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Application of artificial intelligence in biofuel cell catalyst design and system optimization

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Highlights:

- Comprehensive review of artificial intelligence applications in biofuel cells.
- Data-driven modeling and optimization for enzymatic and microbial systems.
- Challenges and prospects toward intelligent bioelectrochemical energy systems.

Abstract: With the global energy transition underway, biofuel cells are gaining increasing attention as a clean energy technology capable of utilizing renewable biomass and organic waste for power generation. Despite the significant advantages of biofuel cells in terms of environmental friendliness and low carbon emissions, challenges related to catalyst efficiency, system complexity, and long-term stability still limit their large-scale application. This review examines the growing role of artificial intelligence (AI) in advancing biofuel cell technology, focusing on its advancements in catalyst screening, system modeling, and optimization. By leveraging AI technologies-including machine learning and deep learning-significant improvements have been demonstrated in material design, system parameter optimization, and performance prediction outcomes. Particular emphasis is placed on AI applications within enzymatic fuel cells and microbial fuel cells, analyzing progress in catalyst material discovery, system simulation, and operational control. By summarizing current breakthroughs and challenges, this analysis aims to offer theoretical support and technical guidance for future development of intelligent, AI-driven green energy systems.

Keywords: artificial intelligence; deep learning; biofuel cells; enzymatic fuel cells; microbial fuel cells

1. Introduction

The global "dual carbon" strategy is promoting the construction of clean energy systems as a central objective of worldwide energy transition [1]. A pivotal challenge within energy science lies in balancing the dual imperatives of energy security with the urgent needs for carbon emission reduction and sustainable development [2]. Among many clean energy technologies, biofuel cells (BFCs) have attracted much attention for their capability to generate electricity through the directly use of renewable biomass or organic waste. This conversion of chemical energy to electric energy is mainly achieved through enzyme or microbial catalysis [3]. Owing to their environmental compatibility, low carbon emissions, and the broad availability of fuel resources, BFCs are considered as a promising pathway for green energy conversion [4]. Based on different catalytic methods and reaction mechanisms, BFCs can be further divided into several types, including Enzymatic Fuel Cells (EFCs) [5,6], Microbial Fuel Cells (MFCs) [7], Photo-Microbial Fuel Cell [8], Enzyme-Microbial Composite Fuel Cell [9], as well as specialized variants for applications such as implantable power and wastewater treatment [6]. Different types of BFCs exhibit inherent differences in energy conversion pathways, biological catalysts, and system configurations, leading to substantial divergence in catalytic mechanisms, operational stability, and application scenarios. Their key characteristics are summarized in Table 1.

Table 1. Comparison of main types and characteristics of biofuel cells.

Type	Advantage	Disadvantage	Typical application
Enzymatic Biofuel Cells	High selectivity, mild reaction.	The enzyme has poor stability and short life.	Glucose battery, biosensor
Microbial Fuel Cells	Sustainable and treatable wastewater	Low power density, mass transfer limitation	Wastewater power generation, environmental monitoring
Photo-Microbial Fuel Cells	Light energy and chemical energy can be used at the same time	Low light conversion efficiency	Ecological energy, environmental restoration
Enzyme-Microbial Composite Fuel Cells	Both high activity and stability	The system structure is complex.	Study on composite electrode
Implantable Biofuel Cells	Sustainable, both power generation and processing functions	Limited power output	Implant medical, environmental governance

As showed in Table 1, different types of BFCs possess distinct characteristics and application profiles [10,11]. Despite their considerable potential in energy conversion and environmental remediation, the widespread deployment of BFCs under practical conditions remains constrained by several persistent technical challenges. Historically, the development of BFCs has heavily relied on experience-driven experimentation and physical modeling [12,13]. However, these methods exhibit significant limitations when addressing the inherent challenges of BFCs systems.

Biological catalytic processes in BFCs are highly sensitive to environmental variations, and enzyme deactivation leads to a pronounced decline in catalytic efficiency [14]. In MFCs, microbial communities undergo dynamic evolution, and metabolic activity directly influences electron transfer and energy conversion. By altering interfacial reaction kinetics and mass transport processes, these metabolic activities further modulate system behavior, resulting in system parameters that display pronounced time-dependent and operating-condition-dependent characteristics [15]. This coupling between metabolic

activity and electrochemical reaction kinetics renders the performance of BFCs systems difficult to predict and control. Consequently, traditional approaches often struggle to achieve effective system scaling and adaptation under varying operating conditions, limiting their practical applicability [16]. There is therefore a pressing need to develop new research paradigms capable of addressing these complexities and to adopt data-driven methodologies to enhance the overall performance and scalability of BFCs systems.

The recent computational power and the accumulation of experimental datasets had positioned AI as a transformative tool in interdisciplinary energy and materials research. Founded on the data-driven modeling paradigm, AI techniques can automatically identify complex, nonlinear relationships between input and output variables, enabling high-precision prediction and optimization decisions without clarifying the physical model a priori. Early on, AI has been successfully applied in the material selection and electrode structure optimization of Solid Oxide Fuel Cells (SOFCs) and Proton Exchange Membrane Fuel Cells (PEMFCs) [17,18], significantly accelerating catalyst discovery and performance enhancement through machine learning (ML) and data analysis. The evolution of fuel cells research, as depicted in Figure 1, illustrates a clear trajectory from initial focus on material and efficiency optimization toward intelligent design and adaptive control. This evolving trend is also reflected in the research on BFCs, where AI techniques have been gradually introduced to address the complex bio-electrochemical coupling issues in BFCs, driving improvements in their performance and stability [19].

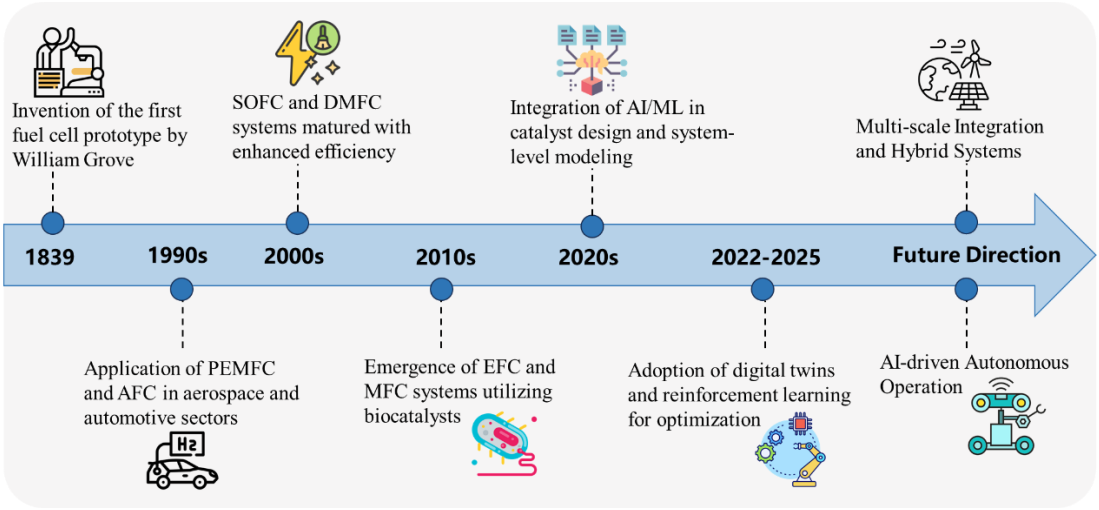

Figure 1. Evolution of fuel cells from traditional to intelligent systems.

Specifically, the application of AI in BFCs is primarily focused on catalyst design, reaction mechanism modeling, and system performance prediction [20]. Through ML algorithms, researchers are able to identify nonlinear relationships between microbial metabolism and electrochemical reactions, thereby optimizing the composition of microbial communities and improving the system's energy conversion efficiency. Deep learning (DL) techniques also play a significant role in catalyst screening, enabling the rapid discovery of efficient catalysts and optimization of their performance by analyzing large amounts of experimental data. In complex multi-scale coupled systems, AI can provide more precise performance predictions and optimization suggestions for operational parameters, thus improving the long-term stability and operational efficiency of BFCs [21]. Given these advancements, the following analysis systematically examines the application of AI in BFCs technology, with a specific focus on research progress and critical challenges in catalyst development and microbial fuel cell system

modeling. The aim is to provide theoretical guidance and technical references for the future development of AI-driven green energy systems.

2. Artificial intelligence technology

AI constitutes a highly integrated technology system, covers multiple levels from data perception and knowledge expression to learning, reasoning, and autonomous decision-making. In engineering and energy system research, practical applications of AI primarily rely on data-driven modeling approaches to characterize the nonlinear relationships between input parameters and system responses in complex systems [22]. In recent years, enhanced computational capabilities and the accumulation of large-scale data resources have positioned ML and DL as key drivers of rapid advancement in AI [23], leading to their widespread adoption across interdisciplinary fields including engineering, materials, energy, and medicine [24–26].

Among many AI methods, ML enables the computing system to learn rules and recognize patterns from data without explicit programming, through the construction of data-driven modeling and prediction system [27]. As its subset of ML, DL shows excellent capability in modeling complex nonlinear system via multi-layer neural network structure, proving particularly effective for tasks such as image recognition, time series analysis and optimization in high-dimensional parameter space [28,29]. With ongoing evolution in model algorithms, derivative technologies such as ensemble learning, reinforcement learning, and transfer learning have gradually become important tools for solving practical engineering problems [5,30]. A structured classification of these AI methods is presented in Figure 2.

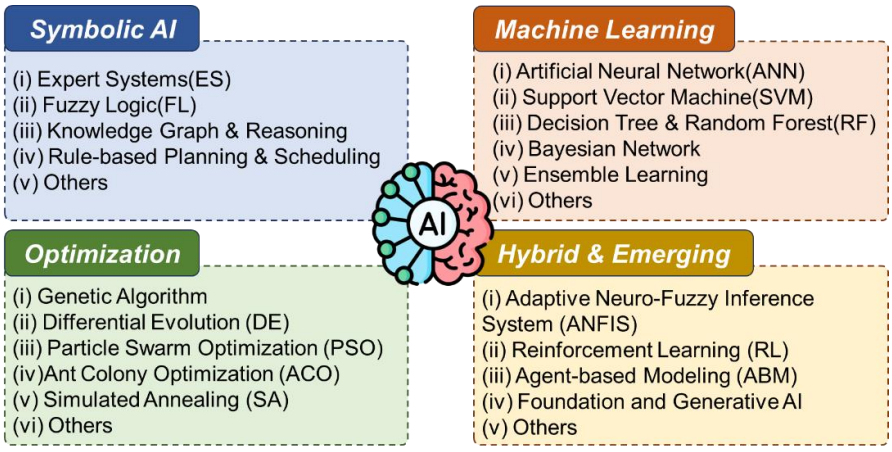

Figure 2. Introduction of artificial intelligence classification.

2.1. Machine learning

ML, an interdisciplinary subfield of computer science, refers to computational algorithms that improve their performance based on learning from experience [31]. Unlike traditional approaches that rely on explicit rules and complete physical models, ML constructs mappings between input variables and output responses by training on experimental or operational data, thereby enabling the prediction and analysis of unseen samples [32–34]. This data-driven modeling paradigm is particularly well suited for complex engineering systems characterized by high dimensionality, strong noise, and significant uncertainty.

In terms of modeling form, common ML models can be divided into several categories according to their structural and training mechanism, including neural networks, support vector machines, decision trees, and ensemble-based methods. Different models exhibit distinct strengths in terms of nonlinear fitting capability, generalization performance, and interpretability, and their fundamental principles and structural features are illustrated in Figure 3.

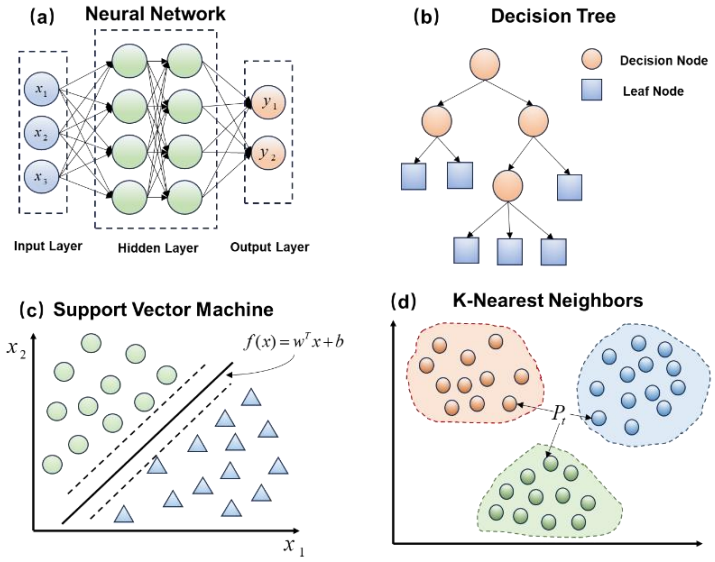

Figure 3. Machine learning model classification. **(a)** Neural Network; **(b)** Decision Tree; **(c)** Support Vector Machine; **(d)** K-Nearest Neighbors.

Moreover, ML has been successfully applied to performance prediction studies of complex engineering systems. Specifically, Ogaji *et al.* employed artificial neural networks (ANN), using operating temperature, pressure, and reactant supply conditions as input variables, to predict fuel cell performance indicators such as output voltage and power [35]. The detailed architecture of the ANN model is illustrated in Figure 4. This approach enabled the characterization of performance response trends under varying operating conditions, thereby facilitating the analysis of the influence of different operating parameters on system performance and supporting the evaluation and selection of operating conditions.

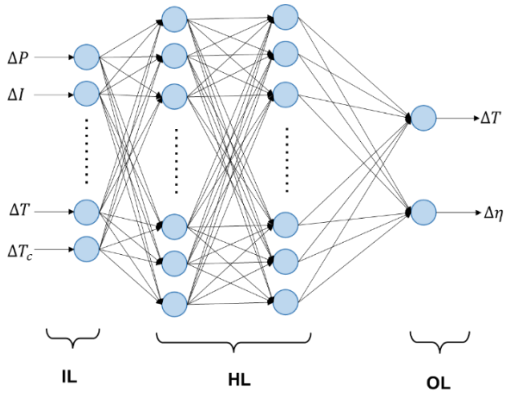

Figure 4. Architecture of the ANN used for fuel cell performance prediction [35]. Reprinted with permission. Copyright 2006 Elsevier.

In ML–based performance prediction studies, model outputs are typically quantitatively compared with experimental data using regression evaluation metrics to assess prediction accuracy and reliability.

Commonly used metrics include the mean absolute error (MAE) [36], root mean square error (RMSE), and the coefficient of determination (R^2) [37]. MAE represents the average absolute deviation between predicted and experimental values and is defined as

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

RMSE is more sensitive to large prediction errors, as it involves squaring the deviations before averaging, and is given by

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

The coefficient of determination, is used to quantify the proportion of variance in the experimental data that is explained by the model and is defined as

$$R^2 = 1 - \frac{\sum_{i=1}^{n}(y_i-\hat{y}_i)^2}{\sum_{i=1}^{n}(y_i-\bar{y})^2} \quad (3)$$

where y_i denotes the experimental value, $\hat{y}_i$ is the model prediction, $\bar{y}$ represents the mean of the experimental data, and n is the number of samples. In practical studies, multiple evaluation metrics are typically considered in combination to provide a comprehensive assessment of model prediction accuracy and generalization performance.

2.2. Deep learning

DL, a transformative branch of AI, realizes automatic feature extraction and high-dimensional mapping of complex data through multi-layer nonlinear neural network structure. This architecture significantly improves the capacity to model nonlinear, time-varying and coupled systems [38,39]. Different from traditional ML that relies on manual feature engineering, DL operates in an end-to-end manner, directly learning abstract, task-relevant representations from raw input data. Supported by advances in computing hardware and algorithmic frameworks, its application has expanded beyond core domain such as computer vision and speech recognition to scientific frontiers such as physics, chemistry, materials and energy. Today, it serves as a vital tool bridging experimental observation [40], theoretical modeling and engineering design. Its unique advantages in high-dimensional data [41], identifying nonlinear relationships, and generating complex patterns provide a new paradigm for exploring intricate energy conversion systems [42,43].

The integration of DL is reshaping how researchers' model and interpret complex structure-property relationships in energy materials and electrochemical systems [44–46]. For example, Ye *et al.* demonstrated that deep neural networks can predict crystal stability using minimal chemical descriptors—Pauling electronegativity and ionic radii—enabling efficient prediction of formation energies for garnet and perovskite crystals and accelerating the discovery of complex mixed crystals [47]. In the realm of energy storage, Yuan *et al.* developed a deep transfer learning framework for real-time health monitoring of lithium-ion batteries, achieving high accuracy in forecasting capacity and remaining useful life while adapting to varying battery chemistries and operational protocols [48]. Further extending its utility to industrial process modeling, Li *et al.* introduced a Supervised Long short-term memory network to capture nonlinear dynamic behaviors, improving prediction quality in applications such as penicillin fermentation and debutanizer column operations [49]. These studies demonstrate that DL methods

exhibit good applicability across diverse tasks, including materials modeling, energy storage system analysis, and prediction of complex industrial processes.

The ongoing evolution DL algorithms, driven by diverse research needs, has expanded their application to non-Euclidean data, such as crystal graphs, molecular graphs and multi-scale topological networks [50]. In crystal graph modeling, graph-based DL architectures directly encode structural relationships between atoms, effectively capturing long-range interactions within molecular and material systems. This approach demonstrates considerable promise for predicting material properties, modeling catalytic mechanisms, and analyzing interface reactions. Figure 5 illustrates a typical convolutional neural network architecture applied to crystal classification [51], where successive convolutional and downsampling layers extract hierarchical features from crystallographic data. Such models have been successfully deployed for property prediction and catalytic studies, enabling the efficient screening and optimization of crystalline materials.

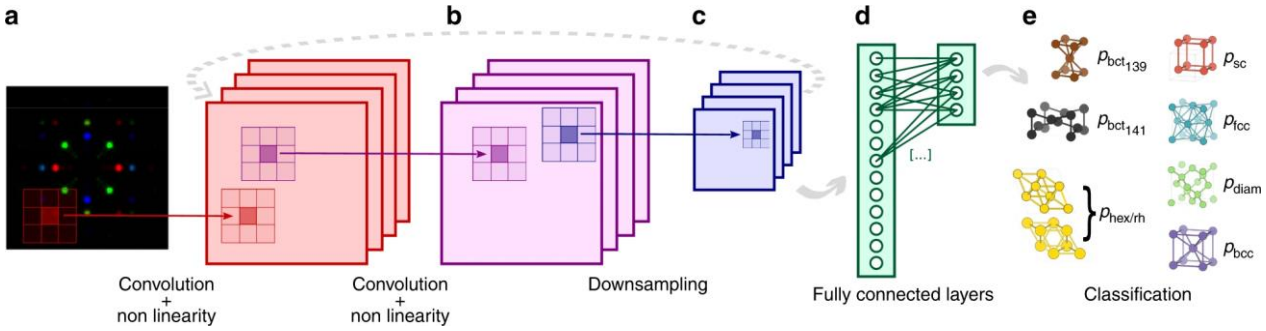

Figure 5. Schematic of a convolutional neural network (ConvNet) for crystal classification. **(a–c)** Convolution and downsampling layers extract hierarchical structural features from crystal images; **(d)** Fully connected layers integrate learned features for classification; **(e)** The network outputs the probability of each crystal structure class [51]. Reprinted with permission. Copyright 2025 Springer.

Attention mechanisms and multimodal fusion strategies enable DL models to integrate multi-source data [52,53], including images, time-series data, structural information, and experimental parameters, within a unified framework, thereby supporting the coordinated modeling of multi-scale and heterogeneous information. For complex and highly coupled systems such as BFCs, these approaches are, in principle, applicable to modeling features across material, interface, and system levels [54]. However, such DL models are typically optimized for predictive performance, and their internal feature representations and decision-making processes often lack intuitive physical interpretability, which to some extent limits mechanistic understanding of the model outputs. Consequently, how to balance predictive accuracy and model interpretability remains a key issue that warrants further attention in AI-driven BFCs research [55,56].

2.3. Large language models

Building upon the continued development of DL, large language models (LLMs), predominantly based on Transformer architectures, have recently emerged as a major frontier in AI. Unlike traditional machine learning and deep learning approaches that primarily focus on structured data modeling, LLMs are capable of processing large-scale unstructured scientific texts, demonstrating unique advantages in

literature mining, knowledge extraction, and the automation of scientific workflows. The architecture and workflow of large language models are illustrated in Figure 6. A recent review by Ramos *et al.* systematically summarized the potential of LLMs in chemistry and materials science [57], highlighting their emerging roles in molecular design, scientific knowledge organization, and automated research processes, thereby driving paradigm shifts in scientific discovery.

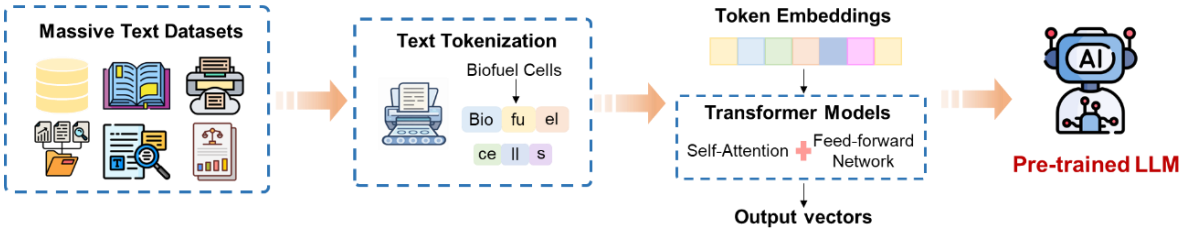

Figure 6. Architecture and workflow of large language models.

Although the direct application of LLMs in BFCs research remains at an early stage and has not yet achieved the widespread adoption seen in drug discovery or conventional catalyst screening, their capability to handle complex multi-physics and multi-scale systems provides valuable inspiration for BFCs studies [58]. Future research may explore leveraging the semantic integration capabilities of LLMs to uncover latent mechanistic relationships from vast corpora spanning chemistry, biology, and electrochemistry. For instance, LLMs could facilitate the identification of electron transfer compatibility between diverse microbial communities and emerging nanostructured electrode materials. Overall, as an emerging direction within the AI methodological landscape, the continued evolution of LLMs offers new methodological support for investigating complex bioelectrochemical systems and lays the groundwork for their future application in biofuel cell research.

3. Artificial intelligence in biofuel cell

AI is increasingly being introduced into BFCs research as a data-driven tool to assist in the analysis of biochemical energy-to-electrical energy conversion processes catalyzed by enzymes or microorganisms. By leveraging ML and DL approaches, researchers can extract key factors influencing BFCs performance from experimental and operational data and establish mapping relationships between performance metrics and various biological, electrochemical, and environmental parameters. Compared with traditional trial-and-error–based research approaches, AI provides alternative pathways for modeling and analyzing bioelectrochemical systems, contributing to improved experimental efficiency as well as enhanced systematicity and reproducibility of research.

3.1. Artificial intelligence in enzyme-based fuel cells

EFCs are bioelectrochemical devices that convert biochemical energy directly into electrical energy through enzyme-catalyzed redox reactions [59,60]. Operating under mild and environmentally friendly conditions, EFCs utilize redox enzymes instead of metallic catalysts, hence offering high substrate specificity, inherent biocompatibility, and improved sustainability. These features establish EFCs as promising candidates for miniature and implantable power sources [61].

A typical EFC, as illustrated in Figure 7 [62], comprises an anode, a cathode, and a proton exchange membrane. At the anode, oxidoreductase enzymes such as glucose oxidase (GOx) or lactate oxidase (LOx) catalyze the oxidation of biofuels, generating electrons and protons:

$$\text{Fuel} + \text{Enzyzme}_{ox} \rightarrow \text{Product} + \text{Enzyzme}_{red} \quad (4)$$

The generated electrons are transferred to the electrode through either direct electron transfer (DET) or mediated electron transfer (MET). Concurrently, at the cathode, reduction enzymes such as laccase or bilirubin oxidase (BOD) catalyze the oxygen reduction reaction (ORR):

$$O_2 + 4H^+ + 4e^- \rightarrow 2H_2O \quad (5)$$

Electrons transit through the external circuit to generate current, while protons migrate through the proton exchange membrane to the cathode, thereby completing the electrochemical cycle and achieving continuous energy conversion [63].

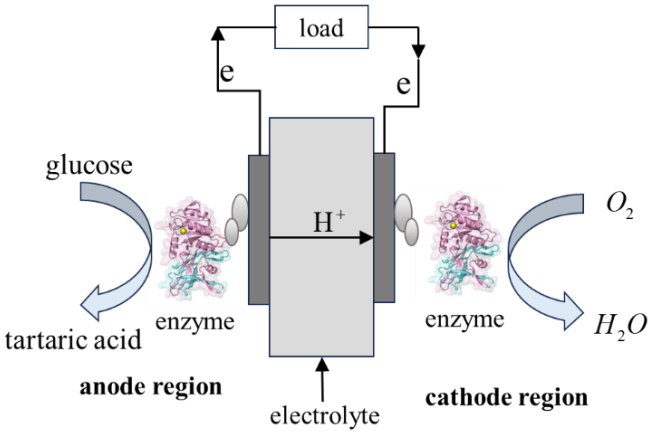

Figure 7. Schematic illustration of the working principle of an enzymatic biofuel cell.

The performance of EFCs is crucially dependent on multiple interrelated factors, including enzyme activity, electron transfer efficiency at the electrode interface, and operational conditions. This complexity necessitates advanced approaches for system optimization, a role increasingly filled by AI. By integrating and analyzing multidimensional data from experiments and simulations, AI techniques can identify key performance-determining parameters, develop predictive models for voltage output and power density, and guide the optimization of critical aspects such as enzyme immobilization, electrode interfaces, and reaction conditions [64]. This integration of AI transforms EFCs research from empirical tuning toward intelligent and mechanism-driven design [65,66].

This data-driven approach is exemplified by the ML–driven Design Build Test Learn cycle illustrated in Figure 8. This framework creates a closed-loop system by integrating cell-free protein synthesis, high-throughput performance evaluation, and sequence–function relationship modeling. This approach significantly accelerates enzyme evolution and gradually establishes an intelligent, self-optimizing design pipeline that offers a new paradigm for the rational design3 of biocatalysts in EFCs.

Early ML models were “black-box” models, focusing solely on the statistical correlation between sequences and functions. However, enzyme catalysis is not a simple sequence mapping but is influenced by the electrostatic environment of their 3D structure [67]. Warshel’s electrostatic preorganization theory suggests that enzymes enhance catalytic efficiency by pre-forming an electrostatic environment at the

active site that complements the transition state's charge distribution, reducing activation energy [69]. Advances in generative AI, particularly Variational Autoencoders and Generative Adversarial Networks, have shown remarkable ability to capture such deep physical constraints.

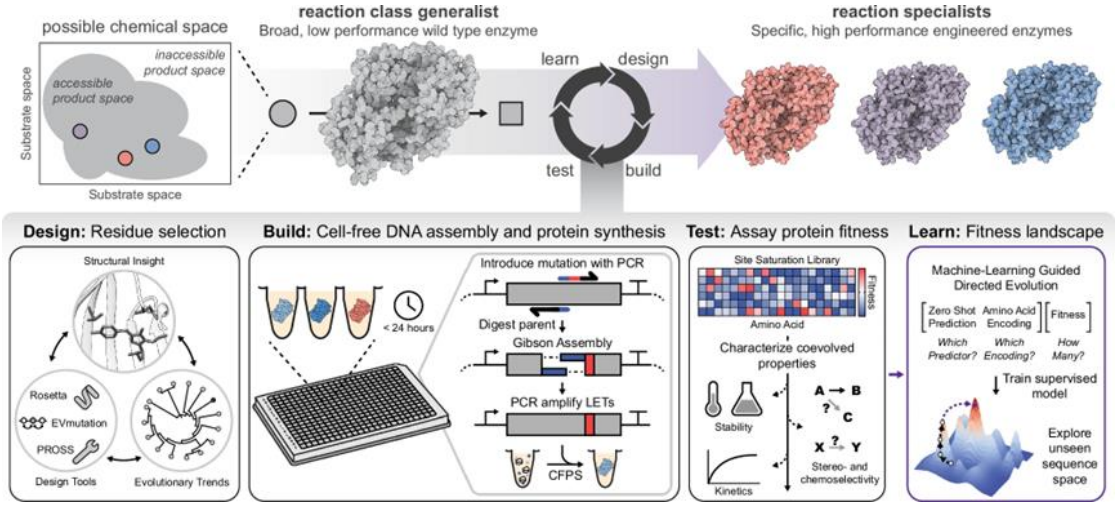

Figure 8. Machine learning guided cell free enzyme engineering workflow [68]. Reprinted with permission. Copyright 2025 Springer.

As shown in Figure 9, AI models not only predict the impact of mutations at the active site but can also accurately identify mutations at distant scaffold sites. These remote sites regulate the electric field vector of the active site through complex hydrogen bond networks and electrostatic interactions. By learning the co-variation patterns in evolutionary data, generative AI effectively "decodes" these hidden mechanisms.

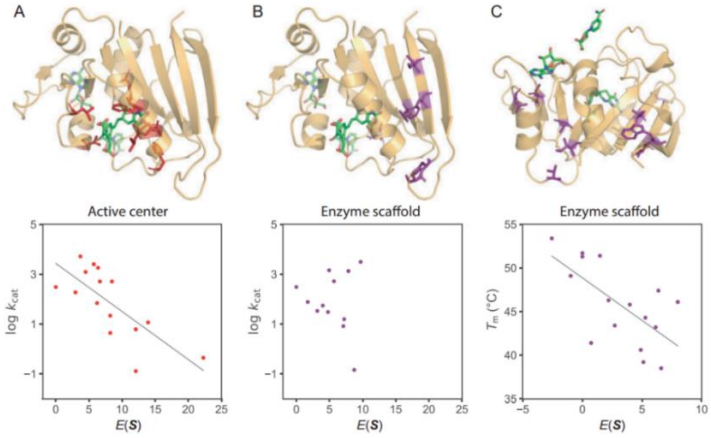

Figure 9. AI-driven Prediction of Enzyme Catalyst Performance via Electrostatic Network Analysis. **(A)** Analysis of the effect of mutations at the active site on the catalytic rate; **(B)** Analysis of the effect of enzyme scaffold mutations, distant from the active site, on the catalytic rate; **(C)** Analysis of the impact of mutations on enzyme thermal stability [69]. Reprinted with permission. Copyright 2023 Oxford Academic.

Simply modifying the internal structure of enzymes through genetic engineering is not enough, we must also regulate their external environment through solvent engineering [70]. Sosa *et al.* proposed an optimized ANN model for predicting laccase activity in different xylitol-based Deep Eutectic Solvents [71].

The model integrates COSMO-RS and ML techniques, effectively capturing the complex relationship between the solvent environment and enzyme activity. During the training process, the ANN architecture successfully extracted nonlinear features between solvent chemistry and enzyme catalytic behavior. As shown in Figure 10, the model demonstrated high prediction accuracy across the training set, validation set, and independent test set. This framework enables data-driven design and optimization, providing a more efficient and reliable system for enhancing biocatalyst performance in enzyme fuel cells.

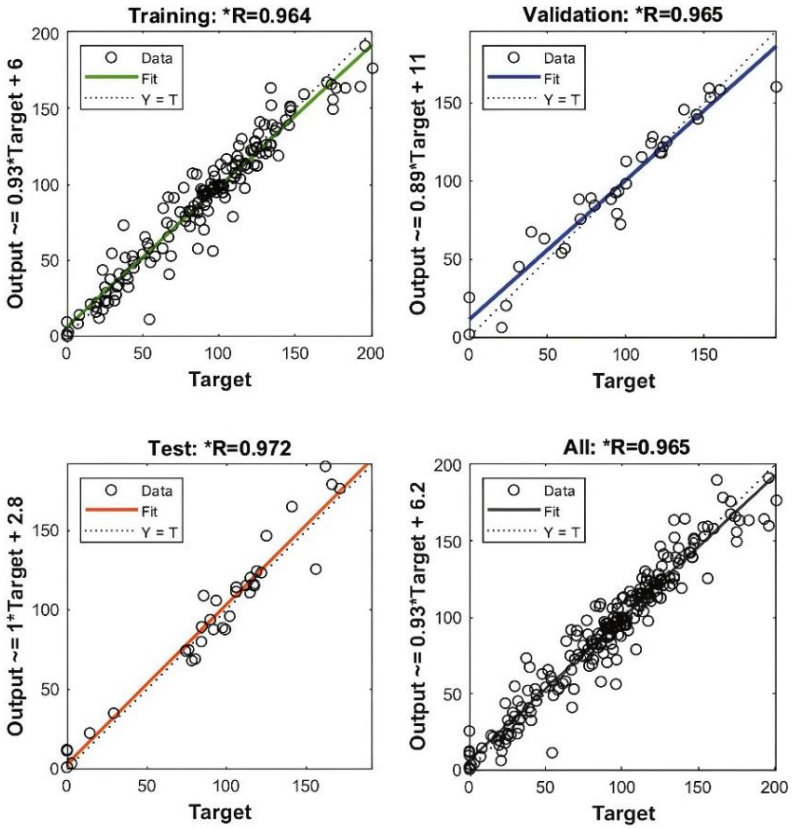

Figure 10. Performance evaluation of laccase activity prediction model based on artificial neural network [71]. Reprinted with permission. Copyright 2022 Elsevier.

Furthermore, Figure 11 illustrates the application of a ML-guided iterative evolution approach to the AtHMT and YmPhytase enzyme systems, resulting in significant improvements in catalytic activity after four rounds of evolution. Through the integration of high-throughput screening and ML models, several enzyme variants exhibited several-fold increases in specific activity compared to the wild type. These results validate the potential of the ML-driven directed evolution framework in optimizing enzyme catalytic performance, significantly enhancing catalytic efficiency in biofuel cell and other biocatalytic applications.

These results demonstrate the efficacy of integrating ML with experimental directed evolution for enzyme engineering. The iterative refinement of predictive models through iterative data feedback allows for the precise identification of high-performance variants and delivers substantial gains in catalytic efficiency. The consistent success of this methodology across diverse enzyme systems underscores the generalizability of the ML-guided framework and lays a robust foundation for intelligent biocatalyst design [72].

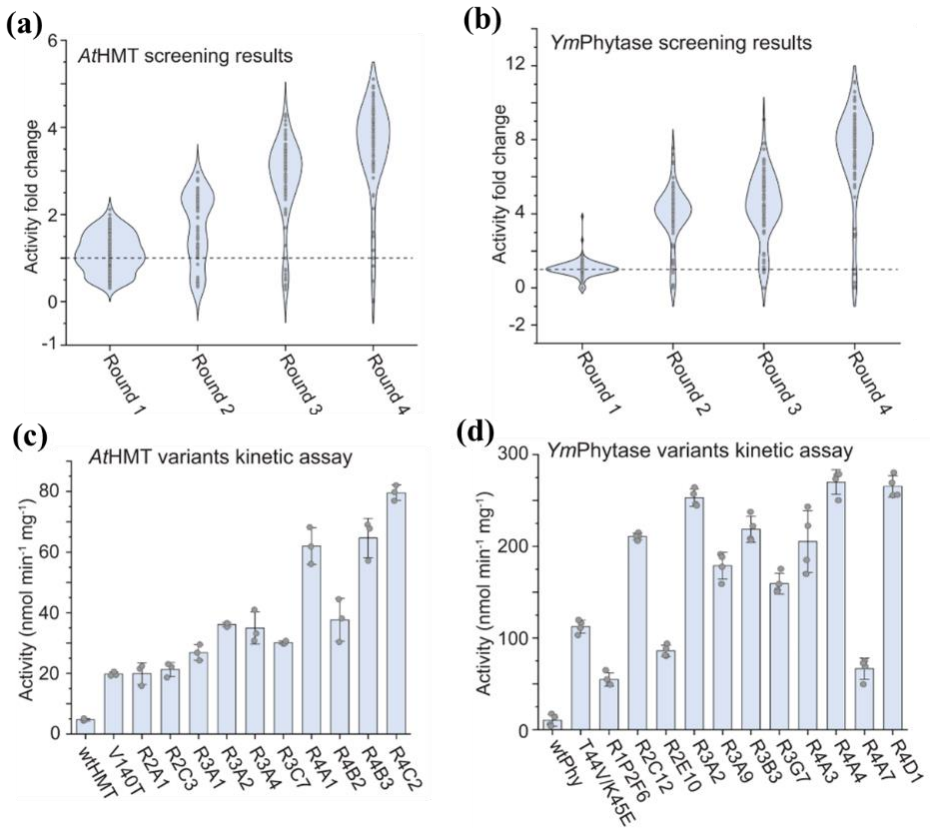

Figure 11. Experimental validation of machine learning–guided enzyme evolution through iterative screening and kinetic assays. **(a)** High-throughput screening results of AtHMT variants across four iterative evolution rounds; **(b)** High-throughput screening of YmPhytase variants over successive rounds; **(c)** Kinetic analysis of AtHMT variants showing increased specific activity compared with the wild type; **(d)** Kinetic analysis of YmPhytase variants confirming enhanced catalytic efficiency after ML-guided evolution [73]. Reprinted with permission. Copyright 2025 Springer.

Having established its utility in enzymatic systems, the section will focus on the application of AI in MFCs. In this context, AI serves as a powerful tool for modeling complex bioelectrochemical interactions, optimizing system components, and enhancing overall power generation efficiency, thereby promoting data-driven innovation in bioelectrochemical energy conversion.

3.2. Application of artificial intelligence in microbial fuel cells

MFCs represent a class of bioelectrochemical systems that convert the chemical energy of organic matter directly into electrical energy through microbial metabolism [74,75]. As illustrated in Figure 12, electroactive microorganisms in the anode chamber oxidize organic substrates, producing electrons, protons, and carbon dioxide [62]. The overall anodic reaction can be represented as:

$$C_xH_yO_z + H_2O \rightarrow CO_2 + H^+ + e^- \quad (6)$$

The generated electrons are transferred from microbial cells to the anode surface through either DET via outer-membrane cytochromes and conductive pili, or mediated electron transfer (MET) using soluble redox shuttles such as flavins and quinones. The electrons then flow through an external circuit to the cathode, while protons migrate across the PEM to maintain charge balance [76].

At the cathode, oxygen is reduced to water following the same reaction as shown in Equation (5). The cell voltage output V of an MFCs can be approximately expressed as:

$$V = E_{anode} - E_{cathode} - I(R_{int} + R_{ext}) \quad (7)$$

where E_{anode} and $E_{cathode}$ are the electrode potentials, I is the current, R_{int} and R_{ext} represent internal and external resistances, respectively.

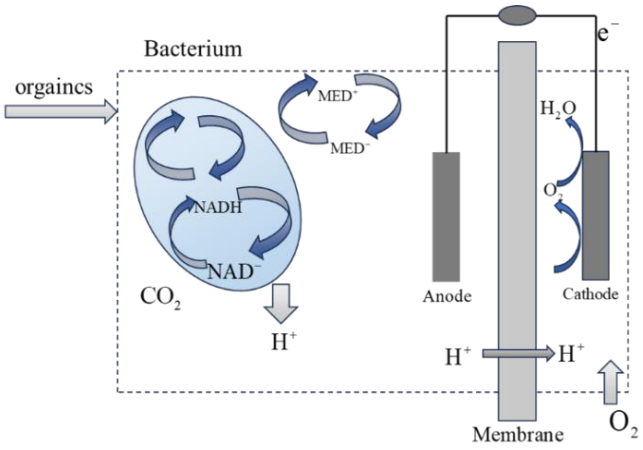

Figure 12. Schematic diagram of the working principle of a microbial fuel cell.

The overall power output and coulombic efficiency of an MFCs depend on multiple interrelated parameters spanning biological and electrochemical domains, including microbial activity, electrode conductivity, substrate diffusion, and internal resistance [77,78]. Optimizing these coupled processes is crucial for achieving high energy conversion efficiency.

As shown in the Figure 13, AI and ML techniques can be integrated into the bioelectrochemical system to analyze complex nonlinear relationships between operational parameters and electrochemical outputs [79]. In this framework, key input variables—such as substrate concentration, temperature, and electrode potential—are processed by ML models to predict critical performance indicators including output voltage, current density, and power density. The incorporation of AI allows data-driven learning and real-time performance estimation, reducing dependence on empirical tuning or mechanistic modeling.

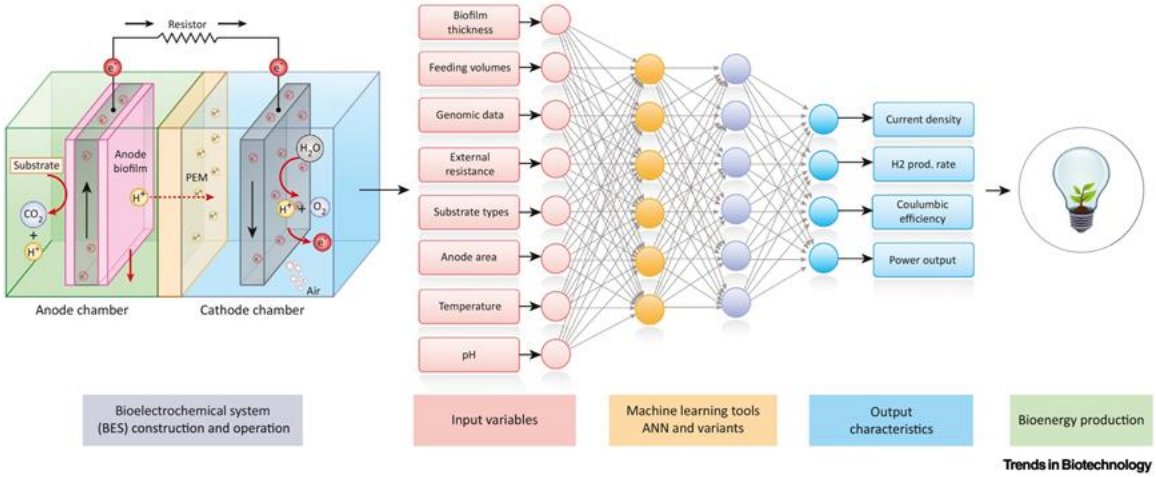

Figure 13. Schematic representation of a BES integrated with machine learning tools for performance prediction [79]. Reprinted with permission. Copyright 2022 Elsevier.

To further explore the broader application of AI in microbial fuel cell research, Table 2 summarizes representative studies that have employed different AI algorithms, such as neural networks, support vector regression, and genetic programming, for modeling and optimization purposes. These examples illustrate the diversity of AI methodologies and their respective advantages and limitations in handling complex bioelectrochemical systems.

Table 2. Application cases of artificial intelligence in microbial fuel cells.

Algorithm Used	Advantages	Disadvantages
NARX neural network [80]	Predict MFCs output with high precision; Optimize feed timing and energy management.	The data size is limited, and the real environment adaptability needs to be verified.
MGGP and SVR and ANN mixed model [81]	The model has strong expression, accurate prediction and certain interpretability; mGGP can automatically generate readable mathematical relations.	Model setting and parameter tuning are complex; the computational cost of evolutionary algorithm (MGGP) is large. It is sensitive to the division of training set and test set.
LSTM quantile regression [82]	It can predict the energy output of SMFCs with high precision and provide confidence interval to optimize energy scheduling.	Data size and environmental diversity are insufficient, and cross-environment generalization and energy consumption problems remain to be solved.
ML model (multivariate regression, random forest, *etc.*) [83]	It can be directly used to predict and optimize power density, identify key operating parameters, and save experimental time and cost.	The model has high complexity and limited generalization, and may need to be retrained under different scales or conditions.
ANN [84]	It can predict the power generation performance of membraneless MFCs with high precision, adapt to nonlinear multivariable system, and reduce the experimental workload.	It requires a large amount of experimental data, easy to overfit, insufficient generalization and lack of interpretability.
ANFIS and PSO [85]	A more accurate model can be established by dealing with nonlinear and a small amount of data. Combined with PSO, it can search the best operating conditions globally.	Multi-objective direct addition is not normalized, the weight is unbalanced, and the extrapolation optimization lacks experimental verification.
VSS and KNN [86]	Without changing the operating state of the fuel cell, only the stack voltage is needed to extract the state of health (SoH) mode; low amount of calculation, suitable for on-line monitoring.	Different databases and working conditions are quite different, which makes it difficult to compare directly between different studies. It is sensitive to noise and needs filtering processing.
SVM [87]	Automatic determination of support vector and model structure without a priori functional relationship assumption.	It is sensitive to data distribution and feature scaling, and depends on experimental design and training data quality.
Random forest regression and gradient boosting regression tree and PSO [3]	There is still high precision under the condition of small sample; it is suitable for dealing with nonlinear and multivariable coupling problems.	Sensitive to changes in data distribution; the interpretability of features is weaker than ANN.
Non-dominated Sorting Genetic Algorithm [88]	Multi-objective optimization algorithm; the error of optimization results is less than 2%.	Larger computing resources are needed; the convergence rate is affected by the initial population.
Gradient Boosting (GB) [74]	High prediction accuracy, suitable for dealing with the impact of multivariate systems; the performance is better than RF and SVR.	Easy to overfit; parameter adjustment is complex.

Although AI has significantly enhanced the modeling accuracy and operational optimization of BFCs by capturing complex nonlinear interactions, its core value lies in driving this technology from the laboratory bench to complex real-world application scenarios. As shown in Figure 14, modern microbial fuel cell systems are gradually evolving into multifunctional industrial platforms that integrate bioelectricity generation, wastewater treatment, and resource recovery [89]. In the face of dynamic industrial scenarios, which are far more complex than laboratory environments, AI algorithms can monitor fluctuating wastewater inflows in real time and dynamically optimize the trade-off between pollutant degradation rates and energy recovery efficiency.

Extensive empirical research has laid a solid engineering foundation for these real-world applications. Tender *et al.* successfully provided long-term stable power supply to weather buoys on the

sea surface by deploying benthic MFCs on seabed sediments, directly validating the survival capability of MFCs in maintenance-free marine environments. In the field of wastewater resource recovery, Roy *et al.* and Bazina *et al.* thoroughly analyzed the reactor structural features and operating parameters when MFCs treated actual industrial wastewater [90,91], quantifying the efficiency differences of various electrode configurations in simultaneously degrading pollutants and recovering bioenergy. Additionally, Santoro *et al.* systematically reviewed the key pathways for the transition of MFCs from microscopic mechanisms to macroscopic applications [76], particularly highlighting the core bottlenecks in system scaling, such as the anti-fouling properties of electrode materials and the engineered cultivation of biofilms. These foundational works not only define the physical boundaries in real-world scenarios but also provide rich experimental data and engineering contexts for the subsequent integration of AI to address multi-physical field coupling and dynamic environmental adaptability issues.

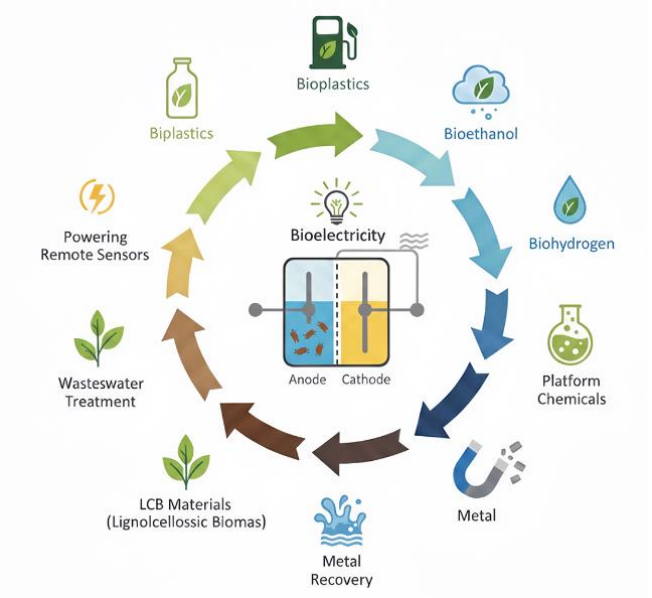

Figure 14. Circular utilization of microbial fuel cell systems in multiple applications. Adapted from [89] under the terms of the Creative Commons Attribution (CC BY 4.0) license.

3.3. Interpretability of AI models in biofuel cell applications

In the study of BFCs, although ML and DL have made significant progress in the predictive capabilities of models, these models typically possess a "black-box" nature, making it difficult to intuitively understand the reasoning process within the model, which is particularly evident when dealing with complex bio-electrochemical mechanisms [92]. Explainable Artificial Intelligence (XAI) aims to reveal the decision logic of ML or DL models, enabling the predictions made by the model to be understood and trusted by humans [93]. Unlike traditional black-box models, XAI methods significantly quantify the contribution of input features to the model output, helping researchers identify which variables or features play a key role in the prediction, thereby enhancing the transparency and interpretability of the model [94]. The Figure 15 illustrates the workflow of XAI methods, which includes the steps of input data, model construction, output prediction, and interpretability analysis. In this framework, the interpretability of the model is achieved through both ante-hoc and post-hoc methods. The ante-hoc method enhances transparency by constructing interpretable model structures during the model design phase, while the post-hoc method analyzes the model using external tools after the model has been trained, uncovering the decision logic of the model. Through

these methods, the model not only makes accurate predictions but also provides an in-depth understanding of the decision-making process, thereby enhancing the credibility and practical value of the model.

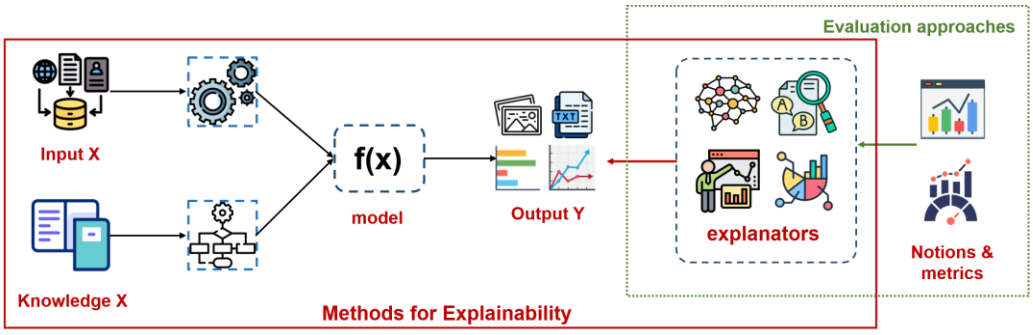

Figure 15. Explainable Artificial Intelligence workflow [95]. Reprinted with permission. Copyright 2021 Elsevier.

In explainability methods, SHapley Additive exPlanations (SHAP) and Local Interpretable Model-agnostic Explanations (LIME) are commonly used feature attribution tools. SHAP, based on a game-theoretic framework, calculates the marginal contribution of each feature to the model's output, providing both global and local interpretability results [96]. LIME, on the other hand, approximates the behavior of complex models by fitting simple linear models around the target points [97]. These methods have been applied in various fields to explain the prediction mechanisms of deep models, including healthcare, natural language processing, and materials performance prediction.

Shiteng Tan *et al.* investigated the electrocatalytic performance of nitrogen-doped carbon materials in MFCs by combining ML with SHAP [98]. They used SHAP to explain the influence of features such as nitrogen content, pore structure, and graphitization degree in nitrogen-doped carbon materials on catalytic performance, helping researchers identify which features played a decisive role in the prediction results, such as the relative importance of pyridinic nitrogen content. Figure 16 shows the feature importance distribution, highlighting the key role of pyridinic nitrogen (Pyrid-N) in the electrocatalytic performance of nitrogen-doped carbon materials, with elemental composition contributing the most to the model output at 42.7%. Through the SHAP method, the study not only improved the predictive accuracy of the model but also enhanced the understanding of the complex catalytic mechanisms, demonstrating the practical potential of XAI in biofuel cell applications. This research provides theoretical support for the design and optimization of catalysts for future BFCs and offers valuable insights for the application of XAI technology in other fields.

In addition to using explainability methods to reveal the decision logic of the model, ensuring the robustness of AI models in dynamic environments is equally crucial for their practical deployment. While explainability addresses the issue of "understanding why," robustness focuses on evaluating whether the model can maintain stable predictive performance when faced with biological variability, data scarcity, or environmental noise. Since the operation of BFCs is influenced by nonlinear factors such as microbial metabolic fluctuations and environmental conditions (e.g., temperature and pH), achieving high accuracy only on the training set is insufficient to ensure the model's reliability under unknown operating conditions. Therefore, researchers must introduce rigorous validation methods, such as using k-fold cross-validation to evaluate model performance on different data subsets, to avoid overfitting. Furthermore, due to the dynamic characteristics of bioelectrochemical systems, uncertainty

quantification for constructing robust models has become a new research trend. Single-point deterministic predictions often fail to cover the potential range of system fluctuations, while predictions based on confidence intervals provide more flexible risk assessment boundaries.

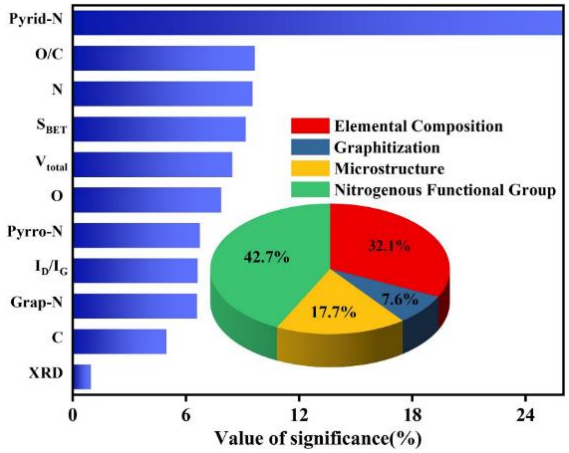

Figure 16. Feature importance distribution in nitrogen-doped carbon materials [98]. Reprinted with permission. Copyright 2023 Elsevier.

Figure 17 intuitively demonstrates the application of this concept in energy generation prediction for MFCs. The study employed a DL-based time series forecasting model, which not only outputs the predicted mean values for power, voltage, and current but also generates a gray shaded area (confidence interval) that includes the lower and upper bounds. As shown in Figure 17 a–d, as the prediction time span extends from 5 minutes to 60 minutes, although the system's uncertainty gradually increases (indicated by the widening shaded area), the actual observed values (blue solid line) are consistently encompassed within the model's predicted confidence interval. This "enclosure" capability strongly demonstrates the robustness of the model: it can dynamically adjust the prediction boundaries in the face of inherent noise and time-varying disturbances in metabolic data, thus providing a reliable decision-making basis for the system's long-term stable operation and energy scheduling.

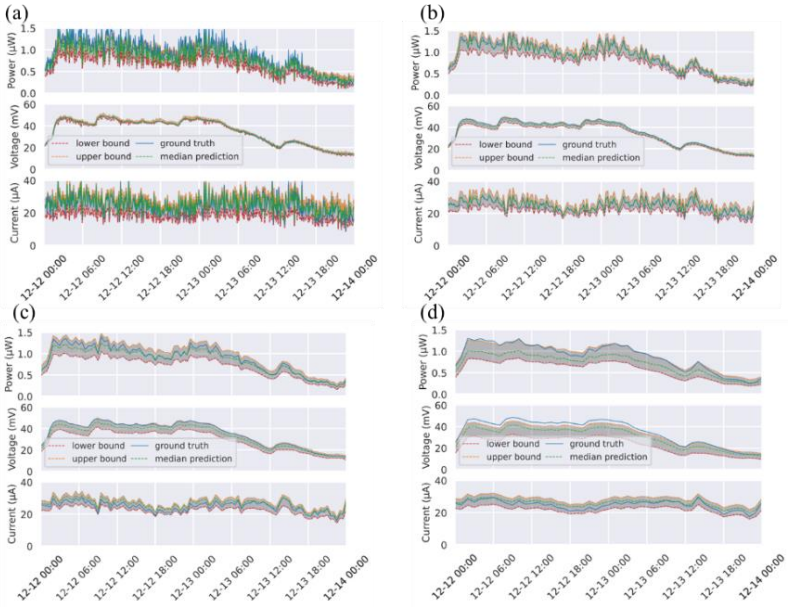

Figure 17. AI-based multi-horizon time-series prediction of microbial fuel cell performance. **(a)** 5 min; **(b)** 15 min; **(c)** 30 min; **(d)** 60 min [82]. Reprinted with permission. Copyright 2025 Frontiers.

3.4. Artificial intelligence in intelligent biofuel cells systems

At higher system integration levels, the application of AI has evolved beyond performance prediction and parameter optimization, extending toward reaction mechanism discovery, adaptive system control, and life-cycle assessment.

Figure 18 illustrates an AI-driven framework for fuel cell design and optimization, which synergistically integrates ML, numerical simulation, and experimental validation into a closed-loop workflow [99]. The framework bridges material characteristics, structural parameters, and electrochemical performance across multiple scales, facilitating efficient interaction between modeling and experimentation. Importantly, this concept can also be extended to biofuel cell systems. By incorporating microbial metabolic models, bioelectrode interface characteristics, and substrate transport parameters [100,101], a data-driven framework for prediction and optimization can be constructed, promoting the development of intelligent BFCs.

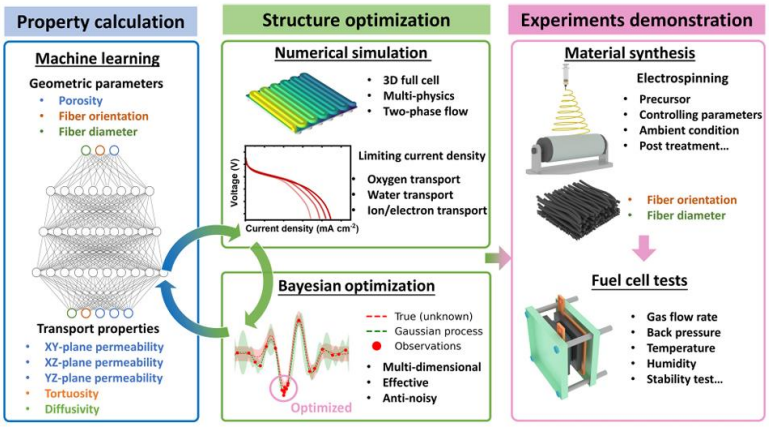

Figure 18. Schematic of an AI-assisted design and optimization framework for fuel cells [99]. Reprinted with permission. Copyright 2025 Springer.

The work of Lim *et al.* serves as a representative example [102]. They developed an intelligent prediction framework based on ANNs. Unlike conventional models that only output electrical parameters, this framework integrates wastewater characteristics (such as COD and pH) to simultaneously predict both bioelectrochemical performance and the internal states of biofilm communities, including the relative abundances of Geobacter and Shewanella. This study demonstrates that the concept of "AI-driven design" can effectively capture the complex bio-electrochemical coupling relationships in BFCs, thereby laying a solid foundation for the future development of intelligent bioenergy systems. The AI-driven dual-prediction framework for BFCs is illustrated in Figure 19.

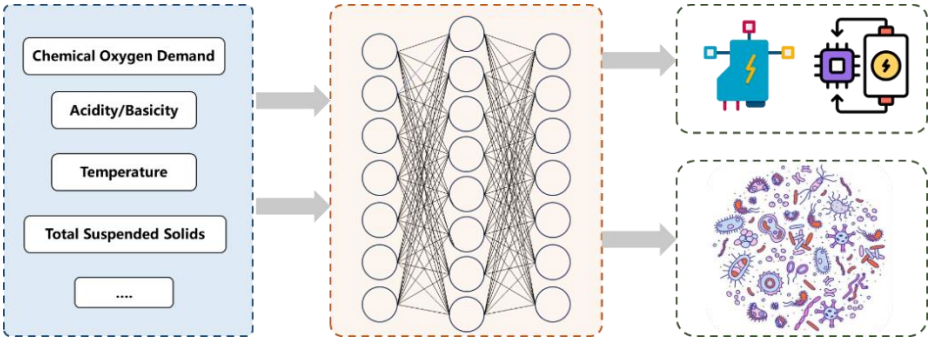

Figure 19. Schematic of the AI-driven dual-prediction framework for BFCs.

4. Challenges and prospects in intelligent biofuel cell systems

Although AI has shown substantial potential in uncovering performance patterns of BFCs, the inherent instability and environmental sensitivity of biocatalysts establish fundamental barriers to the further adoption of data-driven paradigms. The root cause of data heterogeneity originates from the dynamic degradation of biologically active components [103]. Unlike inorganic catalysts, enzymes and electroactive microorganisms tend to undergo structural denaturation or activity loss during prolonged operation, and this time-dependent performance drift results in significant distributional discrepancies among datasets collected at different time points, making it difficult for models to maintain robustness across multi-timescale prediction tasks. Furthermore, the integration of mechanistic understanding with data-driven approaches remains at a relatively superficial stage, as most existing AI models are primarily constructed based on statistical correlations between inputs and outputs, without effectively incorporating biophysical prior knowledge such as enzymatic catalytic kinetics, electron transfer mechanisms, or protein structure–function relationships [104]. The absence of such physical constraints often leads to predictive failure when the system is exposed to substrate concentration fluctuations or extreme pH conditions, because the underlying rate-limiting biochemical steps cannot be adequately captured.

As BFCs advance toward intelligent control systems, the mismatch between biological entities and digital algorithms in terms of both energy and temporal scales constitutes a major engineering challenge. On the one hand, a pronounced energy paradox exists between computational power consumption and biological electricity generation. The electrical output of BFCs, particularly enzymatic BFCs, typically lies in the microwatt to milliwatt range, whereas the execution of complex DL models generally requires substantially higher energy input. Deploying lightweight algorithms on resource-constrained embedded platforms to achieve genuinely self-powered intelligent systems therefore remains a critical bottleneck. On the other hand, an inherent temporal mismatch arises between the sluggish dynamics of biochemical reactions and the instantaneous nature of AI-driven decision-making. Substrate diffusion within porous electrodes and enzyme conformational changes occur over relatively long timescales, while millisecond-level control responses may lead to overcorrection or unstable regulation. In addition, long-term issues such as biocatalyst detachment and interfacial passivation introduce non-stationary system noise, further challenging the robustness and adaptive capability of AI models operating under dynamically degrading conditions.

5. Conclusion and outlook

The application of AI has fundamentally transformed biofuel cell research, shifting its role from a mere auxiliary tool for data fitting to a core engine for elucidating complex bioelectrochemical mechanisms. Beyond conventional performance metric prediction, recent advances demonstrate that AI is increasingly capable of "decoding" the electrostatic preorganization environments of enzymatic active sites as well as the dynamic succession patterns of microbial communities, thereby providing a solid theoretical foundation for the rational design of high-efficiency biocatalysts. By integrating explainable AI approaches, such as SHAP, with DL models, researchers are now able to explicitly quantify the contributions of key features, enhancing the transparency of model decision-making and effectively bridging the gap between black-box predictions and electrochemical interpretability. This paradigm shift

signifies that AI is no longer limited to optimizing output parameters but is actively driving the discovery of underlying structure–function relationships in bioenergy systems.

The realization of truly intelligent BFCs hinges on reconciling the energy paradox between computational power consumption and electrical output, as well as on achieving deep integration between underlying biological mechanisms and data-driven models. Future research must therefore establish hybrid modeling frameworks in which physical constraints, such as Michaelis–Menten kinetics and extracellular electron transfer mechanisms, are explicitly embedded into neural networks to ensure model robustness under small-sample conditions. This also necessitates the development of lightweight edge-AI algorithms that are suitable for deployment on resource-constrained embedded systems and are compatible with the limited power output of BFCs. Ultimately, with the integration of digital twin technologies and real-time biologically informed feedback control loops, BFCs may progressively mitigate temporal-scale mismatches and evolve from passive energy devices into adaptive and self-sustaining intelligent systems, thereby establishing a unique benchmark role in the advancement of data-driven methodologies for complex bioenergy systems.

Data availability statement

No data was used for the research described in the article.

Declaration of generative AI and AI-assisted technologies

During the preparation of this work the authors used ChatGPT in order to grammar checking and language refinement. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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Authors' contribution

Conceptualization, Yuezhou Zhang; software and data curation, Miaomiao Zhang; investigation, Meng Xiao; resources, Yue Wang, Miaomiao Zhang, and Meng Xiao; writing—original draft preparation, Yue Wang; writing—review and editing, Yanhui Chen and Yuezhou Zhang; project administration, Yanhui Chen and Yuezhou Zhang; funding acquisition, Yuezhou Zhang. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflict of interest.

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