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Artificial Intelligence-Enhanced, Closed-Loop Wearable Systems Toward Next-Generation Diabetes Management

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Recent advancements in wearable healthcare have led to commercially accessible continuous glucose monitoring systems (CGMs) for diabetes management. However, CGMs only monitor glucose levels and lack therapeutic functions, prompting the development of closed-loop systems that use monitored glucose levels to guide insulin dosing. While promising, these devices also pose risks, such as insulin overdosing, which can cause hypoglycemia. This review summarizes recent advances in integrating artificial intelligence methods with conventional CGMs. The developments in wearable CGMs and progress in insulin delivery technologies are explored, and existing algorithms for glucose prediction in closed-loop systems are reviewed. Additionally, emerging trends in optimizing these algorithms to enhance the safety and security of closed-loop insulin delivery systems are highlighted.

1. Introduction

Diabetes is a metabolic condition that affects over 500 million people worldwide. Current projections indicate a concerning trajectory, and by 2045, nearly 10% of the global population will be affected by this ailment.[1] At its core, diabetes is characterized by a dysregulated glucose metabolism, which can trigger a range of health complications, such as organ dysfunction, tissue damage, and reduction in lifespan. It is important to note that the scourges of diabetes are not limited to adults only; adolescents and children are also significantly scourged by this disease.[2] Diabetes manifests in multiple forms, notably type 1 diabetes (T1D), where autoimmune responses destroy pancreatic beta cells, leading to insufficient insulin production.[3] Type 2 diabetes (T2D) involves insulin resistance that hampers glucose uptake,[4] while gestational diabetes mellitus (GDM) develops during pregnancy in women without prior symptoms.[5] The disease also includes monogenic syndromes and secondary diabetes from other conditions.[6] As shown in **Figure 1**, this life-sustaining hormone is administered via injections or insulin pumps, forming crucial part of daily care for diabetes patients.[7]

Recent advancements in wearable technology have revolutionized healthcare, particularly through the development of continuous glucose monitoring systems (CGMs) for diabetes management.[8–10] Although CGMs are proficient at sensing glucose levels, they lack therapeutic functions, which has led to the innovation of closed-loop systems that use monitored glucose data to regulate insulin dosing. However, these devices pose both potential benefits and risks; for instance, excessive insulin administration can result in hypoglycemia with life-threatening outcomes, emphasizing the need for precise algorithmic development for practical deployment. This review focuses on the latest progress in the rapidly evolving field, integrating emerging artificial intelligence techniques with traditional CGMs. Deviation from optimal control can result in abnormal blood glucose levels, carrying substantial health risks. It is imperative to recognize that the severity of T1D goes beyond the daily routine, profoundly influencing the overall health, well being, and longevity of those living with this condition.[11,12]

With rapid advancements in technology and biomedical research, new horizons are emerging. The integration of wearable devices and artificial intelligence (AI) is a promising avenue that can revolutionize diabetes care, particularly in closed-loop control. Our review ventures into this exciting domain, examining the current state of commercially available devices, their algorithms, and their potential for achieving tighter and more responsive glucose control. However, incorporating wearable technology and AI is not without its hurdles. Issues related to device accuracy, algorithm robustness, user safety, and data privacy are just a few of the many concerns that researchers and clinicians must address. Our review provides a perspective on the potential benefits and pitfalls of these emerging technologies. We envision the future iteration of closed-loop blood glucose (BG) control systems seamlessly integrating these aspects to emulate the functionality of the natural pancreas, commonly referred to as the artificial pancreas (AP) system. Devices that collect multiple physiological data, paired with AI systems, hold the promise of not just managing but truly optimizing glucose control for individuals with diabetes (**Table 1** and **2**).

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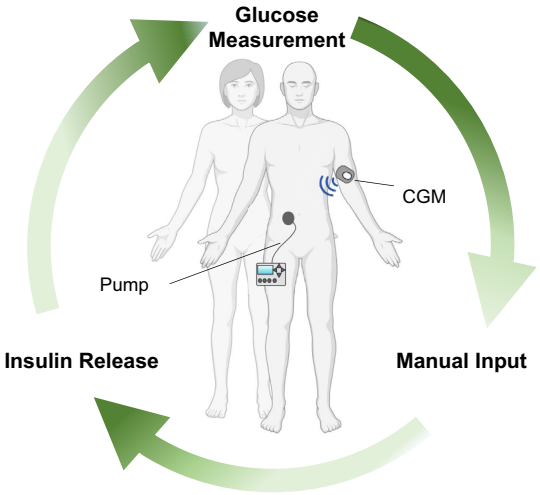


Figure 1. Conventional control system for diabetes management. Conventional system starts with "Glucose Measurement," incorporates "Manual Input," and concludes with "Insulin Release." This approach emphasizes manual interventions for insulin administration.

2. Wearable Devices for Closed-Loop Control

The landscape of care and treatment for individuals diagnosed with T1D is rapidly evolving with the emergence of genetically engineered insulin, advanced glucose monitoring devices, deep neural networks, and sophisticated closed-loop control systems. Wearable devices also play a pivotal role in the precise detection of changes in the body's physiological characteristics.[10,13] These devices are designed to be comfortably worn by patients without disrupting their daily routines, thereby facilitating easier monitoring of vital health parameters unobtrusively.

2.1. Continuous Glucose Monitoring

One remarkable innovation in the field of diabetes care is CGMs. CGMs offer real-time and uninterrupted surveillance of the body's glucose levels by measuring the glucose concentration in the interstitial fluid.[14,15] This technology enables the dynamic assessment of fluctuations in blood glucose levels. Unlike traditional methods that require routine fingerstick blood tests, CGMs operate autonomously, capturing data at regular intervals ranging from 1 to 5 min. The implications of CGMs in diabetes care are significant, as they empower individuals to maintain a healthy and balanced lifestyle by providing immediate insights into their blood glucose levels. This information proves instrumental in the meticulous regulation of dietary choices, physical activity, and timely medication administration.

Presently, advanced CGMs predominantly rely on electrochemical methodologies. Some notable CGM products available in the market include CGMS and its iterative versions by Medtronic (Minneapolis, MN, USA), Dexcom G6/7 by Dexcom, Inc. (San Diego, USA), and Medtronic Guardian Sensor 3 by Medtronic, Inc. (Northridge, USA),[16,17] as detailed in Table 1. To determine the accuracy of CGMs, mean absolute relative difference (MARD) serves as a widely utilized performance metric, which quantifies the discrepancy between glucose concentrations as measured by CGMs and those determined through blood sample analysis.[18] Typically, devices exhibiting a lower MARD value are considered to offer better performance. Moreover, CGMs demonstrate promise in subcutaneous tissue glucose monitoring, with some sensors being implanted beneath the skin. While numerous studies have underscored the potential of subcutaneous tissue glucose monitoring, it is important to acknowledge the inherent constraints associated with implantable sensors, such as sensor size, shape, duration of implantation, and biocompatibility.[19]

Meanwhile, researchers have embarked on a quest to identify and develop alternative CGMs technologies, with a focus on affordability, invasiveness, and user-friendliness. Various noninvasive methodologies for continuous glucose monitoring are being explored, including flexible and stretchable sensors,[20–23] fluid-sampling biochemical sensors,[8,24,25] optical methods (such as near-infrared spectroscopy),[26,27] and electromagnetic methods.[28] Notably, commercial systems like SugarBEAT from

Table 1. Overview of commercially available CGM devices and their features.

Device	Company	Real time/wireless	Connect to insulin pump	MARD[a)] [%]	Predictive alarms	Frequency
STS	Dexcom	✓/✓	✗	16	✗	5 min
G6	Dexcom	✓/✓	✓	9	✓	5 min
G7	Dexcom	✓/✓	✓	8	✓	5 min
Freestyle Navigator	Abbott	✓/✓	✗	No info	✓	5 min
FreeStyle Libre 2	Abbott	✓/✓	✓	9	✓	5 min
FreeStyle Libre 3	Abbott	✓/✓	✓	7.9	✓	1 min
CGMS Gold	Medtronic Minimed	✗/✗	✗	25	✗	5 min
Guardian REAL-Time	Medtronic Minimed	✓/✓	✗	20	✓	5 min
Paradigm REAL-Time	Medtronic Minimed	✓/✓	✓	20	✗	5 min
Medtronic Guardian Connect	Medtronic Minimed	✓/✓	✓	10	✓	5 min
SugarBeat	Nemaura Medical	✓/✓	✓	12.4	✓	5 min
Eversense	Senseonics	✓/✓	✗	8.5	✓	5 min

[a)]MARD, mean absolute relative difference.

Table 2. Comparative analysis of commercially available insulin delivery devices and features.

Device	Company	Type	Infusion accuracy	Basal increments	Glucose monitoring
Medtronic 700	Medtronic Minimed	Infusion pumps	0.025 U h^{-1}	0–35 U h^{-1}	✗
Medtronic 712	Medtronic Minimed	Infusion pumps	0.05 U h^{-1}	0–35 U h^{-1}	✗
Medtronic 712e	Medtronic Minimed	Infusion pumps	0.05 U h^{-1}	0–35 U h^{-1}	✗
Medtronic 722	Medtronic Minimed	Infusion pumps	0.05 U h^{-1}	0–35 U h^{-1}	✓
Dana 2 s	Dana	Syringe	0.01 U h^{-1}	0–16 U h^{-1}	✗
Dana R	Dana	Syringe	0.01 U h^{-1}	0–16 U	✗
IPELE	IPELE	Syringe	0.05 U h^{-1}	0.1–25 U	✗
NovaPen 5	IPELE	Pen	0.05 U h^{-1}	1–60 U	✗
InPen	Medtronic Minimed	Pen	0.05 U h^{-1}	0.5–30 U h^{-1}	✓
AdvantaJet	Activa	Jet injectors	No info	0.5–50 U h^{-1}	✓
Injex 30	Equidyne	Jet injectors	No info	5–30 U h^{-1}	✓
Vitajet 3	Bioject Corp	Jet injectors	No info	2–50 U h^{-1}	✓
Omnipod 5	Insulet	Skin grip	0.05 U h^{-1}	0.05–30 U h^{-1}	✓
Omnipod Dash	Insulet	Skin grip	0.05 U h^{-1}	0.05–30 U h^{-1}	✗

Nemaura Medical (Loughborough, UK), which employs iontophoresis for measuring interstitial fluid glucose; D-sensor from DiaMonTech (Berlin, Germany), which uses optical spectroscopy; and KnowU from Know Labs (Seattle, USA), which uses radiofrequency technology, are examples of these advancements. These new CGM systems have the potential to provide more accurate and objective insights into individuals' metabolic status with minimal invasiveness, liberating them from the reliance on subjective physiological cues and enhancing user comfort.

2.2. Continuous Subcutaneous Insulin Infusion

Complementary to these advancements in glucose monitoring, a spectrum of insulin delivery devices has been developed to precisely administer bioactive insulin, helping maintain blood glucose levels within target ranges of 70–180 mg dL^{-1}.[29,30] The conventional approach involves using insulin syringes, which require manual insulin filling and injection. This is an economically advantageous but potentially less precise method. In contrast, insulin pens offer a more sophisticated approach, injecting insulin via disposable pen needles and allowing dose adjustments through a dial or dose knob, ensuring a higher degree of accuracy and user-friendliness. For instance, the HumaPen Memoir, introduced by Ignaut et al.[31] is an electronic reusable insulin pen that provides multidose memory capabilities for storing data about the previous 16 insulin doses. The InPen system, developed by Bailey et al.[32] exemplifies this trajectory, allowing for Bluetooth-controlled insulin injection. Alternatively, recent research has focused on microneedle patch-based insulin delivery devices, which utilize a glucose-responsive media to control insulin release.[33–35] These devices have demonstrated significant potential in closed-loop glucose control systems. For a comprehensive list of these products, please refer to Table 4.

Improvements have been implemented to enhance the efficiency and patient comfort associated with insulin delivery systems. In the Diabetes Control and Complication Trial (DCCT), nearly 40% of participants in the intensive treatment group benefited from continuous subcutaneous insulin infusion (CSII) therapy.[36] The latest commercial insulin pumps have evolved to prioritize patient-friendliness through a combination of reduced size and advanced features, including integrated dose calculators and alarm systems. Scientific studies have confirmed that CSII is more effective compared to multiple injection therapy in achieving glucose targets, resulting in an approximate reduction of 0.5% in HbA1c, which in turn reduces insulin dosage by ≈14%.[37,38] Wearable continuous infusion pumps also decrease instances of hypoglycemia, leading to an overall improvement in patient satisfaction and quality of life.

3. Closed-Loop Control Framework

The evolution of wearable technologies has greatly facilitated the downsizing, user-friendliness, precision, and automation of both CGM systems and insulin delivery devices (shown in Figure 1). By utilizing the data from CGM, healthcare providers can make informed adjustments to basal and premeal insulin doses, leading to more rational and effective diabetes therapy. Nonetheless, effective glucose regulation, especially during the night, and timely management of hypoglycemia pose unique challenges.[12] To address these challenges, closed-loop AP systems have emerged. These systems employ CGM-informed algorithms to automate insulin administration without continuous user intervention. This seamless and uninterrupted glucose regulation not only alleviates the burden on patients but also enhances their overall quality of life.[39,40]

However, it's crucial to acknowledge that while continuous AIDs can help manage diabetes, they may still cause occasional hypoglycemia and hyperglycemia, which can be life-threatening. Developing accurate and reliable prediction models and insulin dosing algorithms is a significant challenge in closed-loop systems. These algorithms must be adaptable to individual

variations in glucose response and insulin sensitivity, while also ensuring precise control over dosing timing and dosage.[41]

3.1. Glucose Prediction

Glucose prediction models utilize data generated from CGMs to forecast future glucose levels, enabling timely interventions against hyperglycemia or hypoglycemia. These accurate and reliable predictions are crucial for personalized diabetes management, reducing the risks of complications, and enhancing the quality of life.[42,43] However, glucose predictions can be inherently challenging due to interference from various external environmental factors and individual characteristics. Additionally, lifestyle variations introduce further complexity into glucose prediction models. Dietary habits and the timing and intensity of physical activity can cause significant fluctuations in glucose levels. For example, high carbohydrate intake can lead to rapid increases in glucose levels, while physical exercise can cause both immediate and delayed changes in glucose dynamics. These variations necessitate the development of adaptive models capable of accommodating diverse behavioral patterns and environmental influences.

The prediction models not only forecast glucose variations for future time frames but also function as early warning systems for potential hyperglycemic and hypoglycemic risks (as illustrated in **Figure 2**). Addressing the influence of human factors is therefore critical for enhancing the robustness and reliability of closed-loop systems in real-world applications.

3.1.1. Evaluation Metrics

To assess the accuracy of prediction models, various performance evaluation methods are commonly used, including root mean square error (RMSE), mean absolute percentage error (MAPE), and mean square prediction error (MSPE). In the context of blood glucose prediction, y_i represents the model's predicted output and Y_i the actual blood glucose measurement.

$$\mathrm{RMSE} = \sqrt{\frac{1}{N}\sum_{k=1}^{N}(Y_i - y_i)^2} \tag{1}$$

$$\mathrm{MAPE} = \frac{1}{N}\sum_{k=1}^{N}\left\|\frac{Y_i - y_i}{Y_i}\right\| \times 100\% \tag{2}$$

$$\mathrm{MSPE} = \frac{1}{N}\sum_{k=1}^{N}\left(\frac{Y_i - y_i}{Y_i}\right)^2 \times 100\% \tag{3}$$

Clarke error grid analysis (EGA) is a method specifically for evaluating the accuracy of BG monitoring systems.[44] As shown in **Figure 3**, it compares the predicted values from CGMs with reference glucose values to categorize and assess the clinical accuracy of the predictions. Various studies have employed these criteria to compare glucose prediction models. However, each criterion possesses unique advantages and drawbacks, with the selection often depending on the specific objectives of the prediction task.

3.1.2. Machine Learning for Multihorizon Glucose Prediction

Traditional glucose prediction methods utilized mathematical models and statistical assumptions based on glucose metabolism and carbohydrate intake dynamics.[45] However, these models often showed notable prediction biases. A more advanced approach was developed by Sparacino et al.[46] who utilized recursive time series model identification with real patient CGM data, shifting from empirical statistical parametric models to data regression models using first-order polynomials and autoregressive (AR) models, thereby enhancing 30 and 45 min prediction accuracy. Estrada et al.[47] introduced normalized least mean square algorithms (NLMS), integrating anthropological (e.g., HbA1c, disease duration, insulin dosage) into an Autoregressive eXogenous (ARX) model for online identification with T1D patient data. They found that predictive performance improves with physiologically inspired variable gain over constant gain. Kamuran et al.[48] developed an ARMAX prediction algorithm that uses autoregressive (AR) and mean shift (MA) methods for external conditions (X) to better predict blood glucose variations, effectively addressing nonlinearities in glucose prediction and warning the risk of hypoglycemia in the next 30 min ($\mathrm{RMSE} = 18.55\ \mathrm{mg\ dL^{-1}}$) and 60 min ($\mathrm{RMSE} = 38.06\ \mathrm{mg\ dL^{-1}}$) in the experiment.

Machine learning offers a promising method for improving the accuracy and reliability of diabetes management prediction. By analyzing large datasets of glucose measurements, machine learning algorithms can identify complex patterns and relationships that are difficult to detect with traditional statistical models. Georga et al.[49] proposed and extended the support vector regression (SVR) model to predict nocturnal and non-nocturnal (i.e., diurnal) events during sleep by considering recent glucose status, meals, insulin intake, and physical activity. This study reports a high predictive accuracy of 94% for nocturnal hypoglycemic events, as assessed with a sensitivity analysis. Both horizons were found to exhibit comparable performance, with corresponding time lags of 5.43 and 4.57 min, respectively. In the context of diurnal events, their results indicated a sensitivity of 92% and 96% for 30 and 60 min horizons, respectively, when physical activities were not taken into account. The SVR algorithm (SVM model variant) has been one of the most popular methods in the previous years for blood glucose prediction studies. Given the complexity and diversity of external and internal factors affecting blood glucose levels, analyzing their relationship to blood glucose variation is a significant challenge. In another study, Georga et al.[50] used random forest (RF) and RReliefF algorithms to rank the candidate feature sets. A forward selection procedure was then used to build a glucose prediction model and add features to the model in decreasing order of importance.

3.1.3. Deep Neural Networks for Accurate Glucose Modeling

The use of deep neural networks can effectively deal with complex prediction tasks by leveraging their ability to map inputs into high-dimensional latent spaces and identify temporal correlations. In glucose forecasting, Artificial Neural Networks (ANNs) utilize historical glucose data for future predictions. The multilayer perceptron (MLP), a foundational structure in ANNs,

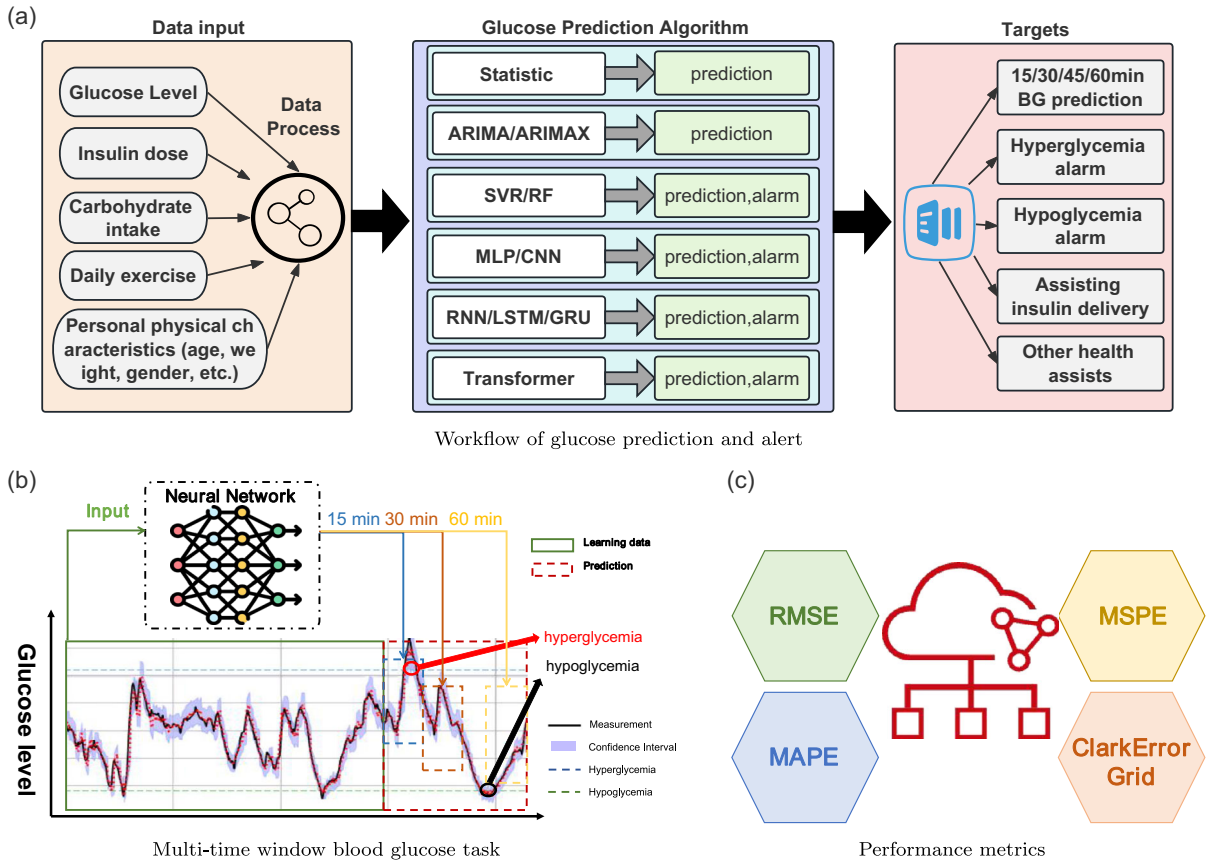


Figure 2. A framework for the glucose prediction and warning task flow. a) The left side shows the input data as well as data preprocessing, the middle part shows multiple machine learning or deep learning algorithms and evaluations, and the right side shows the algorithm objectives. b) Real-time acquisition of the latest CGM data, combined with historically stored blood glucose variation information, is used to predict future trends through neural networks. c) Four common evaluation metrics are used to assess the performance and safety of neural network models.

computes neuron combinations, enabling the learning of nonlinear glucose input–output relationships and adaptation to individual variability. Research demonstrates promising glucose prediction performance with high accuracy, achieving around 15.0 mg dL^{-1} RMSE for 30 min forecasts across various time horizons, such as 15 to 60 min.

Unlike conventional ANNs, which process inputs in isolation, recurrent neural networks (RNNs) capture the temporal dependencies inherent in continuous data by maintaining an internal state that retains information from previous inputs. This makes them particularly useful for glucose prediction, as they can use a series of glucose measurements to forecast future glucose concentrations. RNNs are also adept at managing irregularly spaced data, missing values, and adjusting to the evolving dynamics of glucose responses. Predominantly, glucose prediction employs RNN architectures like long short-term memory (LSTM) networks or gated recurrent units (GRU).[51–54] These structures have the capability to retain or omit information from preceding time intervals. For instance, Idriss et al.[52] employed multilayer LSTM networks to enhance blood glucose prediction capabilities. Their study compared the AR algorithm family, traditional ANN algorithms, and machine learning techniques such as SVR. Experimental results indicated that the LSTM algorithm outperformed others in predicting blood glucose fluctuations. Their model's average RMSE was 12.38 mg dL^{-1}, in contrast to 28.84 mg dL^{-1} for AR and 50.69 mg dL^{-1} for other existing LSTMs. To further improve the prediction accuracy, Sun et al.[51] integrated LSTM and Bi-LSTM, which deepened the network and enhanced its bidirectional sequence learning capacity.

Recently, attention-based methods,[55,56] particularly the Transformer[57] algorithm introduced in 2017, have been investigated for glucose prediction in diabetes management.[58] The Transformer, utilizing a multihead self-attention mechanism, excels in identifying contextual relationships within data, significantly differing from RNNs by processing inputs concurrently for enhanced computational efficiency and handling varying sequence lengths. This feature addresses the limitation of fixed prediction time windows. With a MAPE of 12.78, 13.4, and 13.5 for 12-, 24-, and 36-step predictions respectively, the Transformer's performance in blood glucose prediction showcases its potential in closed-loop diabetes management.

Recently, attention-based methods[55,56,59] have been used for glucose prediction. Zhu et al.[60] integrated RNN with attention structure to capture the local and global information in BG sequences, achieving an RMSE of 35.28 ± 5.77 mg dL^{-1} for 60 min PH on a private dataset. The Transformer model adheres

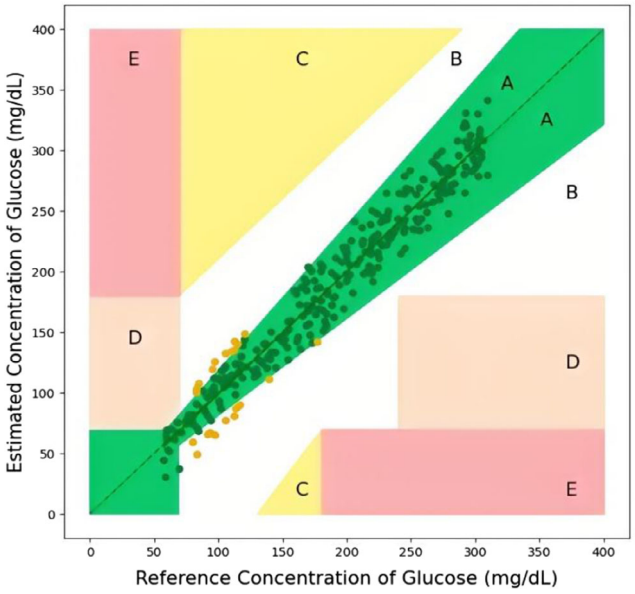


Figure 3. Clarke error grid schematic diagram. A: Clinically accurate; appropriate actions. B: Minor deviations; benign or no treatment needed. C: Overcorrection of normal glucose; potential unnecessary interventions. D: Missed hypoglycemia or false hyperglycemia; potential incorrect treatments. E: Opposite to true condition; severe misinterpretations and interventions.

to the established encoder–decoder framework, yet distinguishes itself by incorporating multihead self-attention mechanisms instead of the traditional RNNs. This architecture excels in parallel processing and is adept at capturing global relationships within sequences across diverse semantic spaces. In the realm of glucose prediction, Lee et al.[58] implemented the Transformer model to perform both prediction and classification tasks using autoregression. This model was evaluated on a proprietary dataset, achieving a MAPE of 17.88 on the OhioT1DM dataset. Additionally, Sergazinov et al.[61] utilized the Transformer model for glucose prediction, innovatively modifying the model's dropout layer to quantitatively assess uncertainty. This modification significantly improved the Transformer's efficacy in blood glucose prediction tasks.

Table 3 presents a summary of various studies and their outcomes. Developing predictive neural networks tailored for specific patient groups remains challenging, especially when the clinical datasets are limited. Neural networks trained on data from certain regions may not perform consistently on globally diverse patient groups. Integrating neural architectures efficiently into devices like CGMs is also a major challenge.

3.2. Clinical and Simulated Diabetes Datasets

Incorporating machine learning and AI into diabetes management necessitates comprehensive datasets for model training, validation, and testing. This section introduces 4 public datasets, which are derived from patients in various regions and collected through different CGM and wearable devices. These datasets can be utilized to train blood glucose prediction models, study closed-loop control algorithms, and research insulin injection feedback. While some of these datasets are open source, others must be procured directly from the respective authors or institutions (**Table 4**).

3.2.1. OhioT1DM

The OhioT1DM dataset[62] comprises 8 weeks of continuous glucose monitoring, insulin dosing, physiological sensor data, and self-reported life events from 12 individuals with T1D. An integrated graphical software tool enables researchers to effectively visualize this extensive dataset. Initially introduced in 2018 for the inaugural blood glucose level prediction challenge, the dataset then encompassed data from merely six participants. In 2020, data from an additional six individuals was incorporated.

3.2.2. UVA/Padova

The UVA/Padova Type 1 Diabetes Mellitus Simulator (T1DMS)[63] serves as a sophisticated simulation tool, enabling researchers to conceptualize and assess simulated therapeutic interventions for T1D patients. It adeptly replicates real-life scenarios, encompassing variations in meal intake, timing, insulin dosages, and administration schedules, while proficiently detecting and quantifying episodes of hyperglycemia and hypoglycemia. By offering precise control over experimental parameters and minimizing the calibration phase, the UVA/Padova T1DMS enhances the efficacy of diabetes research and expedites product development strategies. It plays a pivotal role in the exploration and emulation of closed-loop control algorithms. The research team has refined the simulator, transitioning from the S2008 version to the more advanced S2013[64] iteration, which incorporates an expanded set of parameters and facilitates the simulation of hyperglycemic injections.

3.2.3. D1NAMO

The D1NAMO[65] dataset comprises data from 20 healthy individuals and 9 individuals with diabetes. Uniform wearable devices were employed for both groups, albeit with distinct sampling protocols for blood glucose level monitoring. D1NAMO stands out as the most comprehensive dataset, capturing not only CGM and insulin data but also 34 physiological metrics, including ECG signals, respiratory patterns, and epidermal temperature. However, the continuous monitoring duration for CGM data is limited, leading to challenges associated with a smaller data size during model training.

3.2.4. Shanghai T1DM/T2DM

The Shanghai T1DM/T2DM[66] datasets were sourced from 12 individuals with T1D and 100 with T2D in Shanghai, China. These datasets were compiled under real-world conditions and encompass clinical profiles, laboratory results, medication records, continuous glucose monitoring readings spanning 3 to 14 days, and daily dietary data.

Figure 4 displays the predictive performance of the Transformer model across 4 datasets. Despite the availability

Table 3. Existing machine learning and deep learning glucose control algorithms and performance comparison.

Methods	Authors	Years	Best performance	Data
Mathematical model (prediction)	Cobelli et al.[45]	1982	No quantitative results	No specific data information
AR (prediction)	Sparacino et al.[46]	2007	MSPE = 318 (30 min) MSPE = 1035 (45 min)	28 T1D individuals for 48 h
AR (classification)	Estrada et al.[47]	2010	Hypoglycemia: 97.35% (F1 score 5 min) Euglycemia: 99.8% Hyperglycemia: 98.55%	15 individuals with T1D
MLP (prediction)	Perez et al.[113]	2010	RMSE = 9.74 mg dL^{-1} (15 min) RMSE = 14.75 mg dL^{-1} (30 min) RMSE = 25.08 mg dL^{-1} (45 min)	9 subjects using Medtronic Guardian 6 subjects using Abbot Navigator
MLP (prediction)	Zecchin et al.[114]	2012	RMSE = 14.0 mg dL^{-1} (30 min)	9 individuals from Abbot Navigator 20 simulated virtual individuals generated in UVA-Padova[64]
ARMAX (prediction)	Turksoy et al.[48]	2013	RMSE = 17.47 mg dL^{-1} (30 min)	No specific data information
MLP (prediction)	Bertachi et al.[59]	2018	RMSE = 19.33 mg dL^{-1} (30 min) RMSE = 31.72 mg dL^{-1} (60 min)	6 individuals with T1D in OhioT1DM[62]
SVR (classification)	Georaga et al.[49]	2013	Nocturnal: 91% (F1 score) Diurnal: 86%	15 individuals with T1D
SVR (prediction)	Georaga et al.[50]	2015	RMSE = 21.4 mg dL^{-1} (30 min) RMSE = 24.6 mg dL^{-1} (60 min)	15 individuals with T1D
SVR (prediction)	Xie et al.[115]	2018	RMSE = 19.53 mg dL^{-1} (30 min)	6 individuals with T1D in OhioT1DM[62]
WaveNet (prediction)	Zhu et al.[116]	2018	RMSE = 21.73 mg dL^{-1} (30 min)	6 individuals with T1D in OhioT1DM[62]
LSTM (prediction)	Martinsson et al.[117]	2020	RMSE = 18.87 mg dL^{-1} (30 min) RMSE = 31.40 mg dL^{-1} (60 min)	6 individuals with T1D in OhioT1DM[62]
LSTM (prediction)	Arora et al.[118]	2021	RMSE = 4.03 mg dL^{-1} (5 min)	6 individuals with T1D in OhioT1DM[62]
LSTM (prediction)	Sun et al.[51]	2018	RMSE = 11.63 mg dL^{-1} (15 min) RMSE = 21.75 mg dL^{-1} (30 min) RMSE = 30.22 mg dL^{-1} (45 min) RMSE = 36.92 mg dL^{-1} (60 min)	15 individuals with T1D
Attention (prediction+classification)	Zhu et al.[60]	2022	RMSE = 37.18 mg dL^{-1} (60 min) Hypoglycemia: 87.20% (F1 score-60 min) Hyperglycemia: 88.58%	Dataset used in this study is not publicly available
Transformer (prediction+classification)	Lee et al.[58]	2023	RMSE = 17.88 mg dL^{-1} (60 min) Classification average: 72.00% (F1 score-60 min)	6 individuals with T1D in OhioT1DM[62]
Transformer (prediction)	Sergazinov et al.[61]	2023	MAPE = 10.0 (30 min) MAPE = 22.18 (45 min)	No specific data information

Table 4. A summary of the features of 4 CGM datasets.

Datasets	Data source	Type	Sampling period	Sampling frequency	Patients number	Patients age	Food	Others
OhioT1DM	Real human	T1DM	56 days	5 min	56	20–60	2713	Insulin
UVA/Padova	In silico subjects	T1DM	Customized	5 min	30	Children/adolescent/adult	2713	Insulin
D1NAMO	Real human	T1DM	4 days	5 min	9	20–79	2713	Insulin/ECG/breathing/accelerometer...
Shanghai T1DM/T2DM	Real human	T1DM	3–14 days	15 min	112	20–60	2713	Insulin

of extensive datasets supporting the training and development of intelligent blood glucose algorithms, the quality of these datasets varies significantly. Some have short blood glucose monitoring durations and low sampling frequencies, which profoundly impact model training. We hope to collect more robust continuous glucose monitoring data in the future, sourced from patients of various ages, genders, countries, and ethnicities. Additionally, we aim to integrate a broader range of wearable devices to gather more physiological data, enhancing the accuracy of blood glucose prediction and closed-loop control.

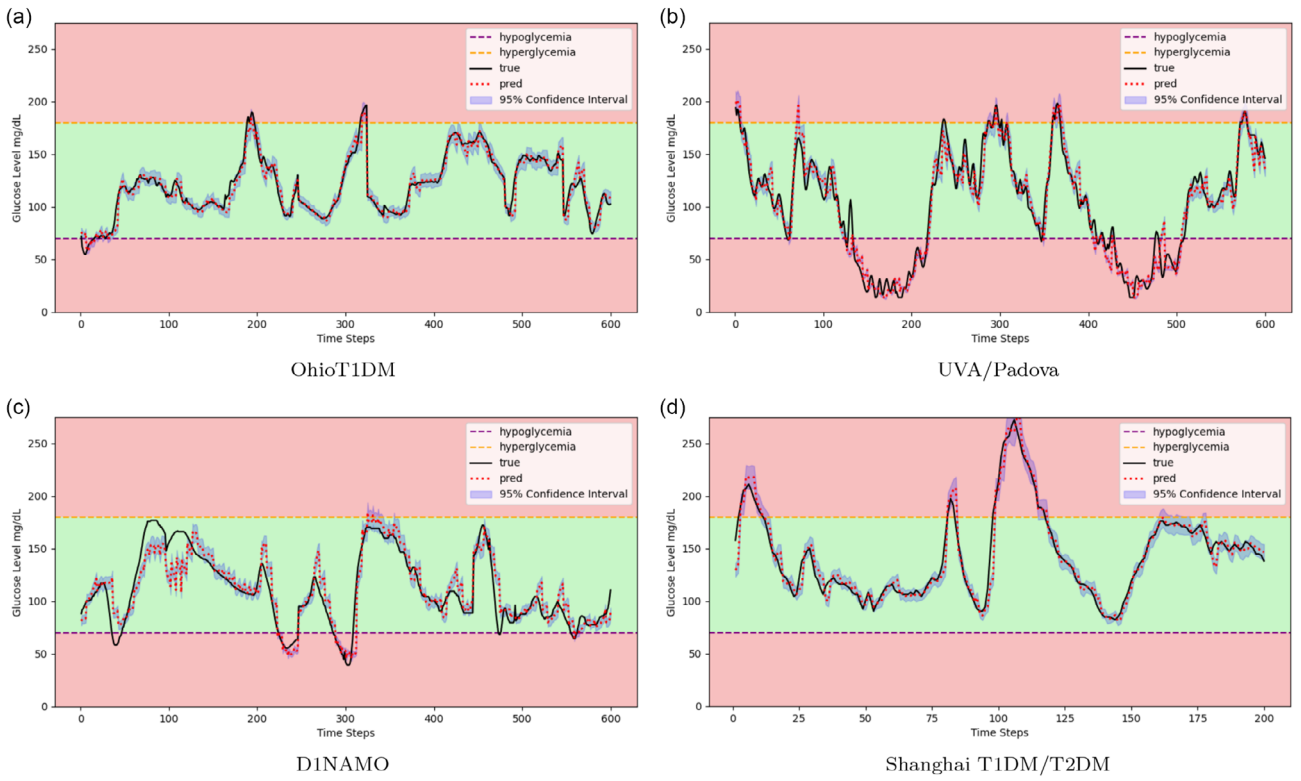


Figure 4. Transformer's prediction results on different datasets. The range of 70–180 mg dL^{-1} represents the normal blood glucose level, depicted in green, while abnormal blood glucose levels are shown in red. The "pred" denotes 30 min prediction window, represented by a red dashed line. a) The prediction results for the OhioT1DM dataset with a time step of 5 min. b) The prediction results for the UVA/Padova synthetic dataset, which exhibits significant fluctuations. This is due to the introduction of CGM noise during data generation. The time step is 5 min. c) The prediction results for the D1NAMO dataset. Due to the smaller size of the CGM data in D1NAMO, the prediction accuracy drops a lot. The time step is 5 min. d) The prediction results for the Shanghai T1DM/T2DM dataset with a time step of 15 min.

3.3. Automated Insulin Delivery Algorithms

As mentioned before, intensive insulin injection therapy stands as the primary treatment approach for T1D. Its goal is to compensate for the lack of endogenous insulin by administering exogenous insulin, thereby regulating glucose levels and preventing complications. However, insulin therapy places a substantial burden on patients due to the need for frequent glucose monitoring and dose adjustments. To alleviate this challenge, AID systems, often referred to as AP, have been developed. These systems automatically monitor glucose levels using wearable devices and calculate personalized insulin doses through specialized algorithms. Various AID systems have emerged, employing different mathematical logic and physiological analyses, as depicted in **Figure 5**.

3.3.1. Standard Formula of Insulin Dose

Early methods of insulin dose calculation were individualized through a simple ratio formula, which is as follows.

$$B = \frac{\text{CHO}}{\text{CR}} + \frac{G_c - G_t}{\text{CF}} - \text{IOB} \tag{4}$$

The calculation of insulin dosages for patients with diabetes involves the use of a formula that takes into account several patient-specific parameters. $\frac{\text{CHO}}{\text{CR}}$ indicates the insulin bolus required to cover dietary carbohydrates, which is calculated by dividing the patient's estimated carbohydrate intake (CHO) by the carbohydrate-insulin specific ratio (CR), which represents the number of grams of carbohydrate covered per unit of insulin. The second term of the formula adjusts the insulin dose based on the patient's current blood glucose concentration relative to the target value. This is calculated as the difference between the patient's blood glucose concentration at the time of insulin injection (G_c) and the target blood glucose concentration (G_t), divided by a correction factor (CF), which is a patient-specific parameter for the amount by which blood glucose is lowered per unit of insulin. The last term of the equation adjusts the insulin dosage based on the amount of previously injected insulin still active in the body, known as the insulin on board (IOB), which is used to avoid overdose.

This standard formula is widely used in clinical practice for calculating insulin dosages in patients with diabetes.[67–69] However, it is important to note that these parameters are patient-specific and may require adjustments based on individual responses and changes in medical status. Further research is

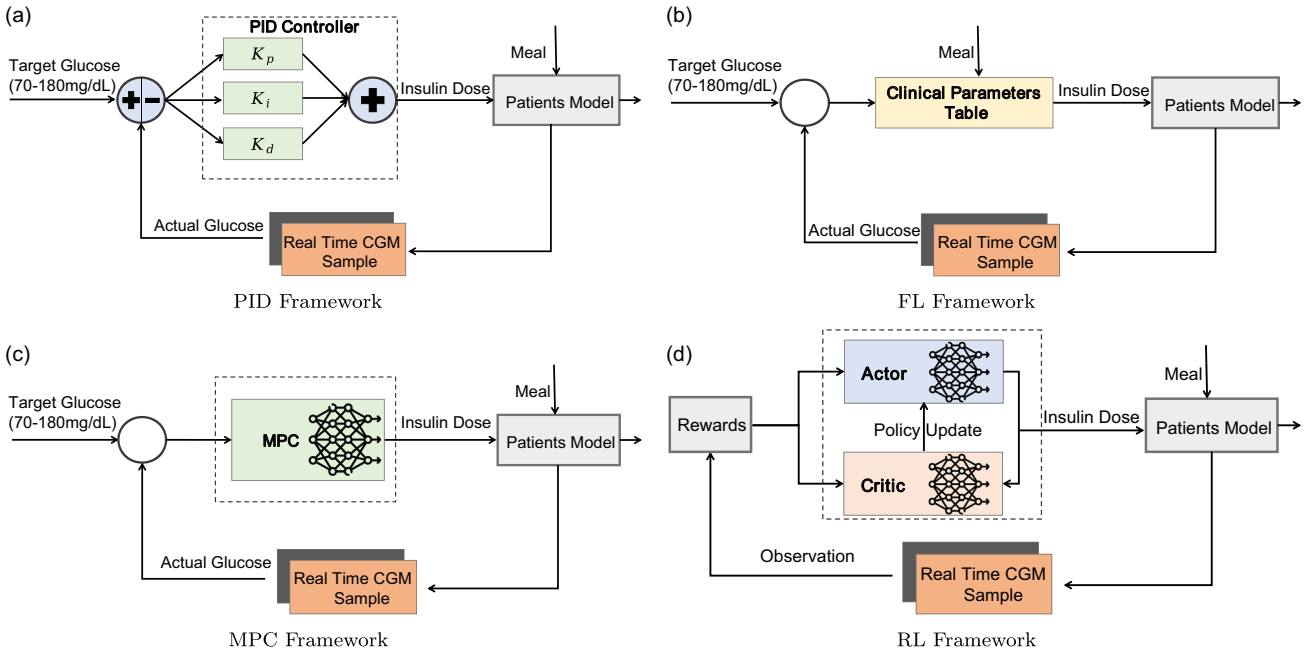


Figure 5. Closed-loop control algorithm flow comparison. a–d) The workflow of the PID, FL, MPC, and RL frameworks, respectively, where the input is the glucose data sensed by the CGMs and the output is the recommended insulin dose.

needed to optimize the use of this formula in clinical practice and improve patient outcomes.

3.3.2. Proportional Integrative Differential Algorithm System

The Proportional-Integral-Derivative (PID) algorithm is a prevalent method for automated insulin delivery in diabetes patients.[70,71] The algorithm determines the insulin infusion rate by considering the discrepancy between the patient's target and current glucose levels, and glucose level rate of change. Specifically, the proportional component adjusts the rate in relation to the glucose deviation from the target. The integral component considers the accumulated difference over time, while the derivative component focuses on the glucose's rate of change. The combination of these components enables the PID algorithm to swiftly and precisely modulate the insulin rate, ensuring consistent glucose control. The computing process is shown in Figure 5a and can be mathematically described as follows.

$$B = K_p(G - G_t) + K_i \int (G - G_t)dt + K_d \frac{dG}{dt} \quad (5)$$

where K_p, K_i, and K_d are the gains of the linear proportional, integral, and differential terms, respectively, and G and G_t represent blood glucose and basal glucose.

Prior research undertook a closed-loop in vivo study using canines as experimental subjects. The investigation employed a CGM named the MiniMed CGMS, paired with an external insulin delivery pump, the Medtronic MiniMed 511 Paradigm.[72] During the initial tests, the closed-loop system was activated under hyperglycemic conditions, intentionally starting with elevated blood glucose levels. This approach aimed to confirm the effectiveness of the PID algorithm's integral component in setting a foundational insulin infusion rate to achieve better glucose level, targeting a set point of 120 mg dL^{-1}. Later stages adjusted the PID algorithm to match the plasma insulin profile typical of someone with standard glucose tolerance.

Even though PID algorithm continually refines its parameters, it is not a form of AI. The calculations are based on real-time glucose data without forecasting future glucose trends. For example, the drug effectiveness is assumed to follow the time-action curve of the medication, ignoring physiological complexities, like glucose regulation after exercise or during illness. Despite its simplicity, the strength of the PID algorithm lies in its ability to mimic the function of endocrine cells using basic parameter calculations.

3.3.3. Fuzzy Logic Computing System

Fuzzy Logic (FL) is a mathematical system that uses linguistic variables and membership functions to capture the uncertainty and imprecision in a system (Figure 5b). Previous works have applied FL to closed-loop glucose control tasks to calculate and deliver the right amount of insulin.[73–75] Unlike PID, FL controllers rely only on glucose management parameters, which are predetermined by diabetes clinical experts and programmed for use in the controller. To maintain alignment with the established practices within diabetes clinical domains, FL quantitative components are commonly forged through collaborative endeavors involving diabetes clinical experts. Glucose attributes are usually confined to five distinct intervals: L (low, <80 mg dL^{-1}), N (normal, 80–120 mg dL^{-1}), H (high, 120–180 mg dL^{-1}), VH (very high, 180–250 mg dL^{-1}), and VVH (very, very high, >mg dL^{-1}). The overarching objective of the rule matrix

construction revolves around the stabilization of glucose concentrations within the desired range of 80–120 mg dL^{-1}.

Operated under the same PID framework, the FL controller operates in a fully automated mode. The present glucose level is ascertained by BG sensors and promptly conveyed to the computational unit. Subsequently, insulin dosages are meticulously computed, thereby triggering the automatic commencement of insulin administration via the pump. In instances where CGM data transmission encounters an interruption, the controller adeptly suspends insulin delivery until the attainment of a steady and valid data stream is established. To ensure the controller's resilience, the input space of the three parameters is judiciously delineated, encompassing a comprehensive spectrum of conceivable dosage scenarios frequently encountered by individuals with diabetes. Concurrently, the rule set necessitates delineation to encapsulate the intricate glucose dynamics inherent in distinctive daily circumstances, such as meal consumption. This adaptability prompts corresponding dose adjustments. For instance, when glucose resides in the normal (N) range, the rate is zero (Z), and acceleration is positive (P), the designated insulin dose amounts to 0.10 units.

FL algorithms can incorporate qualitative and quantitative information into insulin dosing decisions and have shown promising results in clinical studies. However, the FL algorithm is a rule-based insulin delivery structure, which is difficult to adapt to different individuals in complex physical environments and physiological states, and its dosage calculation accuracy and personalization ability can be seriously affected.

3.3.4. Model Predictive Control

Model predictive control (MPC) is an algorithm used to optimize the performance of a system by predicting its future behavior and taking proactive action to achieve a desired outcome. The MPC operates as a dynamic model, generating forthcoming insulin dosages contingent on a computation involving the prevailing glucose concentration.[70,76] This projection hinges upon the current glucose reading and the insulin content extant within the physiological system (on-board insulin). If the calculated glucose value is within the desired range, a trace amount of insulin is delivered. Contrarily, if the calculated glucose concentration deviates from the desired threshold, the dosage is escalated for elevated glucose projections and attenuated for lower projections.

The process of MPC involves constantly adjusting the insulin infusion rate sequence, estimating glucose levels, and evaluating the objective function. The optimization algorithm autonomously explores the optimal sequence of insulin infusion rates that leads to the minimization of the objective function. The initial insulin infusion rate from this optimized sequence (at time t) is then transmitted to the insulin pump, and the comprehensive optimization procedure is reiterated when the subsequent CGM reading is conveyed to the AID system (at time $t+1$).

3.3.5. Reinforcement Learning Control

However, conventional control systems such as PIDs, FL systems, and MPC are based on simplistic chance or linear computation for AID control, which may inadequately address the complexities associated with the human body response.[77,78] Reinforcement learning (RL) excels in scenarios involving sequential decision making, where actions depend on observed states and have delayed consequences. RL eliminates the need for annotated training data, as the RL agent autonomously learns the optimal policy using deep neural networks. Its adaptive nature is well suited for personalized analyses, effectively adapting to the dynamic evolution of user preferences and behaviors.[79] In glucose control, RL algorithms have demonstrated the ability to learn complex and personalized control strategies for individual patients and often outperform PID and MPC algorithms.[80,81]

The AID task in the RL framework can be modeled as a Markov Decision Process (MDP), which is described as a 5-tuple $(\mathcal{S}, \mathcal{A}, r, P, \gamma)$. S denotes the set of states (e.g., glucose at each time point), A denotes the set of actions (e.g., output insulin dose), P denotes the state transfer probability $P(s_{t+1} = s' \| s_t = s, a_t = a)$, $r: \mathcal{S} \times \mathcal{A} \times \mathcal{S} \to \mathbb{R}$ is the reward function, and $\gamma \in [0, 1]$ is the discount factor. The observation of the state is mainly derived from real-time glucose data g_t, historical glucose data $[g_{t-1}, g_{t-2} \ldots g_{t-w}]$, basal insulin dose i_t, bolus doses b_t, and ingested carbohydrates c_t.[82] The composition of observable states in an AID system is generally

$$s_t = [g_t, g_{t-1}, g_{t-2} \ldots g_{t-w}, I_t, C_t] \tag{6}$$

This state represents data for the current time point and the historical window period, utilizing observations from the past $w+1$ time points, where g_t is the glucose value at the current time step and g_{t-w} is the glucose value prior to the w time stamp. Also included are estimates of basal and bolus insulin (insulin on board) combined insulin activity I_t, and estimates of carbohydrate activity C_t.[83]

Several RL methodologies are being explored, including temporal difference learning, a mechanism based on iterative bootstrapping, and updates that rely on the present valuation of the value function. Additionally, the exploration encompasses actor–critic (AC) learning, a composite construct comprising two distinct components: an actor responsible for orchestrating action selection strategies, and a critic tasked with appraising the value function and evaluating the actor's chosen actions. Consequently, these algorithms are distinguished by the incorporation of a dedicated memory framework designed to explicitly encapsulate the strategy, decoupled from the underlying value function.[84] The training goal of an RL agent is to find the best policy $\pi: \mathcal{S} \times \mathcal{A} \to [0, 1]$ that maximizes the cumulative discounted return $\sum_{t=0}^{\infty} \gamma^t r_t$. The reward function is generally set according to the following principles: the reward is maximized when the blood glucose is approximately in the center of the target range (70–180 mg dL^{-1}), too high or too low the reward is negative, and in general special attention should be paid to the reward value during hypoglycemic states, which are more fatal.[80] Other reward functions for glucose control are also mentioned in the studies of Tejedor et al.[85] and Basu et al.[86]

4. Challenges and Future Perspectives

While substantial efforts have been directed toward the advancement of closed-loop diabetes control systems, challenges such as

misalignment between pancreas dynamics, algorithm reliability, and network deployment on edge devices need to be addressed to ensure the effective and widespread implementation of such systems.

4.1. Misalignment between Artificial and Natural Pancreas

Traditional closed-loop control systems employ real-time feedback and insulin delivery through CGM devices. While commonly termed as APs, these systems rely on rudimentary sensory input mechanism, which inadequately account for the complexities of the human body's BG control system. Their operation is solely dependent on glucose monitoring and insulin delivery, contrasting with the sophisticated pathophysiology of a natural pancreas, which involves the interplay of multiple hormones.

In order to address the disparity between the AP and the complexities of the human body, a promising approach is the implementation of a multisensing system. This approach monitors multiple real-time physiological indicators, such as galvanic skin response, heart rate, and blood pressure, obtained from wearable devices, to ensure rapid insulin adjustments. By integrating data from CGM and wearable-derived predictions, the multisensing approach offers a significant advancement for future closed-loop control systems. The implementation of supplementary physiological indicators serves to enhance the accuracy of BG predictions during daily activities,[87,88] thereby facilitating more accurate and personalized dosage administration and glucose control. Additionally, a dual-hormone closed-loop system integrates insulin and glucagon administration, effectively addressing both hyperglycemia and hypoglycemia.[89,90] This system outperforms single insulin delivery in preventing hypoglycemic episodes (**Figure 6**a) and closely mimics the multifaceted functions of a natural pancreas. Within the insulin-glucagon realm, two primary approaches have emerged: modest glucagon dosing to prevent hypoglycemia without increasing insulin administration, and intermittent glucagon infusion to intensify insulin delivery and achieve a more pronounced reduction in BG levels.[90] Studies have confirmed their effectiveness in reducing hypoglycemia, improving BG control, and maintaining longer periods of BG normalization compared to standard insulin pump therapy.[91,92]

Novel devices, such as organic electrochemical transistors (OECT)[93] and microneedles,[9,94] can provide higher accuracy in glucose monitoring, further facilitating the improvement of these algorithms. Addressing challenges related to low hormone concentrations and device longevity, while ensuring clinical accuracy and speed, remains crucial for the future development of sensors and systems. Advances in CGM technology have progressively bridged the perceptual gap between artificial and natural pancreases, significantly impacting the personalization of AI technologies. Modern CGM systems offer more accurate real-time glucose readings, with higher sensitivity and faster response times, inspiring researchers to develop neural network models capable of processing high-temporal-density glucose data. This enables better prediction of future glucose fluctuations and precise insulin injection. Additionally, the integration of multiple sensor systems can provide more comprehensive physiological information for intelligent closed-loop systems. This necessitates the development of new multimodal neural network technologies that can collectively learn from diverse sensor data, thereby enhancing the closed-loop system's ability to more effectively prevent hypoglycemic and hyperglycemic episodes.

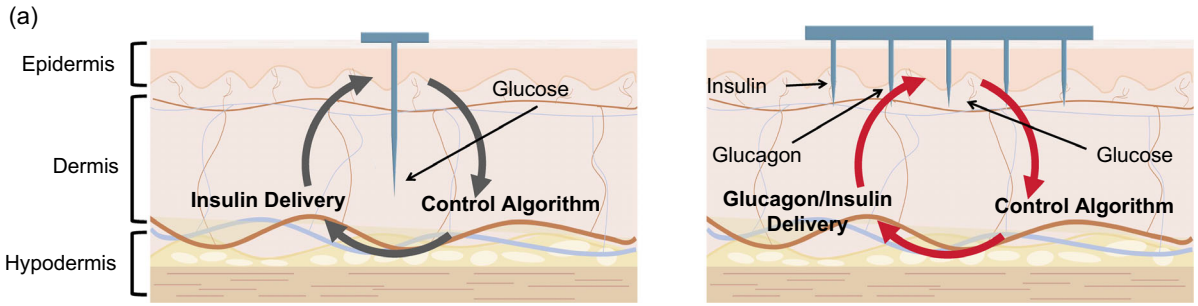
4.2. New Generation of Painless Noninvasive Glucose Monitoring

The evolution of noninvasive techniques has gained attention in CGMs, driven by the need for painless and user-friendly solutions for diabetes management. Traditional methods, involving fingerstick blood sampling, can be painful and inconvenient, leading to poor adherence among users. In contrast, a new generation of noninvasive blood glucose monitoring devices seeks to deliver accurate and continuous glucose measurements without the discomfort associated with the pain of invasive procedures. Novel advancements in sensor technology have paved various ways for innovative noninvasive monitoring solutions, such as fluid-sampling electrochemical, optical, and electromagnetic methods, to detect glucose levels through the skin. Despite the considerable progress made in noninvasive CGM systems, a fundamental challenge persists in the development of robust algorithms for the accurate interpretation and calibration of sensor data, which significantly influences their efficacy. For instance, the fluid-sampling method suffers a physiological time lag between blood glucose levels and interstitial fluid measurements,[95,96] while an optical-based sensor may struggle with disturbance factors like skin tone, temperature fluctuations, and hydration level, which can interfere with light absorption and scattering measurements.[27,97]

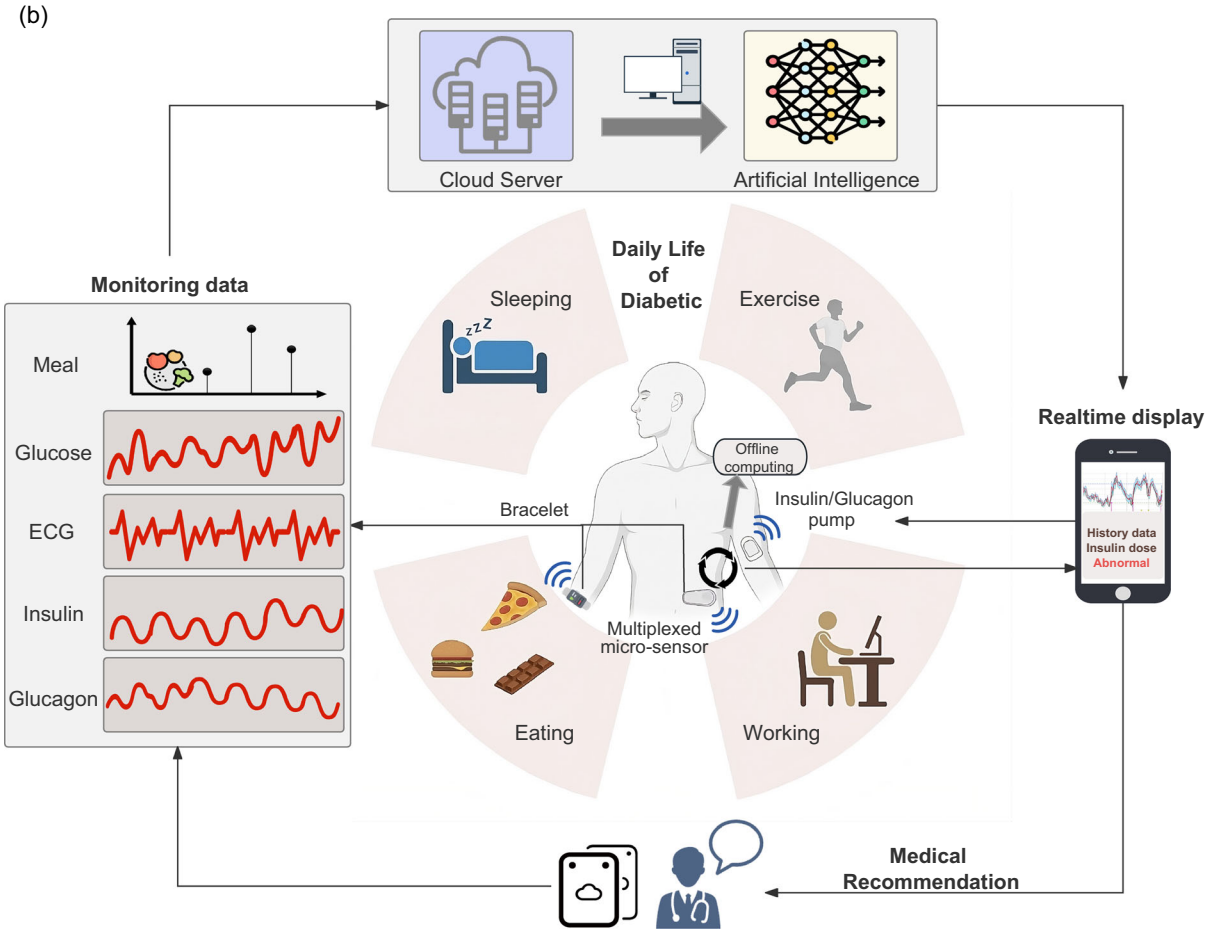
To address concerns about the accuracy of noninvasive CGMs, a promising solution is the implementation of a multimodal system that can monitor various disturbance factors, aiming to enhance sensitivity to changes in blood glucose levels.[28] Additionally, integrating machine learning algorithms into noninvasive monitoring devices offers exciting potential for future advancements. These technologies can analyze large amounts of data from multiple sensors, enabling predictive modeling of glucose fluctuations. By anticipating changes in blood glucose levels, AI-driven systems can facilitate timely insulin delivery, more closely mimicking the natural regulatory functions of the pancreas."

4.3. Reliability of Data Collection and Model Training

Deep learning requires a large number of data to train neural networks; hence, many prediction models opt for training and validation on private or open-source datasets.[29,58] However, due to variations in BG dynamics and physiological characteristics among different patients,[98] validation based on existing data may not reflect equivalent performance in real clinical scenarios. Consequently, the reliability of prediction models in actual clinical settings is challenged. Recently, transfer learning[99,100] has been increasingly recognized for its potential in BG prediction tasks. This approach enables the further generalization of pretrained models on smaller datasets, holding promise for personalized BG prediction. Future efforts to validate models trained on



Glucose detection with single-hormone delivery versus multi-analyte microneedle sensor with dual-hormone delivery



Closed-loop control of artificial pancreas

Figure 6. Our vision for the future of closed-loop artificial pancreas systems. a) Conventional system (left) only regulates insulin based on glucose level, while multisensing system (right) combines multianalyte microneedle array with dual-hormone delivery to regulate BG more flexibly, replicating the function of a natural pancreas. b) We envision the development of a closed-loop AP system. Miniaturized wearable devices continuously capture physiological signals, indicative of the patient's daily activities. This multimodal data is processed by edge AI models, which employ data-driven deep learning algorithms to ascertain the optimal insulin dosage.

existing data in real-world scenarios will require more stable and comprehensive evaluations and techniques to ensure model robustness.

In addition to the challenge of personalized algorithms, another factor affecting the reliability is the issue of imbalanced data distribution in existing datasets.[100] This imbalance originates mainly from two sources: sampling imbalance and BG distribution imbalance. Sampling imbalance often results from the insufficiently diverse collection of clinical datasets, where many datasets include only a limited number of patients who often live in the same area and share similar ethnic and lifestyle. As a result, the capabilities of prediction models and

insulin dosage calculation models tend to be overly focused on populations with similar characteristics. The second type of imbalance is the distribution bias in human blood glucose data, where most datasets concentrate within the normal glucose range, and hyperglycemia and hypoglycemia distributions are scarce. This limits the model's ability to learn about abnormal glucose variations, impacting the performance of alert models.[101,102]

To address these data distribution issues, collaborative efforts from clinical researchers are required to gather more comprehensive diabetes data. Additionally, more preprocessing and algorithmic approaches need to be employed to address imbalanced data, thereby enhancing the learning capabilities of the models.[101,103]

4.4. Edge Computing for Closed-Loop Control

Existing prediction, alert, and closed-loop control networks have predominantly been validated on graphics processing units. However, in real-world closed-loop glucose control scenarios, it is imperative for deep learning models to be deployed on edge devices, such as smartwatches, smartphones, CGMs sensors, and insulin delivery devices.[104] Recent research has underscored the critical role of edge computing in blood glucose computation, as it provides more reliable real-time services on wearable devices.[104,105] This offline computation approach yields extremely low output latency and remains unaffected by internet connectivity issues and improves the medical decision response speed. Deploying neural networks on edge chips with limited computational resources necessitates further model compression. Advanced methods, including quantization[106,107] and pruning,[108–110] offer significant promise in enhancing the application of deep learning for edge-based blood glucose computation. Additionally, the development of more lightweight and efficient algorithms is increasingly being recognized as a key expectation for intelligent closed-loop diabetes control systems.

Another important advantage of edge-intelligent wearable system is the localization of patient's personal data, enabling data processing and analysis to occur on local devices and reducing frequent communication with remote service centers.[111] This fully edge-based computing approach confines user data to local wearable and mobile devices, thereby reducing the risk of data interception or leakage during transmission between edge sensors and remote server centers, and enhancing the protection of user data privacy.[112] To further ensure data privacy and security, wearable devices typically incorporate data encryption technologies and local access control strategies to prevent unauthorized access and potential cyberattacks. This multilayered security design provides users with a more reliable and secure smart wearable experience, meeting the high standards of modern health management and personalized medicine.

Looking ahead, our research will focus on the synergy between AI and emerging wearable devices. The overarching goal in this field is to develop an intelligent wearable cyborg AP that can detect various physiological parameters, facilitate dual-hormone administration, and integrate AI models (Figure 6b) to compensate for the impaired pancreatic function in individuals with diabetes. This endeavor aims to significantly improve the quality of life for people with diabetes by offering a more sophisticated and responsive glucose management solution.

5. Conclusion

AI-enhanced wearable diabetes management systems hold significant promise in improving glucose control and alleviating the challenges associated with insulin therapy in diabetes management. This review has summarized the core components and recent innovations in closed-loop diabetes control systems, including glucose prediction models, automated insulin dosing algorithms, and wearable technology. Significant progress has been made in creating data-driven blood glucose prediction models using machine learning and deep learning techniques. These advanced algorithms, like deep neural networks, capture the temporal nuances in CGM data, offering tailored predictions. In insulin dosing, both traditional systems and RL-based model have proven effective in automating dosage adjustments. Integrating physiological data from wearables can further enhance the performance and safety of closed-loop systems. However, challenges remain. Improving sensor accuracy and miniaturization is crucial for truly wearable systems. Dual hormone systems, which include glucagon, require stable wearable technologies for practical use. The integration of noninvasive glucose monitoring technologies, such as those optical sensors embedded in smartwatches, emerges as a promising avenue for development offering a non-intrusive and continuous monitoring solution, potentially reducing the reliance on traditional invasive methods. The convenience and user-friendliness of such wearable devices could significantly improve adherence to monitoring regimens among individuals with diabetes, fostering proactive glucose management and enhancing overall quality of life. In conclusion, AI-driven closed-loop wearable systems have the huge potential in diabetes care. As this interdisciplinary field progresses, we are nearing the realization of intelligent systems that emulate the pancreas, promising improved outcomes and quality of life for diabetes patients worldwide.

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Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Wei Huang: conceptualization (lead); data curation (lead); formal analysis (lead); investigation (lead); methodology (lead); validation (lead); visualization (lead); writing—original draft (lead). **Ivo Pang**: software (supporting); validation (supporting); writing—review & editing (equal). **Jing Bai**: resources (supporting); software (supporting). **Binbin Cui**: resources (supporting); visualization (supporting). **Xiaojuan Qi**: supervision (lead);

writing—review & editing (supporting). **Shiming Zhang**: conceptualization (lead); formal analysis (lead); investigation (lead); project administration (lead); resources (lead); supervision (lead); writing—review & editing (equal).

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Diabetes management, Continuous glucose monitoring systems, Closed-loop insulin delivery, Control and prediction algorithms, Large health models

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