different sensor types and ML models. Forest plots that enable visualizing summarized individual and pooled effect size with confidence intervals (CI) were generated and is presented in fig. 2. The literatures selected for the analysis included a diverse set of ML-aided glucose sensing platforms with different sensing materials and biofluid contexts. Effect size is a metric that quantifies the accuracy or R2 value. In the present study, this effect size predominantly exceeded 0.85 and in some cases it reached near-perfect values [10]. Further a pooled accuracy effect size of 0.90 was registered in spite of the experimental heterogeneity. Forest plot visualizations facilitate understanding this trend better revealing a confidence interval disparity which indicates robustness of the sensors.

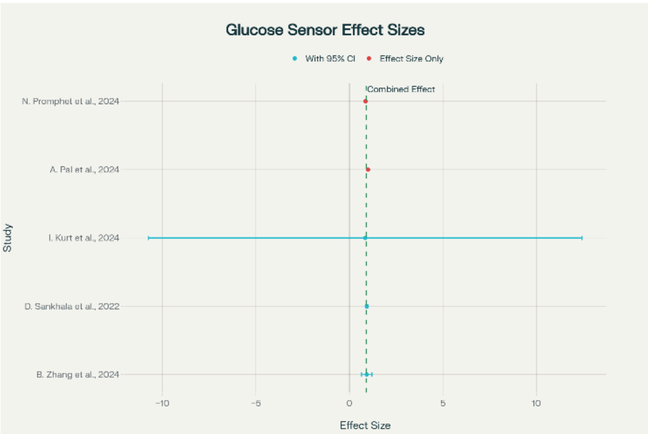

Fig. 2. Forest Plot of ML-Aided Glucose Sensor Predictions.

Forest plot provides a visual comparison of the accuracy (or R^2) effect sizes across the six ML-powered glucose sensors reported in the representative literatures. It presents those methods that have a 95% and above confidence intervals while making predictions. The below are the inferences made from the forest plot.

- Most of the study results presented a higher prediction accuracy (above 0.85), which indicates their strong glucose prediction performance.
- Highest effect size of ~0.996 is registered with MoS_2-SVM based glucose sensor [10].
- EIS-DT, DPV-XGBoost demonstrated a tight confidence interval of 0.93, 0.928 respectively, which reflects their precise estimates[11][9].
- Neuromorphic sensor – FCNN demonstrated a CI of 0.8485 which reveals variance across its predictions. This reflects their uncertainty in making predictions resulting from high error variance [12].
- The combined effect size line at ~0.90 indicates that the ML models achieved around 90% of accuracy/R2 while sensing glucose.
- The unavailability of error metrics in certain studies provide only point estimates which limited certainty on their precisions [14][10][13].

In summary, the Forest plot graph indicates, (i) consistent strong accuracy achieved with ML aided electrochemical glucose sensing as well as, (ii) highlights the variability in precision resulting from sensor and ML method variations. However, combined estimates support the fact that ML inclusions aid in achieving excellent accuracy in predicting glucose. Thus, this meta-analytic visualisation facilitates visual comparison and synthesis of study results as well as enable clarifying uncertainties. However, additional studies with standardized metrics would facilitate strong analytic conclusions.

D. *Comparison with Existing Reviews*

Existing literature reviews on artificial intelligence (AI) based electrochemical sensing of glucose follow a systematic analysis style [3][4]. Further, AI and ML assisted electrochemical sensing of various analytes (not specifically glucose sensing) is presented in certain reviews [5][7][8]. These studies enable understanding the advancements and learning the various AI, ML, methods commonly employed for sensor optimisations. Though these studies highlight the quantitative results obtained with various methods, a more specific analysis (comparison of six potential studies) of cumulative effects and pooled performance analysis with respect to ML assisted electrochemical glucose sensing is feasible with meta-analysis [*present work]. Further, the present study facilitates research planning for a near future development of a similar system. However, there are certain limitations in this study which are discussed in next section.

V. Inferences and Future scope

A. *Significance and Limitations of the study*

Collectively, study findings affirm the potential of ML models in improving the glucose sensor prediction performance. Considering wearable and non-enzymatic sensing platforms, ML methods facilitate improved predictions overcoming noises and biofouling challenges. Diverse range of ML methods ranging from conventional tree-based methods to deep learning networks were investigated for glucose predictions from sensor-specific signal characteristics. However, a major hurdle while conducting cross-study evaluations and meta-analysis is the un availability of standardization of reporting units and inclusion of comprehensive error metrics. Emergence of organic neuromorphic devices and multi-modal sensing architectures enable lightweight, on-sensor data processing based glucose sensing platforms.

B. *Significance and Limitations of the study*

Research direction that drives future advancements in glucose sensing platforms include,

- Sensor hardware miniaturization integrated with light-weight ML models for facilitating sensing system integration with resource-limited wearable devices.
- Enabling access to diverse labelled clinical datasets enhance model generalization and reduce biases.
- Inclusion of Interpretability by explainable AI tools like SHAP and LIME are vastly investigated to gain clinician trust and accelerate regulatory approval
- Multimodal data fusion (that presents physiological markers), combined with electrochemical signals, offers promising prospects for comprehensive glucose monitoring ecosystems.
- Collaborative efforts from experts across diverse disciplines like material science, data science, and clinicians play a pivotal role in overcoming challenges related to data scarcity, noise management, and real-time analytics deployments. This enables streamlining the pathway toward patient-centric precision diagnostics

VI. Conclusion

Meta-analysis of the representative literatures revealed that the integration of ML methods with electrochemical sensing systems, elevates their accuracy and operational resilience. This study enabled comparing the confidence interval with which the various LeSDs make glucose predictions and revealed that sensor variability and ML method variations affect predictions. Further, this review highlighted the present advancements, challenges and future translational opportunities, emphasizing the need for standard metric reporting and clinical validations for realizing a more reliable clinical impact of these devices.

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