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Review

AI-Enabled Electrochemical Glucose Sensing: Towards Intelligent and Modernized Health Monitoring

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Abstract: The rising prevalence of diabetes has made high-precision, continuous glucose monitoring a central challenge in intelligent health management. This review systematically examines recent advances in artificial intelligence (AI)-enabled electrochemical glucose sensing. We overview mainstream machine learning (ML) algorithms and their applications in electrochemical signal modeling, denoising, feature extraction, and adaptive calibration. Four representative platform categories are analyzed: enzyme-based sensors, non-enzymatic and affinity-based systems, electrochemiluminescence (ECL) sensing, and wearable continuous monitoring platforms. Representative studies show that ML algorithms such as support vector regression (SVR), XGBoost, and random forest (RF) can substantially improve analytical performance, with detection limits reduced from 100 nM to 10 nM and R^2 values exceeding 0.9 in selected cases. The deep integration of AI and electrochemical sensing is transforming glucose detection from passive measurement to active cognition, namely to sensing systems that not only record signals but also perform adaptive denoising, drift correction, individualized calibration, and predictive decision support. This transition points toward explainable, low-power, privacy-aware, and wearable personalized health monitoring systems.

Keywords: artificial intelligence; machine learning; electrochemical sensing; glucose monitoring; wearable biosensors; continuous monitoring

1. Introduction

Diabetes represents one of the most challenging metabolic diseases globally, posing unprecedented challenges to public health systems and socioeconomic stability. According to the International Diabetes Federation (IDF), the global diabetic population is projected to exceed 700 million by 2045 [1]. Continuous monitoring of blood glucose levels plays an irreplaceable role in diabetes management, complication prevention, and individualized treatment planning [2–4]. However, conventional glucose monitoring methods, including finger-prick blood sampling and continuous glucose monitoring (CGM) systems, still face limitations in accuracy, invasiveness, cost, and user compliance [5–8].

Electrochemical biosensors have emerged as core technologies for point-of-care testing (POCT), wearable health monitoring, and implantable medical devices due to their high sensitivity, rapid response, low cost, and ease of miniaturization and integration [9–12]. From CGM in diabetes management to sweat electrolyte analysis in exercise physiology and real-time neurotransmitter tracking in neural interfaces, electrochemical platforms

continue to expand their boundaries in precision medicine and digital health [13–16]. The core advantage lies in their ability to directly convert biological recognition events, such as antigen-antibody binding and enzymatic reactions, into quantifiable electrical signals, enabling *in-situ*, dynamic detection of target analytes [17].

Nevertheless, despite continuous technological advancements, conventional electrochemical biosensors still face persistent engineering and biological challenges that severely constrain their long-term stability, individual universality, and clinical reliability. First, signal drift and baseline instability are ubiquitous issues. Biofouling on electrode surfaces, enzyme activity decay, and environmental temperature and humidity variations can all cause non-specific shifts in output signals over time, affecting quantitative accuracy [18,19]. Second, significant inter-individual physiological differences mean that the same analyte concentration may elicit distinctly different electrochemical responses in different users, requiring frequent sensor calibration [20]. Third, complex biological matrix interferences, such as lactate and uric acid in sweat or ascorbic acid in blood, often cause false positives or signal suppression, challenging sensor selectivity [20–23]. Furthermore, in wearable scenarios, motion artifacts and mechanical disturbances introduce significant noise, making true signals difficult to distinguish [24,25]. Finally, most systems still rely on external calibration, such as finger-prick blood sampling, lacking autonomous regulation capabilities and limiting their evolution toward truly closed-loop intelligent systems [26].

These challenges indicate that material innovation or device microfabrication alone is insufficient for qualitative breakthroughs. The core requirement for next-generation electrochemical sensors is intelligence, meaning that systems must possess adaptive, self-correcting, anti-interference, and predictive capabilities [27]. In recent years, the rapid development of AI, particularly ML, has provided a new paradigm for addressing these challenges. AI excels at processing nonlinear, high-dimensional, time-varying data, extracting hidden features from complex signals, establishing individualized models, and enabling dynamic decision-making [2]. Following its success in image recognition and natural language processing, AI is accelerating its penetration into biosensing and driving the transformation of electrochemical systems from passive detection tools to active-cognition systems, that is, platforms that not only acquire signals but also adaptively denoise data, correct drift, update individualized calibration, and support predictive decisions [6]. The overall conceptual framework of this transformation is summarized in Figure 1.

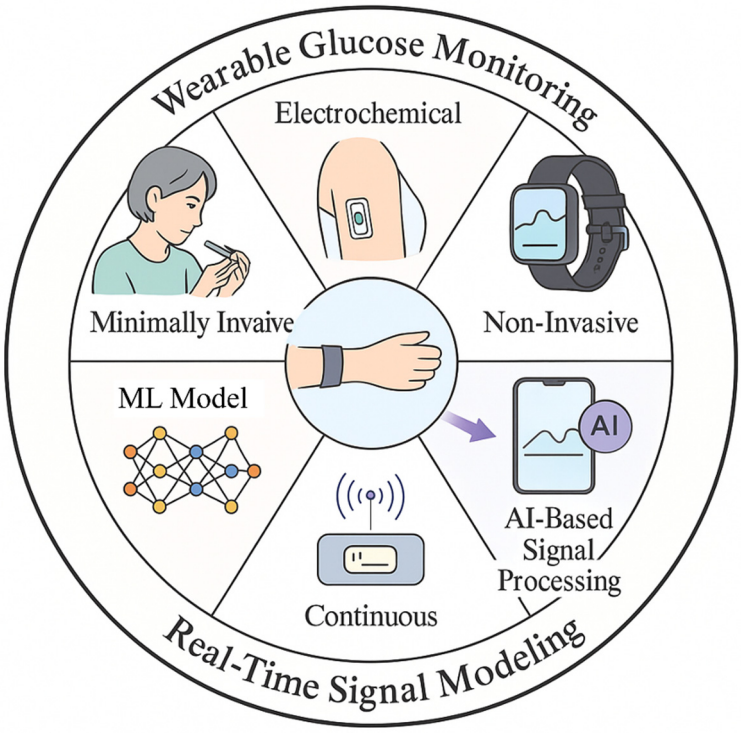

Figure 1. Schematic framework of AI-enabled electrochemical glucose sensing.

In summary, the deep integration of electrochemical sensing and artificial intelligence is reshaping the landscape of glucose detection technology. This review aims to systematically elucidate how AI empowers electrochemical biosensing to address critical bottlenecks. Section 2 overviews mainstream ML methods applicable to electrochemical signal processing and establishes a mapping framework between sensing challenges

and AI solutions. Section 3 demonstrates through frontier research cases how AI achieves signal denoising, adaptive calibration, multimodal fusion, and closed-loop support across enzyme-based, non-enzymatic, and affinity-based, ECL, and continuous-monitoring platforms. Finally, Section 4 summarizes current challenges and future development directions, including edge intelligence, explainable AI, and cross-analyte generalization capabilities. We argue that AI is not merely a data post-processing tool but a core driving force reshaping the design philosophy of electrochemical biosensors.

2. Machine Learning Fundamentals for Electrochemical Sensing

With the rapid advancement of artificial intelligence technology, ML has become one of the core means for promoting the intelligence and automation of electrochemical biosensors. Particularly in recent years, the deep integration of AI and biomedical engineering has given rise to the emerging interdisciplinary field of Digital Biomedical Engineering. This field is dedicated to using AI technology to build intelligent, predictive, and personalized life health solutions, providing a macro theoretical framework and technical pathway for the evolution of electrochemical biosensors from traditional single-detection tools to intelligent, networked health monitoring systems [28]. By learning and modeling complex electrochemical signals, ML can automatically identify hidden patterns, extract key features, and achieve precise prediction of analyte concentrations, system states, or potential interferences. This capability demonstrates unique advantages in addressing traditional issues such as electrode fouling, signal drift, individual differences, and environmental noise [29–31].

2.1. Basic Concepts of Machine Learning

ML is an important branch of AI, representing a collection of algorithms that can automatically learn task patterns from data. Its core idea is to enable computing systems to continuously update model parameters from input data to minimize prediction errors, thereby achieving accurate inference on unknown data [29,32–34]. In the field of electrochemical biosensing, the introduction of ML has gradually transformed signal analysis processes that originally relied on expert experience and manual feature extraction toward data-driven and adaptive optimization approaches [29–31].

According to different learning methods, ML can be divided into two major categories: supervised learning and unsupervised learning. Supervised learning relies on labeled datasets, learning mapping relationships between inputs and known outputs for prediction. For example, in glucose sensing, inputs are electrochemical signal features, while outputs are known glucose concentration values. When output variables are continuous values, such as concentration or current intensity, this constitutes a regression problem; when output variables are discrete categories, such as positive/negative or normal/abnormal, this becomes a classification problem. Unsupervised learning does not require label information and is mainly used for exploring internal data structures, including cluster analysis and feature extraction. Clustering is used to identify natural groupings in data, while dimensionality reduction methods, such as principal component analysis (PCA), reduce input dimensions while maintaining primary information, helping improve model stability and generalization capability [29,32–34].

In recent years, multimodal ML has been increasingly applied in electrochemical biosensing. This method can fuse data from multiple sensing modules, such as electrochemical signals, image signals, temperature, humidity, or pressure data, thereby obtaining more comprehensive feature representations. This multimodal integration strategy can be viewed as an extension of traditional single-modal signal processing, analogous to the comprehensive judgment of multiple detection indicators in clinical diagnosis [35].

2.2. Machine Learning Workflow

ML implementation typically follows a systematic workflow, including data acquisition and preprocessing, model construction and training, validation and testing, and performance evaluation. In electrochemical applications, raw signals often contain noise, baseline drift, and outliers, making data preprocessing crucial [29,33]. Common steps include signal smoothing, denoising, normalization, and outlier removal to enhance data consistency and algorithm learning efficiency [29,33]. For high-dimensional data, feature selection or dimensionality reduction techniques, such as PCA and LDA, can be employed to reduce input dimensions [36,37].

During model training, datasets are typically divided into training sets, validation sets, and test sets, commonly in 60:20:20 ratios. Training sets are used for model parameter learning, validation sets for hyperparameter optimization and overfitting prevention, and test sets for evaluating model performance on unknown data [29,33]. When data is limited, cross-validation provides a more robust evaluation method [38,39]. Its basic concept is to divide data into subsets, with models trained and tested on different combinations sequentially, and average performance metrics taken to reflect overall predictive capability. In the performance evaluation stage, classification

models typically employ metrics such as accuracy, precision, recall, ROC-AUC, and F1 score, while regression models commonly use coefficient of determination (R^2), mean absolute error (MAE), and root mean square error (RMSE) [40]. Overfitting is a common problem in ML models, where models perform well on training data but degrade on new data [41–43]. Through reasonable feature selection, regularization, data augmentation, and preventing data leakage, the model's generalization capability can be significantly improved.

In practice, several methodological factors critically determine whether an ML model is reliable for electrochemical sensing. First, dataset size is often limited because biosensor experiments are labor-intensive and clinical sampling is difficult, which makes complex models vulnerable to overfitting. Under such conditions, simpler algorithms such as SVR, RF, or XGBoost may provide more robust performance than deep neural networks. Second, feature extraction remains essential for electrochemical data. Typical features include peak current, peak potential, impedance magnitude and phase, charge-transfer resistance, baseline drift descriptors, temporal derivatives, and multi-frequency or multi-modal environmental variables. Thoughtful feature engineering can substantially improve model interpretability and reduce data requirements. Third, rigorous validation is indispensable. In addition to train/validation/test splitting, k-fold cross-validation, leave-one-subject-out validation, and external testing on independent batches are particularly important for wearable glucose sensing, where inter-individual variability is significant. Finally, overfitting must be carefully controlled through regularization, feature selection, early stopping, hyperparameter tuning, and avoidance of data leakage between repeated measurements from the same individual.

2.3. Task-Oriented Comparison of Machine Learning Algorithms for Electrochemical Sensing

ML algorithms in electrochemical biosensing should be selected according to signal modality, dataset scale, and deployment constraints rather than model complexity alone. When the input mainly consists of feature-engineered descriptors such as peak current, peak potential, impedance magnitude, charge-transfer resistance, or environmental covariates, shallow models—including SVM, RF, gradient boosting trees (GBT), XGBoost, and shallow artificial neural networks (ANNs)—often provide better robustness, faster training, and easier interpretation under limited-sample conditions [42,44]. By contrast, deep models such as DNNs, CNNs, and RNNs become advantageous when the input retains high-dimensional, spatial, or temporal structure that is difficult to summarize manually. This task-oriented distinction is especially important in electrochemical systems, where limited sample size and matrix heterogeneity often make a more complex model less reliable in practice.

For example, SVM/SVR are well suited to small-sample nonlinear regression and classification, especially when the goal is to map handcrafted electrochemical features to analyte concentration or sample class [29]. Decision trees and their ensemble variants, such as RF, GBT, and XGBoost, can capture coupled relationships among multiple electrochemical variables and are often attractive when interpretability, variable importance analysis, and robustness to mixed feature types are required [45–47]. K-nearest neighbors (KNN) can still perform effectively when the electrochemical feature space is well separated, although their sensitivity to noise and dimensionality limits their utility for more complex problems [48]. ANNs provide flexible nonlinear fitting but generally require more careful regularization and validation than shallow tree-based or margin-based models [49]. CNNs are particularly suitable for ECL images, electrochemical imaging maps, and sensor-array outputs because they can learn local spatial patterns directly from pixels or grids. In contrast, RNN-type architectures and related temporal models are more appropriate for time-series drift compensation, trend prediction, and continuous monitoring because they preserve sequential dependencies across measurements [50,51]. In parallel, PCA remains valuable for dimensionality reduction and feature compression, especially when electrochemical descriptors are collinear, and interpretability still matters [52].

Furthermore, because electrochemical signals are often affected by measurement uncertainty, biological noise, and domain shift, probabilistic ML methods based on Bayesian inference offer a complementary advantage. In particular, stochastic synapse architectures based on GeTex-OTS can support uncertainty quantification and probabilistic reasoning at the hardware level, providing a new computational route toward uncertainty-aware, low-power medical diagnostic systems [53]. By modeling weight distributions rather than single-point estimates, these methods can better distinguish random signal fluctuations from true concentration changes, which is especially relevant for clinical scenarios requiring high-confidence decisions.

2.4. Key Roles of Machine Learning in Electrochemical Biosensing

In electrochemical biosensing, ML algorithms are primarily applied to address core challenges such as electrode fouling, individual variability, noise, and matrix effects [32,33,54]. Through nonlinear models such as SVM and ANN, signal drift caused by electrode surface fouling can be effectively compensated [55,56]. Using

ensemble learning methods, such as RF and XGBoost, model adaptability to different experimental conditions and individual differences can be enhanced, improving system generalization performance [57,58]. For noise and matrix interference, dimensionality reduction techniques such as PCA can effectively identify key features and eliminate interfering signals. Deep learning models such as CNN and RNN can effectively handle complex nonlinear patterns in high-dimensional data, distinguishing target analyte signals from noise. SVM, through kernel function transformation, can improve analyte selectivity in complex matrices. In summary, ML algorithms provide powerful data processing capabilities for electrochemical biosensing through optimized signal processing, feature extraction, and model construction, enabling sensor systems to perform biomolecular detection more accurately and reliably [29,54]. A schematic overview of an AI-assisted wearable glucose-sensing workflow is shown in Figure 2.

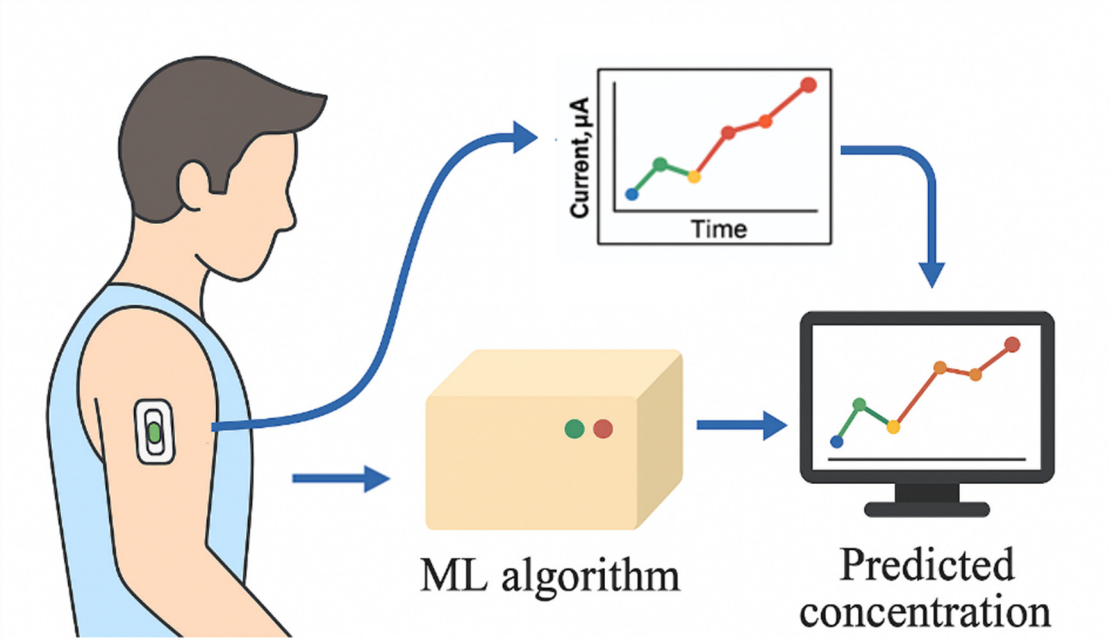

Figure 2. Schematic illustration of an AI-assisted wearable electrochemical glucose sensing system integrating ML for real-time signal analysis and concentration prediction.

3. AI-Enabled Electrochemical Glucose Sensing

3.1. Enzyme-Based Electrochemical Glucose Biosensors

Since Clark and Lyons first proposed the enzyme-based electrochemical biosensor for blood glucose detection by immobilizing glucose oxidase (GO_x) on an electrode surface in 1962 [58], enzyme-catalyzed sensors have become the cornerstone of glucose detection and clinical diagnostics [59–61]. In such biocatalytic systems, specific enzymes recognize the target analyte and catalyze a redox reaction, generating a quantifiable electrochemical signal—typically a change in current or potential due to electron transfer [6,62].

After decades of development, enzyme-catalyzed glucose sensors have evolved through three generations: the first generation uses oxygen as a natural electron acceptor; the second generation introduces artificial electron mediators (e.g., ferrocene or ABTS) to enhance electron transfer efficiency; and the third generation achieves direct electron transfer (DET) between the enzyme and the electrode by constructing conductive interfaces [63–66]. Despite these advances significantly improving sensitivity and dynamic range, critical challenges remain. Enzyme activity is susceptible to decay due to temperature, pH, and biofouling, leading to signal drift and non-linear responses in complex biological fluids such as sweat or saliva [62,67]. To address these issues, ML technology has recently been integrated into enzyme-catalyzed sensing systems for adaptive calibration, environmental compensation, and performance decay prediction.

For instance, Zhang et al. constructed a glucose biosensor based on differential pulse voltammetry (DPV), employing the synergistic action of GO_x and horseradish peroxidase (HRP) with ABTS as the electron mediator [57]. As shown in Figure 3a, hydrogen peroxide (H_2O_2) generated during the enzymatic reaction oxidizes ABTS, producing DPV signals correlated with glucose concentration. However, these signals exhibit non-linear characteristics affected by operational variables such as mediator concentration, scan rate, and electrode activation conditions. By introducing an XGBoost regression model to comprehensively analyze these electrochemical

features and experimental variables, the researchers achieved high-precision prediction of glucose concentration (Test Set $R^2 = 0.928$), significantly improving sensor stability under non-ideal conditions (Figure 3b,c).

In another study, Sharma et al. proposed an ML strategy combined with electrochemical impedance spectroscopy (EIS) to predict sensor sensitivity changes in the presence of biofouling [68]. The results indicated that an RF regression model could effectively identify signal decay trends based on impedance characteristics (Figure 3d,e), providing a new technical pathway for implementing "self-diagnosis" and "self-correction" functions. Similarly, Lee et al. applied regression-based ML to correct redox-sensitive colorimetric paper sensors, further enhancing detection accuracy in complex fluids [69]. Representative enzymatic sensing studies are summarized in Table 1.

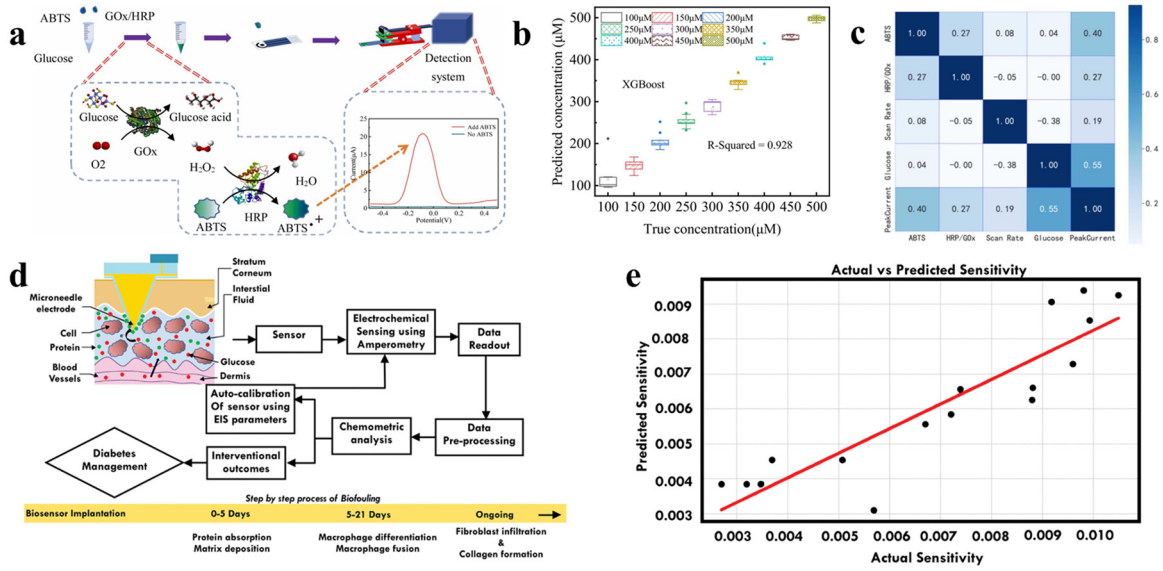

Figure 3. ML-assisted enzymatic electrochemical glucose sensing mechanisms and performance evaluation. (**a**) Schematic of the dual-enzyme cascade reaction where GO_x generates H_2O_2, which subsequently activates Horseradish Peroxidase (HRP) to oxidize ABTS and produce a quantifiable DPV signal. (**b**) Comparison of glucose-concentration prediction performance, showing that the XGBoost model achieves the highest accuracy ($R^2 = 0.928$) with predictions closely matching true values. (**c**) Pearson correlation heatmap of electrochemical and experimental variables (e.g., scan rate, peak current, and enzyme loading), indicating how catalytic activity, mediator transport, and electron-transfer efficiency jointly shape the glucose-dependent response and therefore guide model optimization [57]. (**d**) Functional block diagram of the ML-based signal and data pathway in a continuous glucose monitoring (CGM) system, illustrating the flow from electrochemical sensing to model-based analysis. (**e**) Scatter plot comparing actual versus predicted sensor sensitivity using a Random Forest regression model, demonstrating compensation for biofouling-induced performance decay and enabling self-diagnosis of sensor degradation [68]. Adapted with permission from Refs. [57,68].

Table 1. Standardized analytical summary of ML-assisted biocatalytic electrochemical biosensors.

EC Method	Fluid	Materials/ Platform	ML Model	Linear Range	LOD	Key Statistical Metric	Ref.
DPV	PBS	GO_x/HRP/ Carbon/ABTS	XGBoost	100–500 μM	NR	$R^2 = 0.928$; RMSE = 31.03 μM	[57]
Amperometry + EIS	Artificial ISF	Gold microneedles/ PDMS	RF regression	N/A	N/A	MAE = 1.50 nA·mm^{-1}	[68]
Colorimetric	Buffer	PAni-NPs/ GO_x paper	RF	NR	NR	$R^2 = 0.922$	[69]
Colorimetric (image-based EC)	Sweat	Paper-based GO_x	Regression ML	NR	25 μM	$R^2 = 0.96$	[27]
Amperometry	Serum	GO_x/PDA/rGO/SPE	DNN/ANN	NR	NR	$R^2 = 0.97$; MSE = 0.0012	[70]

In the field of wearable detection, the coupling of enzyme catalysis and ML has also demonstrated potential advantages. Zhou et al. constructed a GO_x-based wearable sweat glucose sensor, utilizing ML regression algorithms to correct colorimetric and electrochemical responses [27]. The model achieved an R^2 of 0.96 in sweat

sample testing from multiple volunteers, with a limit of detection (LOD) reaching 25 μM. This study demonstrated ML's capability to integrate multi-source data (color, humidity, conductivity), effectively offsetting interferences from the complex sweat matrix. Similarly, Abreu et al. demonstrated the quantitative prediction potential of Deep Neural Networks (DNN) in enzyme-catalyzed electrochemical detection [70]. Their multi-model comparison on a GO_x-modified PDA/rGO screen-printed electrode platform showed that the DNN achieved the highest accuracy in predicting glucose in serum samples ($R^2 = 0.97$; MSE = 0.0012).

While enzyme-catalyzed sensors offer excellent selectivity, their practical long-term operation is hampered by enzyme denaturation and biofouling-induced signal drift, necessitating the exploration of more robust affinity-based and bioreceptor-free alternatives. Photoelectrochemical affinity-type transduction further broadens the design space for robust recognition-driven biosensing, especially when optical or electrochemical readouts are jointly leveraged to strengthen analytical specificity [71].

3.2. Non-Enzymatic and Affinity-Based Electrochemical Sensors

To overcome the inherent instability of enzymes, recent research has increasingly expanded toward affinity-based electrochemical biosensors relying on antibodies, aptamers, or molecularly imprinted polymers, as well as portable and non-enzymatic sensing platforms that facilitate robust operation in complex settings [72–74]. In this context, several studies have focused on improving artificial recognition interfaces and biomimetic assay configurations, including strategies based on nano/micro-structured transducers, fluidic assay integration, and molecularly engineered binding layers [75,76]. Molecularly imprinted polymers and related biomimetic receptors are particularly attractive because of their stability, low cost, and compatibility with electrochemical transduction, and their combination with aptamer-based recognition has further broadened the design space of affinity sensing [77–82]. In parallel, auxiliary sample-handling and target-enrichment strategies, including microscale field-assisted manipulation, also highlight the broader importance of controlling analyte transport and confinement in high-performance biosensing systems [83].

However, despite these advantages, such artificial or bioreceptor-free systems often lack the intrinsic specificity of natural enzymes, which can lead to partially overlapping electrochemical responses in complex clinical samples. ML offers an effective way to address this limitation by decoding subtle multidimensional "fingerprint" features embedded in voltammetric or impedance data, thereby improving selectivity and lowering detection limits [34,84]. Nevertheless, this strategy has clear boundary conditions: when structurally similar interferents generate highly overlapping signatures, when interferent concentrations fall outside the training distribution, or when electrode aging and matrix shifts distort the feature space, fingerprint-based models may lose discriminative power.

In the domain of material engineering integrated with ML, Pal et al. developed a frugal paper-based sensor modified with hydrothermally grown MoS_2 microflowers [85]. As illustrated in Figure 4a,b, the MoS_2 nanostructure facilitates glucose adsorption and oxidation. To extract valid signals from the complex DPV background, the team employed a SVR model optimized via a genetic algorithm (Figure 4c). Experimental results (Figure 4d) demonstrated that this ML-assisted approach improved the LOD from ~100 nM (manual analysis) to 10 nM in spiked serum samples, with a recovery rate of 99.64%. They further deployed this model in a desktop application, "GluQuantify" (Figure 4e), enabling end-to-end intelligent analysis.

In the context of wearable continuous monitoring, Sankhala et al. demonstrated a systematic engineering pathway for on-demand sweat glucose sensing [86]. The system (Figure 4f) integrates a ZnO-based sensor array with a portable readout circuit (Figure 4h). Addressing the issues of data loss and environmental noise in sweat analysis, they designed a comprehensive data processing pipeline (Figure 4g) and proposed a reference-point-based signal interpolation strategy (Figure 4i). Comparative analysis showed that tree-based regressors markedly outperformed linear regression, yielding the highest R^2 values and lowest RMSE values in cross-validation (Figure 4j–k). This result underscores how algorithmic calibration can partially compensate for missing data, environmental perturbations, and individual physiological variability in wearable sweat sensing. Representative non-enzymatic and affinity-based studies are summarized in Table 2.

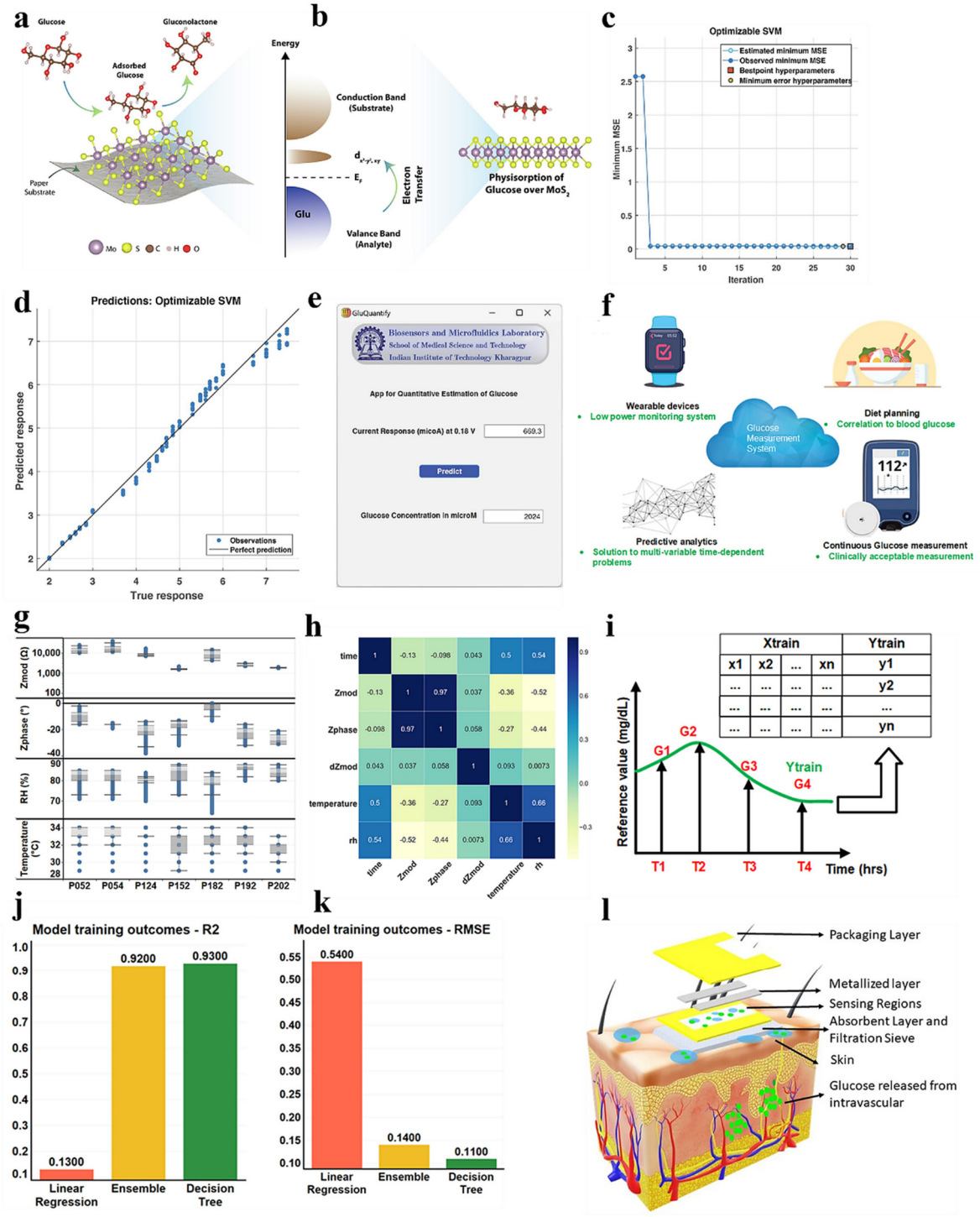

Figure 4. ML-augmented non-enzymatic and affinity-based glucose sensing platforms. (**a**) Schematic mechanism of glucose oxidation facilitated by the MoS_2 microflower structure. (**b**) Illustration of electron transfer during physisorption and oxidation of glucose on the MoS_2/paper electrode interface [85]. (**c**) Optimization curve of the SVR model, showing iterative minimization of mean squared error (MSE). (**d**) Predicted-versus-true response plot obtained with the optimized SVR model, demonstrating strong agreement in complex matrices. (**e**) User interface of the "GluQuantify" desktop application for end-to-end glucose prediction based on the MoS_2-SVR workflow [85]. (**f**) Concept of the wearable sweat glucose monitoring ecosystem [86]. (**g**) Data-processing pipeline showing how raw wearable signals, auxiliary environmental variables, and missing-data handling are integrated before regression. (**h**) Hardware architecture of the wearable sensor patch and signal-transmission module [86]. (**i**) Reference-point-based interpolation strategy used to reconstruct irregular or partially missing time-series data before model fitting [86]. (**j**,**k**) Comparison of regression performance in terms of R^2 and RMSE, showing that tree-based models outperform linear regression under wearable-noise conditions [86]. (**l**) Schematic of the skin-interfaced sensor layers for glucose detection from interstitial fluid [87]. Adapted with permission from Refs. [85–87].

Table 2. Standardized analytical summary of ML-assisted non-enzymatic and affinity glucose sensors.

EC Method	Fluid	Materials/Platform	ML Model	Linear Range	LOD	Key Statistical Metric	Ref.
DPV	Serum (spiked)	MoS_2/paper	SVR	NR	10 nM	Recovery = 99.64 ± 1.60%	[85]
EIS	Human sweat	ZnO thin-film wearable patch	Tree-based regression	NR	NR	R^2 up to 0.93; RMSE as low as 0.11	[86]
CV/DPV	Drug/real sample	Lectin/Prussian Blue	ML optimization	NR	10.2 pM	NR	[87]

These studies highlight two complementary routes for ML-enabled sensing: (i) enhancing signal-to-noise ratios in nanomaterial-based systems (e.g., MoS_2-SVR), and (ii) enabling robust calibration in wearable systems against environmental perturbations (e.g., tree-based regression on ZnO sweat sensing). However, the selectivity gains provided by ML are not unlimited. When chemically similar interferents generate overlapping electrochemical fingerprints, or when the deployed sample matrix differs substantially from the training distribution, model performance can deteriorate rapidly. Robust practical translation therefore requires chemically diverse training sets, hard-interferent testing, subject-level external validation, and preferably uncertainty-aware prediction.

3.3. Electrochemiluminescence Sensing Systems and Intelligent Data Analysis

Electrochemiluminescence (ECL) combines the sensitivity of luminescence with the controllability of electrochemistry [88–90]. Despite its widespread utility in clinical diagnostics [91,92], ECL signals are often non-linear and susceptible to background interference. Integrating ML allows for signal denoising, self-calibration, and the transformation of ECL from simple intensity measurement to "intelligent visual perception" [93]. Furthermore, recent trends have shifted towards portable, smartphone-integrated POCT platforms [94,95], necessitating robust algorithms to handle lower-quality hardware signals. Related mobile phone-based ECL studies likewise show that machine-learning-assisted image analysis can support portable quantitative sensing outside conventional laboratory settings [96].

Kumar et al. developed a smartphone-integrated ECL biosensing platform for the "sample-to-answer" detection of metabolites [97]. As shown in Figure 5a, the portable device utilizes a 3D-printed enclosure containing SE-ECL electrodes. The Luminol/H_2O_2 system serves as the signal generator (Figure 5b), where ECL intensity increases linearly with glucose concentration (Figure 5c). By processing the optical signals via ML algorithms on a smartphone, the system achieved precise quantification ($R^2 = 0.98$) in the 0.05–3 mM range.

Regarding software analysis, Kumar et al. introduced "ECLStat," a tool for automated ECL image processing [98]. The workflow (Figure 5d) includes Region of Interest (ROI) selection, background correction, and feature extraction. The software interface (Figure 5e) allows users to train and deploy various models (RF, SVM, ANN), effectively eliminating subjective errors in manual analysis. Bhaiyya et al. further advanced miniaturization by constructing a closed bipolar electrode ECL platform [99] (Figure 5f). Visual results (Figure 5g) clearly show intensity variations with concentration, and the robust regression model (Figure 5h) demonstrated superior performance ($R^2 > 0.96$) in multi-analyte detection compared to standard linear regression.

Collectively, the studies summarized in Table 3 highlight a transformative trend in ECL biosensing: the shift from laboratory-grade, bulky instrumentation to portable, intelligent point-of-care (POCT) platforms. While traditional ECL analysis relies heavily on precise environmental control to maintain signal linearity, ML algorithms (e.g., RF, CNN) effectively compensate for the non-linear distortions and background noise inherent in miniaturized, low-cost devices [97–100]. By coupling low-cost emitters (like LIG or conductive PLA) with intelligent image processing, these systems demonstrate that algorithmic robustness can offset hardware limitations. This "software-defined" sensing paradigm not only lowers the barrier for high-sensitivity metabolite detection but also establishes a foundation for the integration of optical biosensors into consumer electronics for personalized health monitoring. Beyond glucose-specific demonstrations, this trend is reinforced by emerging miniaturized and wearable electrochemical systems for multiplexed molecular diagnostics, metabolite tracking, non-invasive health analysis, and ML-assisted flexible sensing, which collectively expand the translational scope of intelligent point-of-care devices [17,101–106].

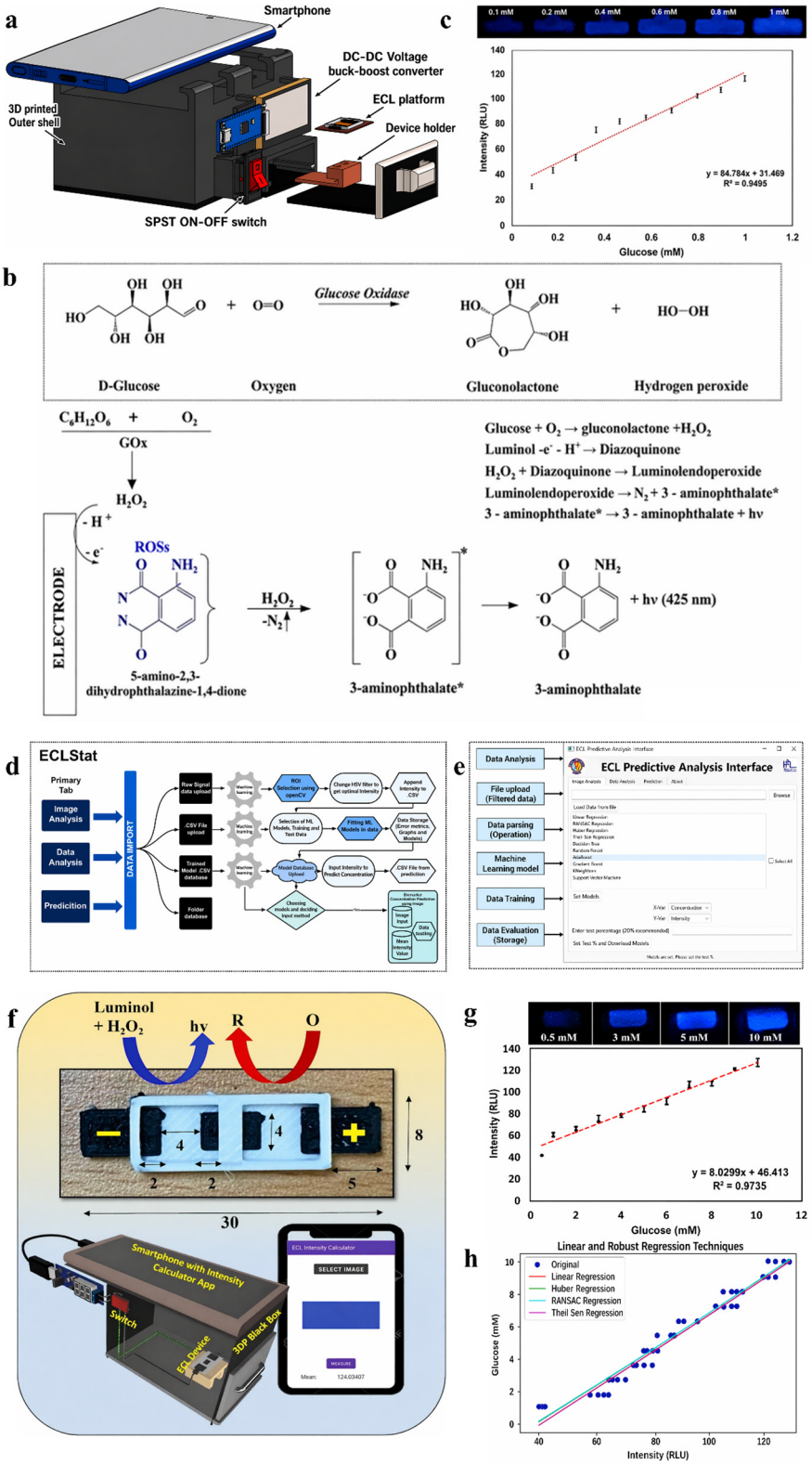

Figure 5. ML-assisted ECL sensing systems and data analysis strategies. (**a**) Exploded view of the 3D-printed portable ECL device integrated with a smartphone for optical detection. (**b**) Mechanism of the Luminol/H_2O_2 ECL reaction on the electrode surface, linking glucose oxidation to light emission. (**c**) Calibration curve and corresponding ECL images (top) showing linear intensity increase with glucose concentration (0.05–3 mM) [97]. (**d**) Workflow of the "ECLStat" software, automating image import, ROI selection, feature extraction, and ML model training. (**e**) Graphical User Interface (GUI) of ECLStat for selecting regression models (e.g., Random Forest, SVM) [98]. (**f**) Structure of the closed bipolar ECL sensor platform, including the microfluidic device and mobile imaging setup. (**g**) Visual ECL output for different glucose concentrations. (**h**) Comparison of linear versus robust regression techniques, showing improved accuracy ($R^2 \approx 0.97$) with robust methods [99]. Adapted with permission from Refs. [97–99].

Table 3. Standardized analytical summary of ML-assisted ECL glucose and metabolite sensing.

EC Method	Fluid	Materials/Platform	ML Model	Linear Range	LOD	Key Statistical Metric	Ref.
ECL	PBS/Serum	LIG/Luminol	RF/AdaBoost	0.05–3 mM	0.04 mM	$R^2 = 0.99$	[97]
ECL	Simulated ECL images	Pt/Luminol imaging	RF/CNN/SVM	N/A	N/A	Accuracy > 95%; $R^2 = 0.97$	[98]
ECL	Artificial serum	Au/Pt/Luminol CBE	Robust regression	NR	NR	$R^2 = 0.96$; RMSE = 0.008 mM	[99]
ECL	PBS	Conductive PLA	Decision Tree	NR	0.033 mM	$R^2 = 0.95$	[100]

3.4. Continuous Monitoring and Self-Calibrating Electrochemical Sensing Systems

Continuous monitoring provides dynamic health insights but is plagued by signal drift and individual physiological variability [107]. ML, with its ability to model high-dimensional time-series data, offers a robust solution for system self-calibration. Recent reviews further emphasize that AI-native wearable sensing architectures are becoming a central framework for digital health, especially when distributed sensor nodes, adaptive analytics, and biosensor networks are integrated into continuous monitoring workflows [108–110].

Sardesai et al. proposed an ML-assisted wearable system for the simultaneous monitoring of sweat glucose and cortisol [111]. The system uses a dual-electrode patch coated with a ZnO semiconductor thin film (Figure 6a), worn on the wrist (Figure 6b). By fusing EIS data with skin temperature and humidity parameters, an ensemble regression model successfully decoupled environmental noise, achieving a high prediction correlation ($R^2 = 0.96$).

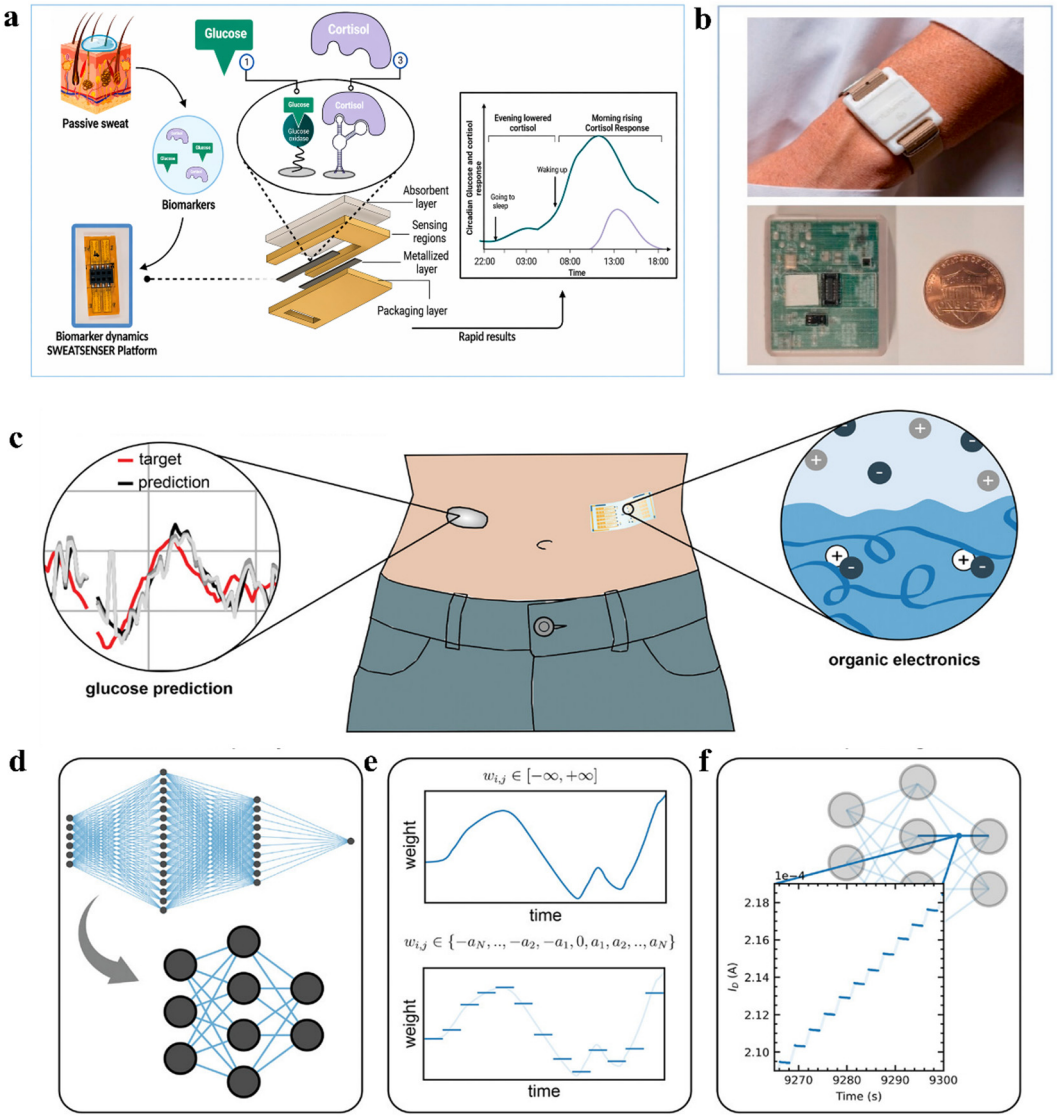

Figure 6. Intelligent continuous monitoring systems and neuromorphic hardware implementations. (**a**) Schematic of the single-channel, dual-electrode sweat sensor patch featuring a ZnO sensing layer (100–200 nm) for glucose and

cortisol detection. (**b**) Photograph of the wearable sensor prototype worn on a user's wrist [111]. (**c**) Concept of an organic neuromorphic micro-network for glucose prediction, mimicking biological synapses. (**d**) Network-size reduction strategy enabling feasible on-chip implementation under edge-computing constraints. (**e**) Comparison between ideal software-based weight updates and the discrete conductance states supported by the organic hardware, showing how quantized updates approximate learned synaptic plasticity. (**f**) Resulting glucose-prediction behavior demonstrates that these hardware-implemented weights still preserve trend-level prediction accuracy over time, thereby linking device-level weight updates directly to system-level glucose prediction performance [112]. Adapted with permission from Refs. [111,112].

In terms of hardware-level intelligence, Kurt et al. demonstrated an organic neuromorphic electronic system for blood glucose prediction [112]. The system utilizes conductive organic materials to create artificial synapses (Figure 6c), capable of analog weight updates in hardware. Although the weight space is more limited than in software neural networks (Figure 6e), experiments proved that these hardware weights are sufficient to support continuous glucose prediction tasks (Figure 6f), providing empirical evidence for low-power, edge-computing smart patches (Figure 6d). Representative continuous-monitoring and self-calibrating systems are summarized in Table 4.

Table 4. Standardized analytical summary of continuous monitoring and self-calibrating systems.

EC Method	Fluid	Materials/Platform	ML Model	Linear Range	LOD	Key Statistical Metric	Ref.
EIS	Sweat	ZnO/Au wearable patch	Regression ensemble	N/A	N/A	$R^2 = 0.96$	[111]
Neuromorphic	ISF	Organic neuromorphic micro-network	Hardware ANN	N/A	N/A	Trend-level prediction preserved; quantitative metric NR	[112]
CGM	ISF	Commercial CGM sensor	MLP/SVR/RF	N/A	N/A	Personalized MARD = 8.2%	[113]
TinyML	ISF	Edge drift-correction pipeline	Random Forest	N/A	N/A	Prediction error within ±16 mg/dL	[114]

Research by Kumari et al. further highlighted that personalized calibration models (e.g., Multi-Layer Perceptron, MLP) can reduce the Mean Absolute Relative Difference (MARD) of CGM systems to 8.2% [113]. Additionally, the "Stress Generation Model" proposed by Sabatini et al., using Tiny Machine Learning (TinyML), can compensate for drift directly at the edge, maintaining prediction errors within ±16 mg/dL [114]. These advances indicate that ML is transitioning from backend data processing to frontend real-time calibration, serving as the core engine for next-generation reliable wearable health monitors. In practical CGM deployment, edge intelligence and cloud computing should be viewed as complementary rather than competing strategies: on-device models provide low-latency, privacy-preserving denoising and drift compensation, whereas cloud infrastructure supports heavier retraining, longitudinal data aggregation, and large-scale personalization. Related dual-mode electrochemical/ECL studies also suggest that optimized neural-network pipelines such as PSO-ANN can support accurate analyte quantification in intelligent biosensing platforms [115].

4. Conclusions

The synergistic integration of AI with advanced electrochemical materials is fundamentally reshaping the design paradigms and detection capabilities of glucose sensors. By incorporating ML, electrochemical signal processing is transitioning from empirical curve fitting to data-driven analytics, enabling sensing systems to achieve high sensitivity and reliability within complex physiological environments. In enzyme-catalyzed architectures, advanced nanomaterials such as multi-walled carbon nanotubes (MWCNTs), gold nanoparticles (AuNPs), graphene, and MoS_2 are employed to enhance electron transfer efficiency and catalytic activity, thereby expanding the linear dynamic range and lowering the limit of detection [116–119]. When coupled with multimodal ML modeling, these systems can achieve signal correction, drift compensation, and adaptive calibration against enzyme activity decay or environmental fluctuations, significantly improving long-term operational stability [61,62].

ML demonstrates comparable potential in affinity-based and bioreceptor-free systems. Since recognition layers such as aptamers and molecularly imprinted polymers (MIPs) are prone to weak binding and signal drift under non-ideal conditions, researchers utilize algorithms like SVM and RF to perform nonlinear fitting on EIS and CV data. This approach effectively extracts characteristic signals from background noise, enabling high-precision recognition

of glucose at low concentrations [117,118,120,121]. In bioreceptor-free sensors, ML can partially compensate for the specificity limitations of conventional methods by analyzing response patterns or "electrochemical fingerprints" from unmodified electrodes to distinguish species with overlapping behaviors [34,122–124]. However, this strategy is not universally reliable: performance can deteriorate when structurally similar interferents produce highly overlapping signatures, when interferent concentrations fall outside the training distribution, or when sensor aging and matrix shifts distort the feature space between calibration and deployment. Therefore, robust translation requires chemically diverse training sets, explicit hard-interferent testing, subject-level external validation, and preferably uncertainty-aware prediction. Furthermore, ML-driven modeling of material layer structure, pore distribution, and electrode surface states facilitates the prediction and optimization of material parameters, enhancing electrode performance and signal consistency. More broadly, rigorous benchmark design and lightweight deployment concepts drawn from the wider ML literature remain instructive for electrochemical AI systems, particularly when models must be evaluated carefully and executed on resource-constrained hardware [125,126], while deep learning has also shown strong potential for decoding complex voltammetric signals in living systems [127].

Despite the significant performance enhancements empowered by ML, several challenges remain for widespread application. Firstly, the inherent noise and non-linear characteristics of electrochemical data increase the difficulty of model training, particularly in wearable and body fluid detection, where signals are susceptible to interference from multiple factors such as temperature, pH, sweat composition, and motion-induced artifacts. Secondly, the scarcity of high-quality, annotated datasets is not only a matter of sample number but also of sample diversity and representativeness. Many published studies still rely on benchtop measurements, spiked samples, or small volunteer cohorts, which may not fully reflect the variability encountered in real-world users. The collection of real patient data is often restricted by ethical and privacy considerations, making models prone to sampling bias and potentially leading to uneven performance across different populations [128–130]. This issue is particularly critical for wearable sensing, where inter-individual variability in sweat rate, skin condition, hydration status, medication, diet, and circadian rhythm may substantially alter sensor response even at similar glucose levels. Additionally, the "black box" nature of many ML models reduces clinical interpretability and physician trust, raising regulatory concerns regarding liability attribution, data transparency, model auditing, and the definition of clinically interpretable failure modes. From a translational perspective, regulatory acceptance will also depend on whether calibration procedures are traceable, model updates are auditable, and failure modes are clinically interpretable, making prospective multi-center validation and subject-level external testing essential.

Looking forward, research on ML-assisted electrochemical glucose sensing should focus on three strategic directions: (1) Data Level: establishing open, shared multi-source bio-electrochemical databases and introducing transfer learning, data augmentation, and synthetic data generation technologies to mitigate sample scarcity, support subject-level external validation, and better address individual variability; (2) Algorithm Level: promoting the integration of deep learning with explainable artificial intelligence (XAI) to develop models that possess not only high predictive precision but also physical interpretability, uncertainty awareness, and improved robustness against distribution shift; (3) Hardware Level: strengthening the integration of sensors with edge intelligence to achieve low-power, low-latency, privacy-preserving denoising, drift compensation, and dynamic self-calibration directly on the device, while allowing cloud-based infrastructures to support heavier retraining, longitudinal data aggregation, and large-scale personalization when needed. Through interdisciplinary collaboration combining the strengths of materials science, electrochemistry, data science, and clinical engineering, AI-enabled electrochemical glucose sensing is poised to transition from laboratory validation to practical clinical and wearable health monitoring applications [131].

In summary, the fusion of ML and electrochemical glucose sensing represents not merely a technological innovation but an evolution in the philosophy of health monitoring. It transforms electrochemical detection from "passive measurement" to "active cognition," in which sensing systems not only record signals but also perform adaptive denoising, drift correction, individualized recalibration, and decision-support functions, laying a solid foundation for the future construction of interpretable, personalized, and persistently operating bioelectronic health systems.

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Data Availability Statement

The data generated during this study are available in the main text.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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