Augmenting Sensor Performance with Machine Learning Towards Smart Wearable Sensing Electronic Systems

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Wearable sensing electronic systems (WSES) are becoming a fundamental platform to construct smart and intelligent networks for broad applications. Various physiological data are readily collected by the WSES, including biochemical, biopotential, and biophysical signals from human bodies. However, understanding these sensing data, such as feature extractions, recognitions, and classifications, is largely restrained because of the insufficient capacity when using conventional data processing techniques. Recent advances in sensing performance and system-level operation quality of the WSES are expedited with the assistance of machine learning (ML) algorithms. Here, the state-of-the-art of the ML-assisted WSES is summarized with emphasis on how the accurate perceptions on physiological signals under different algorithms paradigm augment the performance of the WSES for diverse applications. Concretely, ML algorithms that are frequently implemented in the WSES studies are first synopsized. Then broad applications of ML-assisted WSES with strengthened functions are discussed in the following sections, including intelligent physiological signals monitoring, disease diagnosis, on-demand treatments, assistive devices, human–machine interface, and multiple sensations-based virtual and augmented reality. Finally, challenges confronted for the ML-assisted WSES are addressed.

1. Introduction

Advances in new materials and soft and stretchable circuits have given rise to the interests in wearable sensing electronic systems (WSEEs) for a broad range of applications, including health monitoring, disease diagnosis, personalized healthcare, on-demand treatment, assistive device, human–machine interface (HMI), and virtual and augmented reality. Generally, a WSES consists of several heterogenous components: the sensor unit, power unit, wireless communication unit, data collection/storage/transmission unit, and data processing unit. Each of these components is essential to be intelligent and smart, thus enabling the potential large-scale use of WSES. First, sensors must be sensitive, reliable, durable, and wearable, of which high-quality sensing data is the prerequisite for obtaining excellent performance of WSES. Second, current solutions to powering units can be categorized into three strategies: self-powering, integrated battery, and wireless power. Third, data collected from the sensor system can be stored in a memory within the WSES or wirelessly transmitted to an external device (i.e., tablet or cellphone). Note for some cases, collecting sensing signals are still assisted with external sources (i.e., special equipment for spectroscopy data acquisition), which makes the wearability of the devices compromised to some extent. Fourth, processing data can be configured into an online mode within the WSES or offline mode by using external devices (i.e., cloud computing or cellphone).

On the one hand, optimizing each component in the WSES on various aspects has witnessed many achievements, such as deliberately tailored materials, excellent permeability for wearing, long-term stability, carefully designed soft circuits, etc. On the other hand, the popularity of the WSES as healthcare devices or for other applications is still limited. This is probably because the useful information output from current WSES still does not meet the expectations of users even though a large volume of raw data can be readily collected. This is true, especially when sensor arrays with different data modalities are configured into one system. Therefore, it makes the large volume of multimodal data interpretation difficult under the paradigm of conventional data processing techniques. Without further complexing the device structure designs, a promising approach is to extract as much information as possible from the collected raw data using current WSES. Fortunately, advanced data processing strategies could narrow the gap between users’ expectations and devices’ performance with the fast-rising of artificial intelligence (AI).

The combination of abundant data from the WSES and AI technique could make a game-changer that further boosts the performance of current WSES and revolutionizes many applications in personal healthcare, public health sector, sports, and games. As an important subset of AI, Machine learning (ML) has already been widely implemented in many fields of
Mathematics, physics, chemistry, engineering, and materials science.[22–25] As a powerful tool for processing and analyzing raw data collected from wearable devices, ML algorithms facilitate the practicality of the WSES for a potential application as medical devices in many aspects. For instance, a simple biosensor device consisting of gold nanoparticles[23] enables the fast screening of coronavirus disease 2019 (COVID-19) with the assistance of ML algorithms.[24–27] Several vital signs of health status can be readily assessed with the help of ML algorithms to efficiently and accurately extract useful information from the WSES.[28–35] Sufficient disease treatment with optimal dose adjustment has also been demonstrated for type 1 diabetes.[36] Other important achievements have been demonstrated in the past few years, including sign language translation,[37,38] human–machine haptic interface,[39] and brain-to-text communication, etc.[40] The wide implementation of ML algorithms in research fields of engineering and materials science has already been emerging.

In this review, we focus on how to utilize sensing data from the WSES to the fullest with the assistance of ML algorithms, which, in turn, is expected to further optimize the performance of the WSES at a system level for applications of healthcare, HMI, and virtual/augmented reality (VR/AR) (Figure 1). First, the basics of several typical ML algorithms are introduced, along with demonstrated examples. Then the tracking and monitoring of physiological signals using the ML-assisted WSES are summarized in Section 3, along with discussions on proof-of-concept applications of on-demand disease treatment and assistive devices for people in need. The possibility of using ML-assisted WSES for applications of intelligent HMI and multiple sensations-based highly immersive VR/AR demonstrations is outlined in Section 4 and 5. Conclusions and perspectives are presented in Section 6, including challenges and proposed prospects.

2. ML Algorithms and Augmented Sensing Performance

Using wearable devices, abundant raw data of different physiological signals can be collected, which, however, require further processing and analyzing. For instance, many physiological signals from our daily activities are detected in the form of concentrations of biochemicals, patterns of biopotentials, and intensities of biophysical activities.[41–44] An accurate understanding of the information conveyed by these data from wearable sensors makes it possible for both users and clinicians to adjust treatments or further actions conveniently and efficiently. Conventional data analysis paradigms, including threshold limits, simple mathematical models (i.e., linear or polynomial regressions), or manual selection, are insufficient for a large volume of raw data handling from many aspects, such as data structure complexity and high dimensionality, multiple modalities, and, etc. Hence, ML algorithms have come to play a critical role in forging a new paradigm of data analysis that further facilitates the advances and practicality of smart and intelligent wearable electronics.[45–48] Through implementing appropriate ML algorithms, useful information of various signal features can be extracted from raw data and utilized to the fullest, which, in turn, would make these wearable devices perform better in an intelligent manner.[49–53] One should note that selecting an appropriate algorithm for different types of raw data is important to establish the correct and robust correlation between the sensing signals and the physiological status. In this section, we summarize major data processing techniques reported in previous studies on wearable electronics. Two major types of algorithms are included: data preprocessing algorithms such as principal component analysis (PCA)[54] and hierarchical cluster analysis (HCA),[55] and classification algorithms such as support vector machine (SVM),[56] decision tree (DT) and random forest (RF),[57,58] and artificial neural network (ANN).[59–61] Additionally, a few key examples of how ML algorithms optimize and augment the performance of wearable devices are discussed.[48,50,51,60–64]

2.1. Data Analysis Algorithms in WSES

2.1.1. Principal Component Analysis

As a typical unsupervised ML algorithm, principal component analysis (PCA) is widely used for data dimensionality reduction, increasing interpretability while minimizing information loss. PCA also enables feature clustering and classification for disease diagnosis.[65] The raw dataset is projected into a lower-dimensional space via a set of principal components (PCs) to maximize the variance while preserving as much data information as possible. By computing the values of PCs, clear data visualization can be realized by only showing the first few PCs, which are reduced from a large set of high-dimensional data. Generally, the first two or three PCs (PC1, PC2, and PC3) are the most selected features, thus forming a 2D or 3D plane visualization (Figure 2a). There are also other versions of PCA, such as contrastive principal component analysis, which enables visualization of dataset-specific patterns missed by PCA.[52] It is worth mentioning here that other approaches of data dimensionality reduction can also be implemented for analysis on sensing signals collected from wearable sensors, such as linear discriminant analysis (LDA) for human activity recognition,[66] t-distributed stochastic neighbor embedding (t-SNE) for speakers’ voice recognition,[67] and non-negative matrix factorization (NMF) for electroencephalography (EEG) spectral analysis.[68] More information can be found in other references.[48,69–70]

2.1.2. Hierarchical Cluster Analysis

Hierarchical cluster analysis (HCA) is an unsupervised algorithm of multivariate analysis for clustering, including two types: agglomerative (bottom-up approach) and divisive (top-down approach). Results of PCA are often represented as a dendrogram by building a hierarchy of cluster. First, the dissimilarity between datasets of observations is calculated, which is usually done by selecting an appropriate metric (a measure of distance between pairs of observations). Then the measure of dissimilarity dictates the observations to be combined into clusters (for agglomerative) or split into clusters (for divisive). Some commonly used metrics for hierarchical clustering include Euclidean distance, Squared Euclidean distance, Manhattan distance, Maximum distance, and Mahalanobis distance.[12,53] Note the choice of an appropriate
metric will influence the hierarchy of the clustering results, as some elements or features may be relatively closer to one another under one metric than another.

2.1.3. Support Vector Machine

Support vector machine (SVM), as a supervised algorithm for binary classification tasks, can also be reconfigured for multiclass classification by dividing multiclass problems into multiple binary classification problems. To separate the input dataset into potential classes, one or more hyperplanes in high-dimensional spaces are constructed by calculating the largest margin among the input datasets. With a well-chosen multivariate function (i.e., a tunable kernel) including linear function, polynomial function, and sigmoid function, etc., the hyperplanes divide the input dataset (i.e., support vectors) into groups linearly or nonlinearly (Figure 2c). The classification results quality can be described by the so-called margin distance, the boundary distance between the hyperplane divider and support vectors. A larger margin distance indicates a more accurate classification result. SVM finds many applications for WSES, such as drug discovery,[71] and convulsive seizure detection.[72]

2.1.4. Decision Tree and Random Forest

Decision tree (DT) solves classification and regression problems by using a set of tree-like hierarchy decisions (Figure 2d).[49] DT
consists of a root node as the highest-level decision at the top level of the hierarchy, followed by many subtrees (i.e., branches). Each subtree, representing a decision node, is used to split the data into smaller branches until no further branches can be separated, thus building \( n \) decision nodes (i.e., \( n \)-leaf node). For each \( n \)-decision node, a threshold is obtained through impurity metrics (e.g., Gini, information gain) to proportionally separate the data features.\(^ {73} \) One obvious advantage of DT is the comprehensiveness of including all possibilities at each path for all subdatasets. Building on multiple single decision trees, random forest (RF) inherits results of classification and regression from DT and assembles them into one result, thus eliminating any overfitting issues and reducing the forecasting variance which may arise by using DT.\(^ {64} \)

2.1.5. Artificial Neural Network

Inspired by the biological neuron networks in animal brains and the understanding of the interactions between neurons and physiological activities of the human brain and body, an algorithm, called neural network, has gone through significant advances in the past decade, along with the computation power improvements of graphics processing unit (GPU). As a popular deep learning technique, the neural network stands itself out of other non-neural methods in three main ways: 1) comprehensive consideration of all features extracted from the raw dataset using the nonlinear model; 2) a huge amount of parameters involvement to include as many optimizers as possible; 3) a large amount of data required to train the model to achieve optimal performance. With the advances of flexible and wearable devices as biosensors, the large volume of physiological signal datasets from body activities can be readily collected. Thus, by exploiting these data, an artificial neural network algorithm can be efficiently trained, facilitating the further performance enhancements of WESE.\(^ {74} \) Here, we introduce three common types of neural networks that are of great importance for physiological signal data processing and analyzing, including fully connected neural network (FCNN), recurrent neural network (RNN), and convolution neural network (CNN).

**Fully Connected Neural Network**: FCNN is a type of neural network architecture where all the nodes (i.e., neurons) in one layer are connected to the nodes in the next layer (Figure 2e-i). A typical FCNN consists of three layers: an input layer, a hidden layer, and an output layer. Two or more hidden layers can be configured. Input data initialize each neuron with randomized weights and bias values into the input layer nodes. Then data directionally propagates throughout the neural network. Each \( n \)-neuron node in the hidden layer is activated once a threshold value is reached through a mathematical function. Eventually, regression or classification problems are solved when data reach the nodes in the output layer after applying specific mathematical functions. Note the data flow of FNN is in one direction, from the input layer through hidden layer(s), then to the output layer. Performance enhancement of the FCNN algorithm can be obtained by the learning technique of backpropagation. Briefly, once data propagate to the output layer, the errors from
the neural network are calculated by comparing the output results to the expected values. If errors are not in the desired range, then these errors propagate back through the neural network. Consequently, this learning approach further optimizes the internal model parameters.\footnote{[58]} The contributions of errors at each node are computed, which facilitates the automatic adjustments of the algorithm to reduce the error gradients further until optimal convergence values are reached at output layers.

**Recurrent Neural Network:** Inheriting many same attributes of FNN, an RNN presents a temporal dynamic behavior because the connections between nodes form a directed graph along a temporal sequence (Figure 2e-ii). Each neuron node in the hidden layers acts as a memory element.\footnote{[75]} This indicates that the recurrent neuron nodes can hold the active information from their previous hidden states and integrate this information with the new input state. Such capability makes RNN of great significance for temporal and sequential data from texts (handwriting) and voice (speech) recognitions. One shortcoming of an RNN is the difficulty in model training with data that present temporal contingency (i.e., long-term dependency). As the state-of-the-art variants of RNNs, long short-term memory (LSTM) and gated recurrent units (GRUs) are put forward to this “contingency” challenge, leading to excellent performance in model training.\footnote{[61]}

**Convolutional Neural Network:** By far, CNN is the most widely implemented neural network algorithm for computer vision-related tasks, such as object detection, image recognition, and facial emotion decoding. The basic components of CNN are convolutional, pooling, and fully connected layers (Figure 2e-iii). Convolutional layers, consisting of several convolution kernels, are for learning local features of the input datasets. Pooling layers are for dataset dimensionality reduction. Fully connected layers inherit similar attributes of a regular nonconventional artificial neural network.

### 2.2. Performance Improvements of WSES with ML Algorithms

From the perspective of data processing and analyzing, the tasks of ML algorithms designed for WSES applications (i.e., health monitoring, diseases analysis and diagnosis, and assistive devices) mainly fall into two types: regression or classification. First, the readily collected datasets of physiological signals from the human body facilitate the establishment of a smart algorithm model. Usually, a continuous collection of physiological signals can be achieved for most sensing devices of WSES, which indicates the availability of a large number of raw datasets. Then, the dataset can be split for the ML model establishment, for instance, 80% of the dataset for training and 20% for validating and testing. Note the partition ratio of a dataset is algorithm-specific and related to the quality of the raw dataset.\footnote{[76]} When selecting the partition ratio of the dataset, the goal is to maintain the statistical stability of prediction performance with minimum underfitting or overfitting at a reasonable computing cost. Then implementing the well-trained model on new datasets usually achieves the accurate outcome of classification or regression, which also relies on the overall quality of the raw datasets. Nevertheless, underfitting or overfitting may present in ML algorithm models due to insufficient or excessive training datasets, respectively. However, compared to conventional data processing of threshold limit-based techniques, ML algorithms after appropriate training are still much advantageous and adequately sufficient for improving the performance of WSES. Here, we discuss a few examples to illustrate how the ML algorithms boost the function qualities of WSES for various applications.\footnote{[50,51,61–64,77,78]}

#### 2.2.1. Classification

Analysis of many physiological signals from the human body usually presents a binary result: yes (i.e., normal) or no (i.e., abnormal) for disease diagnosis. Such analysis is called classification, on which ML algorithms could facilitate to achieve high efficiency and accuracy of predicting data features. One example of early-stage lung cancer detection is illustrated in Figure 3a using surface-enhanced Raman spectroscopy (SERS) data of the exosomes.\footnote{[61]} The data is analyzed through a residual neural network (ResNet)-based deep learning model, which achieves a 95% accuracy of classifying exosomes derived from normal and lung cancer cell lines (Figure 3b). ResNet model performs better compared to results from other multivariate statistical methods, including PCA-linear discriminant analysis (84%), partial least-squares discriminant analysis (88%), SVM and other CNN with five convolutional layers (90%). This deep learning analysis-based technique for detecting lung cancer cell-derived exosomes in blood could serve as a routine prescreening tool as a noninvasive, safe, and sensitive analytic method. Similarly, by implementing a 3D CNN model, data from low-dose computed tomography can also be used for lung cancer screening with absolute reductions of 11% in false positives and 5% in false negatives.\footnote{[77]} In another example of using molecularly modified gold nanoparticles and carbon nanotubes, Nakhle et al.\footnote{[60]} reported a 86% accuracy of noninvasive diagnosis and classification of several diseases from exhaled breaths via a series of discriminant factor analysis binary classifiers. Aside from obtaining an accurate classification of diseases diagnosis, Gehrung et al.\footnote{[78]} also achieved 57% workload reduction at a comparative diagnostic performance of experienced pathologists through comparative transfer learning of multiple CNN architectures. In short, these results demonstrate that ML-assisted data analysis could achieve comparable results for disease diagnosis as similar as clinician specialists. More importantly, with the assistance of the ML algorithm and WSES, the review and diagnosis of the disease could be automatic that is expected to save medical resources and reduce burns on individuals and society.

#### 2.2.2. Multiple Data Processing

False-positive or false-negative diagnosis results may result in overtreatments or insufficient treatments. This might be the incapability of a single sensor to accurately track and monitor multiple biomarkers of the relevant disease. Thus, a combination of multiple biomarkers shows promise to boost the prediction performance through a cross-validation strategy. However, such a design brings difficulties in analyzing data from different sensor channels, which is not feasible in the conventional data processing paradigm. Kim et al.\footnote{[64]} reported a cross-validation approach by detecting multiple biomarkers of urine samples. Taking advantage of data of multiple biomarkers from different
sensors along with ML algorithms, the authors achieved better prediction outcomes for prostate cancer screening compared to that of cases with fewer biomarkers (Figure 3c). Specifically, the authors selected four biomarkers, naming annexin A3 (ANXA3), prostate-specific membrane antigen (PSMA), erythroblast transformation-specific related gene protein (ERG), and endoglin (ENG). Each of these biomarkers could generate electrical signals that were detected by a biosensor. After applying the FCNN algorithm with three hidden layers, more than 99% accuracy was obtained for totally 76 naturally voided urine specimens, which is much higher than that of a single-biomarker approach (i.e., 62.9% accuracy) (Figure 3d). The authors also found that the simple inclusion of multiple biomarkers did not necessarily increase the prediction accuracy without ML algorithms. Similarly, Zeng et al.\[50\] established epidermal electronics systems (EES) and electronic tattoos (E-tattoos) to simultaneously monitor multiple physiological signals with six different features, which facilitates accuracy of 89% for metal fatigue status prediction after implementing the DT algorithm. What is expected is that a specific algorithm should be deliberately configured for different cases of multiple data analysis. For instance, RF performs better than neural

![Classification](image1)

**Figure 3.** Augmented sensing performance of ML-assisted WSES. a,b) Classification of normal and lung cancer cells with an accuracy of 95% was achieved using a deep learning model: a) schematic of the deep learning-based model for early-stage lung cancer prediction; b) output of classification results after training. Reproduced with permission.\[61\] Copyright 2020, American Chemical Society. c,d) Multiple data processing with high efficiency via ML algorithms: c) schematic of urinary biomarker sensor data from four channels used for prostate cancer detection; d) monotonic accuracy increase for the screening results along with the increase of the number of data channels. Reproduced with permission.\[64\] Copyright 2021, American Chemical Society. e–h) Fusion of multiple modal (somatosensory and visual) data using ML algorithms leading to a recognition accuracy of 100% for hand gestures: e) CNT-based strain sensor; f) digital images from camera; g) schematic of the somatosensory–visual (SV) dataset consisting of 3000 samples (top) along with the illustration of how visual and somatosensory information is processed in the fusing algorithm (bottom); h) best accuracy was achieved via bioinspired somatosensory–visual (BSV) associated learning algorithm. Reproduced with permission.\[51\] Copyright 2020, Springer Nature.
networks when examining the importance of each single biomarker as it directly allows to understand the variables.\(^{[64]}\)

### 2.2.3. Multiple Modal Data Fusion

Performance enhancements of WSES could also be realized by utilizing multiple modal data, which can capture the features of body activities from different perspectives. With ML algorithms, a processing technique termed data fusion plays an essential role in analyzing datasets with multiple modalities. In 2012, Riera et al.\(^{[63]}\) described a data fusion system for stress detection using EEG and facial electromyography (EMG) data. When only taking a dataset from EEG, classification of 79% accuracy can be reached via Fisher discriminant analysis. While integrating EEG and EMG dataset into one system through a fusion operator tree, the observed real-time stress level classification reached an average accuracy of 92% with a maximum of over 97%. Data fusion is demonstrated to be efficient for data feature extraction and result prediction even when one type of dataset is nonideal and noisy. For example, Wang et al.\(^{[51]}\) found that by combing data from both visual (camera images) and somatosensory (stretchable strain sensor made from carbon nanotubes) signals (Figure 3e-h), the accuracy for human gesture recognition can be significantly boosted. Note that it is of critical importance to match the characteristics of the multimodal data to the analyzing capability of specific algorithms. So that the performance improvement of WSES benefiting from the multimodal data fusion can be achieved. For instance, the key strategy proposed by Wang et al. is the bioinspired somatosensory-visual (BSV) data fusion learning architecture that consists of a CNN algorithm for visual data processing and a sparse neural network for somatosensory data processing at the feature level. As demonstrated, the BSV architecture achieved 100% recognition accuracy even when visual data are noisy (i.e., under-over-exposed). Consequently, the BSV model of fusing two modal data performs better than that of single modal data approaches (i.e., only visual or somatosensory) or other algorithm-assisted data fusion methods, including weighted-average fusion (SV-V), weighted-attention fusion (SV-T), and weighted-multiplication fusion (SV-M) (Figure 3h). Thus, it is essential to select an appropriate algorithm architecture for specific combinations of multi-modal datasets based on their characteristics. It is worth pointing out that multiple modal data fusion is not a universal solution of “One-for-All” for boosting the performance of WSE. For instance, Zhou et al.\(^{[17]}\) achieved an accuracy of 98.63% for hand gesture recognition by using only somatosensory data from a sensing glove, which is infinitely approaching the result from the BSV model. Therefore, the resource cost of the complexity of processing multimodal data and the number of devices required to collect the corresponding multimodal data should be taken into account for practical application.

### 3. ML-Assisted WSES for Healthcare

Along with the achievements of materials development and data processing, WSES is becoming popular in individuals’ modern lives and healthcare. They also play critical roles as a reliable resource for clinicians to track and monitor diseases and enable interactive and evolving clinical decisions, thus making medical suggestions for patients. Additionally, personalized healthcare monitoring and disease treatment can be realized with the assistance of WSES and intelligent algorithms. In this section, we outline the applications of WSES assisted with ML algorithms for physiological signals monitoring (i.e., biochemical, biopotential, and biophysical signals),\(^{[30,41,79–82]}\) disease diagnosis,\(^{[83–89]}\) and personalized healthcare (i.e., on-demand treatment and assistive devices).\(^{[7,90–93]}\) Some recent examples are highlighted in Table 1.

#### 3.1. Physiological Signals Monitoring

##### 3.1.1. Biochemical Signals

Health status can be readily assessed by analyzing body fluids noninvasively through wearable biochemical sensors for the prognosis, diagnosis, and management of diseases or just for keeping fitness. Many fluids can be efficiently sampled, such as sweat, interstitial fluids (ISF), tears and saliva. Various biomarkers from these fluids, such as molecules, electrolytes (e.g., $\text{Na}^+$, $\text{K}^+$, and $\text{Ca}^{2+}$), and major metabolites (lactate, urea, and glucose), are closely related to health conditions and chronic diseases.\(^{[13,14,15,44,94–96]}\) By tracking and monitoring these biomarkers, screening and predicting related diseases can be done by identifying the abnormal concentration variations. Therefore, timely detection and accurate monitoring of relevant biomarkers are of great importance to avoid any incorrect diagnosis or unnecessary treatments.

Gao et al.\(^{[97]}\) reported a simultaneous analysis on multiplexed biomarkers including sweat metabolites (i.e., glucose and lactate), electrolytes (i.e., $\text{Na}^+$ and $\text{K}^+$), as well as the skin temperature using a flexible integrated sensing array (FISA) (Figure 4a, b). Amperometric sensors are selected for glucose and lactate detection based on the oxidation reactions. Ion-selective electrodes (ISEs) are used to measure $\text{Na}^+$ and $\text{K}^+$ levels, and Cr/Au metal microwires for resistance-based temperature sensing (Figure 4b). With these sensors integrated into one system, the FISA can real-time assessments of detailed sweat profiles even when engaged in prolonged indoor and outdoor physical activities. Figure 4c displays the on-body real-time perspiration analysis when an individual is conducting the stationary cycling at graded load. The FISA monitored each of the signals after the complex signal processing using a silicon integrated flexible circuit board. Note the raw data for sweat metabolites, electrolytes, and skin temperature are in different modalities (i.e., Ampere, Voltage, and Ohm). Therefore, the authors established linear relationships between the target biomarkers and the detected electrical signals (i.e., current, potential, and resistance). So that the level of each target biomarker can be displayed as the units designed. Nevertheless, as a continuous analyzing and monitoring platform, the capability of processing abundant and detailed data of various biomarkers needs to be extended to track the absolute levels and explore the pattern changes of each signal at a system level. Thus, useful output information can be obtained as decision supports for either practical clinic assessment and personalized diagnostic or physiological monitoring applications. One advantage of the FISA is the feasibility of collecting a large volume of datasets relevant to various biomarkers once more voluntary community participation is involved. The next
### Table 1. Progress in ML-assisted WSES for healthcare and human–environment interactions applications.

| Sensor descriptions       | Sensing mechanism        | Data modality | ML (i)   | Model type          | Applications                              |
|---------------------------|--------------------------|---------------|----------|---------------------|-------------------------------------------|
| Ion optics                | Mass spectrometry        | Discrete      | GBDT (i) | Classification      | CF (i) diagnosis                        |
| SF (i) integrated with PPy (i) | Potential               | Time series   | RNN (i) | Classification      | ECC (i) signal monitoring, emotion recognition |
| Printed electrode array   | Potential                | Time series   | HD (i), PCA (i) | Classification      | Hand gesture recognition                        |
| Textile-based capacitor sensor | Capacitive             | Time series   | ANFIS (i) | Classification      | Walking gait analysis, disease prognosis (100) |
| Multilayered pressure sensor | Piezoelectric          | Time series   | DWT (i) | Classification      | Heart health assessment, blood pressure detection (10) |
| CNT (i)-based strain sensor | Triboelectric           | Time series   | N/A | Classification Regression | Pulse and blood pressure monitoring (47) |
| AuNP (i)-based gas sensors | Resistive                | Time series   | PCA | Classification      | VOC (i) detection, lung cancer diagnosis (45) |
| AuNP-based gas sensors    | Raman spectroscopy       | Discrete      | PCA, Resnet (i) | Classification | Lung cancer diagnosis (41) |
| PdNi (i)-based strain sensor | Resistive               | Time series   | L1-distance | Classification | Swallowing monitoring, dysphagia diagnosis (46) |
| Accelerometers            | Potential                | Time series   | DTW, SVM (i), KNN (i) | Classification | Alzheimer disease prognosis (113) |
| Blood glucometer          | Multiple                 | Discrete      | MLP (i), LSTM (i) | Classification Regression | Diabetes monitoring (114) |
| Accelerometers            | Potential                | Time series   | LSTM | Regression          | Parkinsonian tremor severity monitoring (207) |
| AuNP/ligand-based gas sensor | Resistive              | Discrete      | DFA (i) | Classification      | COVID-19 detection (23) |
| PE (i)-based TENG (i) sensor | Triboelectric           | Time series   | SVM | Classification      | Sign language recognition, virtual communication (18) |
| Textile-based TENG sensor | Triboelectric            | Time series   | CNN, PCA | Classification | Prosthetics, human-robot interactions (132) |
| Tattoo-like skin electrode | Potential                | Time series   | LDA (i) | Classification      | Silent speech recognition, emotion detection (127) |
| Tactile glove             | Resistive                | Mapping       | CNN | Classification Regression | Prosthetics, human-robot interactions (132) |
| Tactile vest              | Resistive                | Mapping       | CNN | Classification      | Sitting poses detection, motion monitoring (127) |
| Flexible ECG (i) electrode | Potential                | Multiple      | CNN | Classification      | Brain–machine interfaces (100) |

(i): machine learning; (i): GBDT: gradient-boosted decision tree; (i): CF: cystic fibrosis; (i): SF: silk fibron; (i): PPy: polypyrrole; (i): RNN: Recurrent neural networks; (i): ECC: Electrocardiography; (i): HD: hyperdimensional; (i): PCA: principal component analysis; (i): ANFIS: adaptive neuro-fuzzy network; (i): DWT: dynamic time warping; (i): CNT: carbon nanotube; (i): AuNP: gold nanoparticle; (i): VOC: volatile organic compound; (i): Resnet: residual neural network; (i): PdNi: palladium nanosilads; (i): SVM: support vector machines; (i): KNN: k-nearest neighbor; (i): MLP: multilayer perceptron; (i): LSTM: long-short term memory; (i): DFA: discriminant factor analysis; (i): PE: polyester; (i): TENG: triboelectric nanogenerator; (i): LDA: linear discriminant analysis; (i): ECG: electroencephalography.

The possibility of FISA is to exploit the collected datasets to train predictive algorithms. Consequently, through cross-analyzing the correlation and pattern features of the target biomarkers’ levels, the FISA might further validate the understanding of the health status of individuals. In another example of analyzing perspiration samples, Zhou et al. [49] presented an ML algorithm based on gradient-boosted DT (Figure 4d) to identify cystic fibrosis (CF) using mass spectrometry data, obtaining 98% accuracy by cross-validation. Although the sensing data are not from a wearable device, the concept of implementing ML algorithms to establish understandings on which metabolites and lipids contribute to the prediction of disease state has a far-reaching influence. Therefore, advanced analysis techniques with ML algorithms are of great interest to interpret the sensing data from the WSES, thus enabling the evaluation of the health status of deep tissues via a noninvasive way.

Different data modalities are usually presented for biomarkers monitoring, as shown in the above FISA example. For instance, quantifying the pH and uric acid levels of open chronic wounds is important for monitoring the status of healing and recovery. The signals of these two target biomarkers, as reported by Pal et al. [98] can be detected as current change in (a unit of µA) due to the uric acid oxidation reaction, and resistance change (in a unit of ohm) due to reversible variations of emeraldine salt (ES) form and emeraldine base (EB) form of polyaniline. Using omniphobic paper-based smart bandages (OPSBS), the authors achieved status monitoring by printing conductive carbon and polyaniline inks as electrodes (Figure 4e). Although excellent correlations between current/resistance changes and the pH/uric acid levels can be established through linear regressions, more analysis on the data of biomarkers’ levels via intelligent algorithms is still in need. Then it would become possible to acquire insights into the relationship between the sensing signals of OPSB and the healing process of chronic wounds.

Other types of fluids, including tears and saliva, can also be accessed noninvasively. For instance, Sempionatto et al. [93] (Figure 4f) reported a wearable bioelectronic platform on eyeglasses that is capable of tear alcohol detecting, showing a good correlation to the parallel blood alcohol concentration (BAC) measurements. García-Carmona et al. [94] demonstrated a pacifier-based wearable sensor platform focusing on chemical saliva sensing in newborns, obtaining real-time Amperometric monitoring of glucose with a linear relationship (Figure 4g). Nevertheless, appropriate algorithms will be required to report the concentrations of the corresponding biomarkers for both of these two examples.

#### 3.1.2. Biopotential Signals

Electrophysiological signals recorded from human skin as electrical potential changes can be great indicators of body conditions for healthcare, sports management, and modern lifestyle. Many
Figure 4. Physiological signals monitoring using ML-assisted WSES. a–c) A wearable flexible integrated sensing array (FISA) for in situ sweat analysis: a) A FISA-based smart “wristband” (top) and “headband” (bottom); b) schematic of the FISA’s operation for multiplexed perspiration analysis; c) real-time sweat analysis results from FISA on a subject’s forehead, including multiple biochemicals Na⁺, K⁺, glucose, and lactate. Reproduced with permission. d) Schematic of the bootstrap methods for identifying cystic fibrosis (CF) from perspiration samples. Reproduced with permission. e) An omniphobic paper-based smart bandages (OPSB) for open chronic wounds monitoring. Copyright 2019, Elsevier. f) An eyeglasses-based wearable device on a subject’s forehead, including multiple biochemicals Na⁺, K⁺, glucose, and lactate. Reproduced with permission. g) A pacifier-based sensor for noninvasive saliva biomarker monitoring, including glucose. Reproduced with permission. h–k) A wearable surface electromyography (sEMG) biosensing system for hand gesture recognition with in-sensor adaptive machine learning capabilities, reaching 97.12% accuracy for 13 hand gestures classification: h) the flexible device on a subject’s forearm (left and right bottom) along with the device’s block diagram displaying several main components; i) examples of single-DOF and multi-DOF gestures including finger flexion (flex.); j) three examples data of sEMG and MAV feature values; k) classification of 13 single-DOF gestures based on principal component analysis. Reproduced with permission. l–o) A wearable textile triboelectric sensor for continuously and precise measurement of both systolic and diastolic pressures: l) schematic of the textile cardiovascular monitoring system; m) processing flow of the blood pressure estimation from the measured pulse signal using a machine learning algorithm; n,o) systolic and diastolic blood pressure and result comparisons between the textile triboelectric sensor and a commercial cuff. Reproduced with permission.
noninvasive on-skin electrodes are developed for continuous data collections of electrophysiological signals such as electroencephalogram (EEG)/electrooculography (EOG) of the central nerve system, action potentials of the peripheral nerve system, electrocardiogram (ECG), electromyogram (EMG), and electrooculogram (EOG). From the point-of-view of materials, advances of flexible/stretchable, conformal, self-adhesive, and air-permeable electrodes to tackle the biodevice interfacing issues have been witnessed in the past five years. These material improvements could further facilitate high-quality data collection from stable and reliable signals. For instance,Yang et al.[28] fabricated biocomposite electrodes using silk fibroin as the adhesive layer and polypyrrole (PPy) as the conductive layer via interfacial polymerization. The electrodes can be conformally attached to the skin to reliably collect real-time ECG signals even with skin deformations during sporting and sweating. Therefore, by simply measuring the ratio value of T to R waves from ambulatory ECG when increasing running speed to 8 km h⁻¹, the health status of being healthy or not can be inferred.

From the point of view of data processing, advanced algorithms have attracted great interest in analyzing electrophysiological signals. These algorithms are capable of feature extractions at different levels for various signals that are expected to enable smart health monitoring applications. As demonstrated by Yang et al.[28] further useful information could be inferred from the continuous recordings of ECG by implementing an RNN algorithm. For instance, the classification of human emotions (i.e., “sad” or “happy”) was achieved using their RNN model with 169 features (extracted from ECG signals) for each of the motions. This RNN model is also reliable to analyze ECG signals from different individuals with data variations such as flipped signal, varying heart rate, and translation of heartbeats. This intelligent ECG system is expected to help emotion management to maintain a better mental and physical condition. Note that ECG signals are collected in real-time, but the identification of emotions is done separately afterward, which makes further studies necessary to explore a system-level approach for smart health monitoring and management.

Moin et al.[102] reported a surface electromyography (sEMG) biosensing system for hand gesture recognition using a wearable and conformal electrode array (totally 64 channels) via screen-printing (Figure 4h). Unlike other ML-assisted wearable electronics with external sources for data processing, this sEMG biosensing system is capable of in-sensor adaptive learning and model training and updating through hyperdimensional (HD) computing algorithm locally. Thus, this sEMG system performs better with the inference-resistance ability for real-time hand gesture classification compared to other studies. HD computing has presented profound advantages to execute complicated classification tasks via very high-dimensional vectors (hypervectors) from input information such as physiological signals of sEMG. Figure 4i displays the examples of making gestures with single-DOF (degree-of-freedom) and multi-DOF that would generate different wave forms of sEMG signals. Mean absolute value (MAV), indicating the local amplitude of the sEMG, was used as a color code to segment each waveform at a unit time window of 50 ms (Figure 4j). Then signals are processed and projected into hypervectors using an HD computing algorithm. Figure 4k presents the projected spatiotemporal hypervectors from trial data of single-DOF gestures via PCA. Their results demonstrated a 97.12% accuracy for classifying 13 hand gestures from two participants with algorithm training by only a single trial per gesture. Such in-sensor computing capability with advanced algorithms makes real-time predictions available that would broaden the WSES for instant-response-required applications such as sign-to-speech translation of American sign language.

3.1.3. Biophysical Signals

Physical body motions can be assessed to identify various physiological activities, including movements as subtle as small skin deformations[30,31] and as intensive as hand/arm/leg joint bending and extending.[10,81,103–106] For instance, tracking the walking gait during daily activities was demonstrated using textile socks that are embedded with strain sensors.[105] The pressure from foot pressing during walk induces capacitance changes, which makes it possible to differentiate the four walking gait phases: heel-strike (HS), hell-off (HO), toe-off (TO), and mid-swing (MS). Using data from four strain sensors on the sock as input, the authors applied an adaptive neuro-fuzzy system to analyze strain sensing data, thus classifying phases of walking gait. A hybrid of two learning algorithms is configured: 1) varying the membership functions values to minimize the error through the sum of the squared difference between the output and the real signal; 2) optimizing the fuzzy sets and the fuzzy inference rules through designing fuzzy c-means algorithm. The proposed neural network model reached a mean performance accuracy of 93% (for TO phase), 94% (for MS phase), 96% (for HO phase), ≈100% (for HS phase). What remains important and challenging is to correlate these data from walking gait analysis with body health status, thus facilitating disease prognosis and management (i.e., Parkinson).[107]

One example of exploiting subtle skin movements for biophysical signals is pulse wave monitoring at the wrist. The gentle due to systolic and diastolic behavior of the heart will cause the intra-arterial pressure to rise and fall, which can be detected as perceptible yet gentle pulse beating at the shallower part of the radial artery surface. Given this, high sensitivity of pressure sensors is required for such subtle motion monitoring and tracking. Chu et al.[101] developed an active pulse sensing system using piezoelectric sensors, reaching a sensitivity of roughly 32.6 nA kPa⁻¹, which was demonstrated to capture precision and stable pulses from different individuals. The pattern features of pulse wave forms are important during medical assessments, which, especially for traditional Chinese medicine, are one of the four main diagnostic approaches to predicting and preventing diseases early. To analyze the changes of pulse wave form patterns, the authors deployed a dynamic time warping (DTW) algorithm. The similarity and dissimilarity for each pair of pulse waves from the same or different individuals are reflected through calculating a DTW distance, reaching a true positive rate of 77% accuracy. Note the differentiation of different pulse waves is determined by setting the threshold at different DTW distances, which might be problematic to capture the full spectra of features for each individuals’ pulse wave forms.
In a recent example by Fang et al.,[31] a neural network model was established to conduct an in-depth analysis on pulse wave data for continuous and personalized cardiovascular system characterization. The authors developed an intelligent and durable textile triboelectric sensor as a biomonitoring device integrated with a flexible data processing circuit, a Bluetooth module, and a customized cellphone APP (Figure 4). Two triboelectric materials are selected for their appropriate electron affinity difference: fluorinated ethylene propylene (FEP) and single-walled carbon nanotubes (SWCNTs).[108,109] The triboelectric textile sensor reached a sensitivity of 0.21 μA kPa⁻¹. The perceptible pulse beating at the wrist can bring the periodical contact-separation process between FEP and SWCNTs. Thus, the generated alternating current patterns can be explained as pulse wave forms, of which the characteristics closely reflect the blood pressure changes for the early diagnosis of atherosclerosis diseases. The authors implemented a machine learning model to predict blood pressure in real-time with the collected pulse wave form data. As shown in Figure 4m, after preprocessing the raw data, the extracted pulse wave features are used as input to train a neural network that is configured to output two representative results: the systolic and diastolic blood pressure. Figure 4n displays the continuous results predicted through the ML algorithm for systolic (117.3 ± 3.06 mmHg) and diastolic (70.2 ± 3.5 mmHg) pressure, nicely correlating with results obtained from commercial cuffs (Figure 4o). This example shows that abundant useful information can be obtained from the collected raw biophysical signals with the assistance of implementing appropriate data processing and analyzing techniques. One point is worth noting here is that instead of integrating the computing component in the wearable sensors themselves, developing a customized cellphone APP with a built-in data processing algorithm is a feasible approach that can take advantage of the cellphone’s computing power, thus boosting the prediction performance of WES along with simplification of device structure designs.

3.2. Disease Diagnosis

Data are important indicators of health status. And algorithms facilitate the diagnosis process in terms of efficiency, accuracy, and workload for physicians.[110] When appropriate features are extracted from physiological signals data using WSES, these features could be exploited and correlated with the characteristics of existing health conditions. For example, the pattern changes of physiological signals data might indicate any possible disease formation. Therefore, utilizing the sensing data to monitor and track health status would bring a step forward as decision support for various disease diagnosis. It is commonly known that specific volatile organic compounds (VOCs) in exhaled breath can be linked to various diseases at early-stage formation.[60,65,111,112] For instance, electronic nose (e-nose) or other devices of a similar concept are widely adopted for breath sample detections. Early in 2009, Peng et al.[65] showed a rapid distinguishment of lung cancer patients from the exhaled breath using an array of gold nanoparticles-based sensors (Figure 5a,b). The sensors can rapidly and reversibly respond to a wide range of concentration levels of biomarkers in the breath. The detection is based on the difference of the normal concentration levels of 1–20 ppb in healthy subjects and 10–100 ppb in lung cancer subjects for specific VOCs. The authors analyzed the responses from sensor arrays (through PCA method), accounting for >90% variance of the two groups with clear discrimination of the lung cancer and healthy patterns. Further validation on the prediction model was done using artificial VOCs of the cancerous mixture and healthy breath. Testing results presented a well-confined classification with no overlap between the simulated mixtures of healthy and lung cancer VOCs. It should be mentioned that in the original work by the authors, the sensor array is not designed to be wearable, although it can be easily configured to be portable. Nevertheless, applying an appropriate algorithm to analyze the collected sensing data is still the key to enabling an efficient way for target disease diagnosis by learning the extracted features.

Learning data features is essential as hidden information on specific diseases might be ignored, which is detrimental for cases where early detection and timely/adequate treatment are of great importance. As an example presented by Saidi et al.,[111] they established a detection approach for monitoring urinary creatinine levels without directly measuring any related signals. First, they analyzed the VOCs from breath to identify chronic kidney disease (CKD), diabetes mellitus (DM) and healthy subjects (HS) using e-nose. Totally six sensors are configured with the e-nose, which is sensitive to ammonia (VOC characteristic to CKD), ethanol and acetone (VOC characteristic to DM). Then, they used 18 variables (i.e., three features from each of the six sensors) to describe each measurement by the e-nose. Via the PCA method, the authors demonstrated good classification between CKD, DM, and HS (96.64% of total variance for the first three PCs) using training (80%) and testing (20%) datasets. The classification model is also valid for new VOC samples from new human subjects (Figure 5c). What is more important is the discrimination of healthy subjects with high or low creatinine (HSHC or HSLC), which is usually done via sampling urine. They further conducted partial least squares (PLS) regression on collected data to achieve this goal, revealing a relationship between breath VOC and urinary creatinine concentration level (Figure 5d). Although the whole e-nose device is not readily wearable, the concept of appropriately processing the raw data via a set of algorithms to extract hidden useful information on disease management is profound, especially when the relevant sensing data are incomplete. While miniaturization of sensing units and data processing units is still undergoing, the development of wearable devices for sampling VOCs and intelligent data processing algorithms could promise a fast, easy and cost-effective diagnosis approach for various diseases diagnosis and management.

As discussed earlier, the configured algorithms should also be specific when handling various kinds of data. Thus, the prediction accuracy, model robustness and computing cost could be optimized. For instance, Alzheimer disease classification can be obtained by analyzing patients’ foot movement data. Varatharajan et al.[113] made a comparison of the prediction performance between different algorithms, including the DTW algorithm, inertial navigation algorithm, k-nearest neighbor classifier, and SVM. Results have shown that DTW performs better than others for this specific task since DTW is efficient in
Figure 5. Disease diagnosis using ML-assisted WSES. a and b) An array sensor based on gold nanoparticles for lung cancer distinction by analyzing exhale breathings: a) TEM image of gold nanoparticles (top) and a photo of exhale breathing testing; b) principal component analysis (PCA) of both real and simulated breathing. Reproduced with permission.© 2009, Springer Nature. c,d) An electronic nose (e-nose) capable of distinguishing several diseases from breaths: c) visualization of PCA results on chronic kidney disease (CKD), diabetes mellitus (DM) and healthy subjects with high or low creatinine (HSHC or HSLC); d) prediction of creatinine content in the urine. Reproduced with permission.© 2018, Elsevier. e) illustration of the sensor comprising palladium nanoislands (PdNIs); f–h) illustration of the classification machine learning algorithm for bolus identification with an accuracy of 94.7%. Reproduced with permission.© 2018, American Chemical Society. i,j) A nanomaterials-based sensor array for COVID-19 detection: i) schematic of sensor operation from breathing; j) data classification from sensor responses to breathes achieving 90% and 95% accuracy in discriminating patients with COVID-19 and patients with other lung infections. Reproduced with permission.© 2020, American Chemical Society. k) A model based on eight binary features including five initial clinical symptoms just by asking basic questions to estimate the risk of COVID-19 infections. Reproduced under the terms of CC BY 4.0.© 2021, the Authors. Published by Springer Nature.

warping and aligning data from different patients, thus reducing the side effects of any potential artifact datasets.

Multiple modal data contribute to the robustness and accuracy of disease diagnosis as patients may present more than one abnormal physiological signal for a target disease. Therefore, simultaneously taking the relevant data with different modalities into account is significant for health monitoring and disease management. One example is that patients with diabetic disease usually present abnormal levels on several vital sign data, such as blood glucose, heart rate, blood pressure, and weight. Taking these four vital signs into account, Alfian et al.© 2022 The Authors. Advanced Intelligent Systems published by Wiley-VCH GmbH
WSES, as discussed earlier. Therefore, the concept presented in this work is expected to arouse more interest and efforts to develop system-level devices capable of collecting and processing specific multiple vital sign data for the target disease diagnosis and management.

One advantage of using WSES for disease diagnosis is that the target physiological signals are usually collected in an unperceptive way which will not exert any discomfort on people’s daily activities compared to conventional bulky equipment. This feature becomes even more demanding when onsite physical examinations by the clinician will alter the levels of vital signs. An example presented by Hssayeni et al. investigated the Parkinsonian tremor severity during patients’ various activities of free body movements. By combining algorithms of gradient tree boosting and LSTM with wearable sensors, the authors demonstrated a high correlation \((r = 0.96)\) with results from literature when using unconstrained body movements data. Such a technique could provide a large dataset consisting of a full spectrum of the patients’ tremor history in their natural environment, enabling continuous and accurate monitoring of the true health status.

In contrast to identifying relevant biomarkers of diseases, monitoring biophysical signals of different body regions using WSES could also provide important indicators for disease diagnosis. One example is the discrimination of dysphagic and non-dysphagic swallows by monitoring the swallowing muscle movements at the neck. Ramírez et al. selected a flexible strain sensor (Figure 5e) for muscle motion monitoring. The collected data from different swallowing behaviors were analyzed with the assistance of the ML algorithm (by calculating the LI-distance of the per-class average). So that a new swallowing behavior can be recognized. As shown in Figure 5f-h, first, the given swallowing signals (i.e., 10 mL of water, 15 mL of yogurt, and 6 g of a cracker) were collected (gradient red in Figure 5f) and used to develop the classification model (blue in Figure 5f). Features of each of bolus signals were separately extracted via unsupervised learning. Thus, a new swallowing signal (green in Figure 5g) can be identified by passing through the three classifier models, reaching an 86.4% accuracy. Building on these results, the authors further developed the subject classification model of identifying bolus swallowing signals from a healthy person or patient with dysphagia with an accuracy of 94.7%. One should note that integrating a wireless data transfer module to the wearable strain sensor may be required to enable a comfortable way as noninvasive and home-based systems for monitoring swallowing function and improved quality of life.

Due to the coronavirus 2019 (COVID-19) outbreak, detection and diagnosis are urgently needed, especially for countries and regions where medical resources are limited. Because of the rationale that the emergence of VOCs could occur in the early stages of the infected people, Shan et al. proposed a method to detect at-risk subjects or existing COVID-19 infection by analyzing VOCs from the exhaled breath (Figure 5i). The sensors could generate electrical resistance changes by the relevant VOCs of COVID-19, from which data features can be extracted and exploited to identify a wide range of chemical patterns by developing recognition algorithms. The authors did the statistical analysis using discriminant factor analysis model on three binary comparisons: COVID-19 versus control; COVID-19 versus other lung infections; and COVID-19 first vs COVID-19 s sample. Figure 5j presents the classification results on the binary comparison of COVID-19 versus other lung infections, indicating 90–94% accuracy for the training set and 76–95% for the test set. This rapid test for screening COVID-19 may be a useful rule-out tool as part of a triage process due to its simplicity of highly sensitive signals compared to others using spectroscopy characterizations. A more powerful envision of using such sensors and pattern recognition algorithms is to configure them into smart surgical masks as an epidemic control tool for continuous and real-time monitoring and diagnosis of individuals who may be at risk. A super simple approach was reported by Zoabi for COVID-19 testing using only eight binary features, including five initial clinical symptoms of cough, fever, headache, sore throat, and shortness of breath (Figure 5k). Although bias reporting of symptoms may negatively affect the prediction accuracy, such a simple framework of quick and efficient diagnosis of COVID-19 is still useful when testing resources are limited.

3.3. On-Demand Treatment

Taking advantage of results from continuous and real-time monitoring and diagnosis using WSES, therapy or clinic treatments become a natural next step to achieve disease management. On the one hand, the challenge relies on establishing the appropriate correlation between the drug level and the disease stage. On the other hand, on-demand drug delivery becomes necessary during the evolvement of the individual’s health status to avoid any overtreatments or insufficient treatments. Given this, Keum et al. combined two functions of disease monitoring and treatment into one system. The system, configured into a smart contact lens, is capable of continuous diabetic diagnosis and diabetic retinopathy therapy (Figure 6a-d). First, biosensing of tear glucose levels was achieved based on the electrochemical glucose reaction on the working electrode (WE, Figure 6a). Note the strong correlation between blood and tear glucose levels were confirmed. Thus, it is feasible to use tear glucose level change as an alternative for diabetic disease monitoring and detection. Figure 6b displays the real-time response of electrical current when the glucose concentration is leveling up in vitro, indicating a clear linear relationship with a slope of 0.06 \(\mu\)A/(mg·dl\(^{-1}\)). The authors then combined this biosensor with a flexible drug delivery system (f-DDS) as a smart contact lens for in vivo diagnostic and therapeutic demonstrations (Figure 6c). The functions of glucose sensing and drug delivery were enabled by powers via resonant inductive coupling that is regulated using an application-specific integrated circuit (ASIC) chip. Figure 6d presents the cornea, sclera, and retina fluorescence images of groups with and without genistein drug release by applying the on-demand electrical potential. These results demonstrated the possibility of sensitive glucose monitoring and effective drug delivery using WSES. Nevertheless, limited discussions were presented by the authors on the regulation of on-demand drug delivery by utilizing the glucose-sensing data. Therefore, ubiquitous healthcare with real-time medication may be realized by implementing algorithms on analyzing monitoring data along with the feedback from treatments, thus achieving...
the real on-demand drug delivery for sufficient treatments at the right locations and timing.

As the symptoms or levels of biomarkers of relevant diseases may vary daily, weekly, or monthly, therefore, an appropriate mechanism to trigger the on-demand drug release has to be carefully designed. Two aspects are essential: 1) the drug release procedure should bring about no side effects; 2) the drug release should be timely and sufficient. Lee et al.\textsuperscript{[115]} presented a solution that realized on-demand drug delivery by using phase-change material (PCM) based on the threshold limit of the levels of relevant vital signs. The authors showed a graphene-based wearable patch for sweat-based diabetes monitoring and feedback therapy (Figure 6e). First, the glucose sensor was confirmed to be sensitive and selective to glucose in sweat with no interference from other biomarkers such as lactate, ascorbic acid, or uric acid. Second, the microneedle-based drug loading system is triggered to release the drug once the needle coating layer of phase-change material (PCM) is heated up to the phase transition temperature ($T_c$) (Figure 6f). The authors demonstrated the feedback treatment on diabetic mice when hyperglycemia was detected based on results from glucose level monitoring (threshold limit basis). Figure 6g displays the digital and infrared images with the wearable patch on the skin near the abdomen. The high temperature on the patch region is because of the thermally actuated drug release process, which is triggered once a threshold value of glucose level is reached (i.e., hyperglycemia detected). Treatment effectiveness was demonstrated after the drug was delivered compared to control groups (Figure 6h). One open question which is not discussed in detail by the authors is that how the threshold value of glucose levels is set so that hyperglycemia can be timely and accurately detected as the levels of some biomarkers may rise and fall for unexpected reasons in a short time.
range which might falsely trigger the drug delivery command. A more robust analyzing algorithm on sensing data of vital signs is essential. Therefore, reliable and systematic output information derived from WSES via a deliberately configured algorithm would make a difference in treating chronic diseases such as diabetes mellitus.

For disease treatments, drug dose adjustment at the appropriate treatment stage is critical so that the therapy can be effective and safe with minimum possibility of insufficient treatment or over treatment. However, the suggestions from a physician are usually delayed, especially for chronic diseases, either due to the bias-report from patients or the limited medical resources. Given this, Nimri et al.\[^{[146]}\] reported an automated artificial intelligence-based decision support system (AI-DSS) on adopting insulin pumps and continuous glucose monitoring (CGM) technologies. The data flow of the AI-DSS is shown in Figure 6i. DMS (diabetes management system) was used to upload routine diabetes care data, such as CGM readings, insulin delivery history and carbohydrate intake. These data are passed to the cloud server of AI-DSS, where an algorithm model is configured to comprehensively analyze glucose patterns and insulin dosing events in a similar approach to that used by a physician. One big difference is that the AI-DSS is designed to request the most recent 21 days of data with at least 12 valid days before producing any recommendations or personalized diabetes management tips. Consequently, as demonstrated by the authors, the AI-DSS would not be inferior to physician-guided recommendations in terms of statistically significant reductions in mean glycated hemoglobin level (Figure 6i). This model with intelligent dose adjustment capability is especially useful for intensive insulin management, thus saving patients frequent clinic visits. When properly integrating the AI-DSS with the WSES mentioned above, an envision is that disease diagnosis and treatment would be done in an “imperceptible” way with optimal treatment outcomes. Nevertheless, most reported studies on on-demand drug delivery focus on controlling release rate or release success to the target regions. What might be less addressed is to regulate the drug release process by utilizing feedbacks from biosensing data on relevant biomarkers and assessment data on the disease treatment progress.

### 3.4. Assistive Devices

Functionalities loss, either for newborn babies or for impaired people for various reasons such as accidents or aging effects, is becoming a great burn for the disabled themselves and their families and society.\[^{[117-119]}\] Wearable devices provide an efficient and straightforward way for the disabled to interact and communicate with environments. For instance, one way for speech-impaired persons to communicate with others is sign language which is conveyed by the hands, face and body. However, communication barriers still exist between signers and nonsigners as often prior knowledge is required for non-signers to understand sign language. Alternatively, many combinations of finger motions convey information of single words or simple sentences. Monitoring and analyzing these motions may be feasible to convert the “silent” language into a conversational medium that nonsigners could understand, especially in the natural communication environment. In 2020, Zou et al.\[^{[37]}\] presented an intelligent sign-to-speech translation system that can be worn on a hand for real-time hand gestures translation into the speech of sign language (Figure 7a). The first key is accurately monitoring each finger motion which is realized using yarn-based stretchable sensor arrays. As shown in Figure 7b, the sensor array can detect each finger movement while making signs of number 1, 2, and 4 through hand gestures. By implementing the ML algorithm, features of each hand gesture are extracted, and then they are used for hand gesture classification via a multi-class SVM algorithm. The authors demonstrate a recognition accuracy of 98.63% for 11 sign language hand gestures using 660 samples from four persons. Furthermore, the accurately detected gesture can be converted into speech in a real-time manner using a customized app with a built-in classification algorithm. One limitation might be the recognition accuracy of any unknown hand gestures not in the database or a series of hand gestures consisting of sentences (i.e., multiple words).

An improved model of sign language recognition was reported recently by Wen et al.\[^{[38]}\] using a similar glove solution. Two advances are presented in this work compared to the work mentioned above.\[^{[37]}\] First, the authors included more sensors for detecting the dexterous motions of hands, including ten on fingers, two on the wrists, two on index/middle fingertips, and one on the palm (Figure 7c left). Second, both nonsegmentation and segmentation AI frameworks are implemented for sign language recognition, including various discrete words and sentences from the database and new/never-seen sentences. Figure 7c (right) displays representative sensing signals of the 15 triboelectric sensors when making gestures of the word “Better” and sentence “Do you know the doctor.” The authors utilized the 1D CNN algorithm for processing time-series signals from 50 words and 17 sentences. Recognition effectiveness is further optimized by adjusting the kernel size, the number of filters, and convolutional layers. The visualization of the classification results via PCA presented no overlap, achieving high recognition accuracy of 91.3% for 50 words and 95% for 17 sentences (Figure 7d,e). By further modifying the CNN algorithm via a segmentation manner where signals of sentences are fragmented, analyzed, and reconstructed, new/never-seen sentences can be recognized with an 86.67% accuracy. Such capability of the sign-to-speech translation gloves along ML algorithms may present a step forward to minimize the communication barriers between signers and nonsigners.

For an individual with impaired throat or voice loss, their silent speech can be detected by decoding the sEMG from the jaw that contains lots of voice information.\[^{[120]}\] Liu et al.\[^{[121]}\] reported a demonstration using a flexible epidermal tattoo-like patch capable of recording sEMG for silent speech recognition (Figure 7g). Three patches were attached to a subject’s lower jaw and the left and right sides of the face (i.e., three channels of sEMG signal from targeted muscle groups). While the subject is saying different words such as action instructions (i.e., front, right, and stop) and emotion instructions (i.e., sad, hello, happy), the combined sEMG signals are collected as a dataset which is then processed through linear discriminant analysis model. For instance, a total of 150 and 180 feature vector sets were recorded for five action and six emotion instructions, respectively. Figure 7h presents the visualization of classification results.
Figure 7. Assistive devices for the disabled using ML-assisted WSES. a,b) A wearable yarn-based stretchable sensor arrays (YSSA) system assisted with machine learning algorithm demonstrating a recognition accuracy of \(\approx 98.61\%\) and a recognition time of less than 1 s for sign language hand gesture patterns: a) a subject’s hand with the skin-attached YSSA and the wireless PCB; b) numbers 1, 2, and 4 are expressed using analog signals generated by the YSSA. Reproduced with permission.\(^\text{[37]}\) Copyright 2020, Springer Nature. c–f) Sensing gloves for sign language communication with capabilities of both words and sentences recognition after being equipped with nonsegmentation and segmentation assisted deep learning models: c) locations of total 15 triboelectric sensors on both left- and right-hand gloves, and the corresponding sensing signals (i.e., voltage) of word “Better” and sentence “Do you know the doctor?”; d) Cluster results of word signals from CNN output layer; e) Cluster results of sentence signals from CNN output layer; f) Diagram for the design of the sign language recognition and communication system. Reproduced under the terms of CC BY 4.0.\(^\text{[38]}\) Copyright 2021, the Authors. Published by Springer Nature. g–i) An imperceptible, flexible epidermal surface electromyography (sEMG) tattoo-like patch for silent speech recognition with an average accuracy of \(89.04\%\) for action instructions and \(92.33\%\) for emotion instructions: g) Schematic of the epidermal sEMG patch for patient voice loss; h) visualization of features from sEMG for six emotion instruction; i) flowchart of the augmented reality (AR) interaction via sEMG signals. Reproduced under the terms of CC BY 4.0.\(^\text{[121]}\) Copyright 2020, the Authors. Published by Springer Nature. j–l) A self-powered triboelectric auditory sensor (TAS) as an external hearing aid for hearing-impaired person: (j) schematic of using TAS to allow fully hearing music; k) frequency spectrum of a TAS-based hearing aid; l) sound waves and corresponding acoustic spectrograms of normal, weakened, and restored voices. Reproduced with permission.\(^\text{[122]}\) Copyright 2018, American Association for the Advancement of Science. m–o) A flexible piezoelectric acoustic sensor (f-PAS) assisted by machine learning algorithm for speaker recognition at an accuracy rate of \(97.5\%\): m) schematic of the f-PAS system with multiple channels; n) the trained short-time Fourier transform (STFT) features visualized in t-distributed stochastic neighbor embedding (t-SNE) plot by 2800 training data of 40 people. o) Comparison of recognition error rate between the f-PAS and commercial phones. Reproduced with permission.\(^\text{[19]}\) Copyright 2018, Elsevier.
for six emotion instructions via PCA, demonstrating a 92.7% accuracy. The authors further utilized this sEMG patch for the HMI application, where the emotion instructions from voice loss/impaired person can be vividly represented by a virtual character (Figure 7i). In another example reported by Zhou et al., they decoded the muscle motions information using a bionic triboelectric nanogenerator-based electromechanical sensor. Because of this triboelectric sensor’s high sensitivity (54.6 mV mm⁻¹), the signal intensity from face muscles is much higher (i.e., 206 times) than that of the sEMG approach aforementioned above. The authors further demonstrate the Morse code-based communication aid application by leveraging machine learning algorithms, achieving a 96.3% accuracy of conveying natural conversational information.

Wearable devices are also used for an assistive auditory system to present an efficient and straightforward communication strategy for intelligent robotics and hearing-impaired people. Guo et al. reported a self-powered triboelectric auditory sensor (TAS) with a broad response frequency range (100–5000 Hz). TAS can effectively recover the weakened voice and amplify a specific sound wave naturally (Figure 7j-l). Another advantage of TAS is recording music and accurately recognizing individuals’ voices for realizing intelligent HMI applications. Nevertheless, the authors achieved speakers’ recognition through a simple similarity comparison of the power spectral density estimation and joint time-frequency analysis among different speakers. An advance was presented by Han et al. using a machine learning-based speaker recognition platform by implementing the Gaussian mixture model (GMM) for voice data processing (Figure 7m). The authors designed a self-powered flexible piezoelectric acoustic sensor (f-PAS) to record speech waveforms from which frequency signals were obtained through fast Fourier transform (FFT) and a short-time Fourier transform (STFT). STFT features of different speakers were extracted via GMM analysis which is then displayed in a t-distributed stochastic neighbor embedding (t-SNE) plot (Figure 7n), demonstrating a 97.5% speaker recognition rate with the 75% reduction of error rate compared to reference group (Figure 7o).

In summary, we reviewed the applications of using WSES for healthcare monitoring, disease diagnosis, on-demand treatment, and assistive devices. The physiological signals collected from WSES are analyzed through various algorithms for different applications, such as detecting the concentration levels of relevant biomarkers, tracking and monitoring the disease evolution, optimizing drug dose adjustment for on-demand treatment, and providing health support for people in need.

4. ML-Assisted WSES for Human–Environment Interactions

The intelligent WSES equipped with ML algorithms is a key platform for human-environment interactions. Owning to the powerful capability of data processing of ML algorithms, these WSES can interact with environmental objects in both virtual and real spaces through an imperceptible way because of the excellent wearability, in contrast to the conventional bulky devices. Additionally, when coupled with the visual and auditory devices, the WSES-based tactile and thermal interfaces can further strengthen users’ interactions between reality and the virtual environment with much more realistic and immersive experiences. In this section, we highlighted the WSES-based human–machine interfaces and their applications for virtual and augmented reality. Some representative examples are listed in Table 1.

4.1. Human–Machine Interfaces

The application of a human–machine interface (HMI) using WSES requires efficient and accurate data acquisition from different human body locations. For instance, when the information from various physiological signals (i.e., biophysical, biopotential, and biochemical signals) is continuously transferred to the external machines. Therefore, the potential instructions from these signals can be correctly executed on the machines, thus achieving the designed human-machine interactions. For one thing, some high-intensity movements with a very large extension or contraction range, such as arm and leg swinging during walking, can be easily detected. Some other dexterous movements, such as muscle motions, require highly sensitive sensors which should be soft, stretchable, and compliant. Consequently, the information from these subtle movements can be accurately conveyed to the environment through compliant sensory feedback mechanisms. For instance, a very high gauge factor (>85,000) within a small strain range (<5%) was presented by Araromi et al. The sensing mechanism is based on Ohmic contact changes between conductive meanders embedded within elastic films. The designed sensor is highly suitable for subtle motion monitoring. Given this, the authors constructed a sensorized textile-based arm sleeve (with three sensors integrated) that can track and classify discrete and continuous hand gestures and motions through detecting small muscle contraction in the arm during hand moving or making gestures. By implementing different algorithm architectures, including varying the numbers of hidden nodes and the numbers of both fully connected and LSTM layers for distinguishing dynamic gestures, an 88.29% accuracy of classifying a fist, an open palm and a finger pinch was achieved. They also demonstrated the tracking of the compound, continuous hand moving, such as wrist pronation and supination. With high sensitivity and intelligent algorithms, such textile-based WSES are significantly promising for HMI applications that exert no restrictions for daily human activities under natural conditions. Note that for subtle muscle motions detection, the sensors must be closely attached to the target region, which is realized by wearing a very tight sleeve, thus possibly bringing in issues like discomfort for long-term use. Nevertheless, the trade-off might be overcome through advanced algorithms to analyze quality-compromised data collected from wearing comfortable WSES but less sensitive. In a similar work by Kim et al., the authors proposed an ultrasensitive skin-like sensor based on laser-induced nanoscale cracking that achieves a gauge factor >2000 at 0.55% strain. By attaching this skin-like sensor to the wrist for small skin deformations detection, signals from multiple finger motions were picked up and then were realized for finger motions classification via coupling with the LSTM network, demonstrating an accuracy of 96.2% on average. With the
Figure 8. ML-assisted WSES for human–machine interfaces. a) A textile-based strain sensor-integrated sleeve for hand motion detection to enable human–computer interfaces. Reproduced with permission.© 2020, Springer Nature. b–e) A printed nanomembrane hybrid electronics (p-NHE) enabling the deep learning-embedded electrophysiology mapping to allow all finger motions capture at 99% accuracy; b) schematics of the target muscles with three p-NHE sensors; c) EMG signals from four gestures of an open hand, closed hand and index finger and wrist flexions; d) EMG mapping data showing RMS signals of a hand closed, thumb and index finger motions (left) and the demonstration of controlling a robotic hand; e) 3D plot visualization of the seven gestures based on the EMG RMS signals from three channels. Reproduced under the terms of CC BY 4.0.© 2020, the Authors. Published by Springer Nature. f–h) A scalable tactile glove (STAG) capable of estimating the object weight and exploring the typical tactile patterns that emerge while grasping objects: f) schematic of the STAG to learn the human grasp; g) typical interaction sequence when grasping an object; h) The circular plot shows the relative correspondences between different parts. Reproduced with permission.© 2019, Springer Nature. i–m) A portable, wireless, flexible, skin-like hybrid scalp electronic system (SKINTRONICS) as a universal brain–machine interface to accurately classify the real-time steady-state visually evoked potentials (SSVEP) in the occipital lobe: i) overview of the flexible wireless electronics attached on the back of the neck; j) signal quality comparison three devices; k) EEG data in the time domain with features linearly rescaled between 0 and 1 (top), along with a representative grayscale image (bottom); l) time-domain data using CNN model showing a correct choice with 99.89% probability; m) a confusion matrix representing the real-time tests of time-domain data with an overall accuracy of 94.01%. Reproduced with permission.© 2019, Springer Nature.
assistance of advanced algorithms, this type of skin-like sensors may find their applications in various fields, especially for one-time use in special cases of HMI applications.

Biopotentials from muscle motions at various body regions can be utilized to command machines using WSES. Kwon et al.\[^{190}\] reported a fully printed nanomembrane hybrid electronics (p-NHE) to allow hand-gesture captures by analyzing the sEMG signals from muscles at the forearm (Figure 8b). As three data channels, three sensors are attached to target muscles on the arm of palmaris longus, brachioradialis, and flexor carpi ulnaris (Figure 8b). The p-NHE can pick up the sEMG signals during moving fingers or making hand gestures (Figure 8c) that can be plotted as heat maps using average root-mean-square (RMS) values. Features of RMS are studied through CNN and k-nearest neighbors algorithms. Figure 8e presents the classification results of individual digit controls and multiple hand gestures based on three sEMG signals, with clear separation and overall accuracy of 99% for one channel and 98.6% for three channels. The authors showed the successful replication of human hand motions on a robotic hand, including making a fist and bending single fingers (Figure 8d).

Hand motions are dexterous and informative, which makes hand gesture learning is challenging yet important. Sundaram et al.\[^{192}\] reported a scalable tactile glove (STAG) that consists of 548 sensors for decoding the signature of human grasps (Figure 8f). One advance claimed by the authors is the capability of the sensing glove to differentiate characteristics of objects such as identity, weight, and representative tactile patterns during object grasping. First, the reliability of STAG allows recording videos that consist of tactile pattern evolutions during object grasping (Figure 8g). Therefore, exporting specific frames that have interaction information when objects are in contact with the glove is feasible, which can then be input into a CNN model for training, therefore enabling object identification. Nevertheless, failed trials were observed for objects with similar shapes, sizes or weights, which demand more intelligent devices and algorithms with materials-based texture classification ability. Second, weight estimation was predicted using a dataset from multi-fingered grasps as input to a CNN model, showing a better performance than a linear model. Third, the authors conducted a correlation analysis on the sensors located on different parts of the glove when grasping different objects (Figure 8h), indicating that the thumb usually works with the distal phalanges of large fingers when performing object pick-up. With these results, hand pose can also be identified through tactile maps of the glove with an 89.4% accuracy. The temporal and spatial information of the dynamic human-object interactions is significant to bring a step forward to life-like robotics with the capability of dexterous object manipulation just like human beings.

Brain–computer interface (BCI) is another important way to facilitate human–computer interactions or other external devices, thus enhancing or restoring people’s ability to communicate with others. In 2019, Mahmood et al.\[^{190}\] introduced a wearable and skin-like hybrid scalp electronic system (SKINTRONICS) that is portable, wireless, flexible. The authors claim that the first advantage is the fully integrated packaging of EEG sensors and circuits to enable continuous monitoring and data transmission. The miniaturized skin-conformal system consists of three components: elastomeric hair electrode, skin-like electrode, and wireless electronics (Figure 8i). The SKINTRONICS recorded the steady-state visually evoked potentials (SSVEP) with only two channels on the occipital lobe with a high signal acquisition performance and comparable data transmission rate (122.1 ± 3.53 bits min⁻¹). A closer comparison of the 12.5 Hz SSVEP data demonstrates a reliable and stable signal acquisition property for SKINTRONICS compared to the other two control groups (Figure 8j). The collected SSVEP data were transmitted to a cellphone where an CNN model was trained for real-time EEG signals classification. A two-layer CNN model was configured to identify low-level features of all five SSVEP classes at an accuracy of 94.01% via a real-time manner (Figure 8k–l). As demonstrated by the authors, all six subjects, while wearing SKINTRONICS system at their necks, were able to accurately control three target machines including a wireless electric wheelchair, a wireless mini-vehicle, and a presentation software just by just conducting five simple tasks (null task [eyes closed for alpha rhythms] and gazing at four different LED locations). A recent example was reported in 2021 by Willett et al.\[^{190}\] which successfully demonstrated the translation of the neural activity in the motor cortex into texts by implementing an RNN decoding approach. This is achieved only by imagining to write on a paper with a pen for a subject with paralysis from the neck. First, the neural signals were recorded using microelectrode arrays. Then a series of algorithms, including PCA, t-SNE, and k-nearest-neighbor classifier, are applied to classify each character (i.e., “a” to “z”) with a 94.1% accuracy. The authors also demonstrated the real-time handwritten sentence decoding through an RNN architecture at a comparable typing speed of 90 characters min⁻¹. While intracortical microelectrode array technology is still developing, keeping the robust recording and decoding when changes occur in neural activities, especially for a wireless version with excellent wearability, is still challenging.

### 4.2. Virtual and Augmented Reality Applications

Generally, visual and auditory stimuli are widely used to create virtual reality (VR) and augmented reality (AR) experiences for humans through eyes and ears, thus enabling virtual sensations associated with the physical world. While haptic stimuli, widely detected and monitored by WSES, have not been fully explored for VR/AR applications.\[^{133–137}\] Some applications of haptic systems are already present in the market, such as smartphones and watches, game joystick, and vests and gloves, which are integrated with modular tactile devices.\[^{138,119}\] However, one potential limitation for these products is the difficulty of conformably attaching them onto one or all regions of the human body. Consequently, thin, lightweight, soft/stretchable, and skin-integrated devices represent a promising direction for haptic interfaces. In 2019, Yu et al.\[^{139}\] described a wireless, battery-free platform of electronic systems for VR applications through haptic interfaces. Figure 9a shows the schematic design of the haptic platform, including millimeter-scale vibration actuators in soft, conformal sheets. This epidermal VR interface enables information communication via spatio-temporally programmable vibration patterns by compliantly attaching it to the skin. One example, as demonstrated by the authors, was virtual social interactions. During video chatting, if one touches his/her friend’s
hand through the touch-screen interface of a laptop, this virtual touch sensation can be experienced by the friend when wearing epidermal VR interfaces on his/her forearm through a form of continuous vibration excitation (Figure 9b). For prosthetic devices, this epidermal VR interface can help establish tactile feedback for users. As shown in Figure 9c,d, the characteristics of object grasping by the prosthetic hand, such as object shapes and estimated weight, can be used as input data on the epidermal VR interface mounted on the lower arm. Thus, users virtually experience the sensations of the objects when picking up. As shown in the schematic, the tactile feedback was created by the array of miniature actuators, which may have a limited capability to mimic the spatial tactile sensation in terms of resolution. Thus, the accurate information conveys (i.e., the hand gesture) from one to another via this epidermal VR interface might be compromised. Potential improvement could be made by physically increasing the density of the actuator array. Alternatively, advanced and precise interpretation of the interaction information with ML algorithm could further facilitate the control and execution of epidermal tactile interface devices, expanding the sensation from 2D to 3D with ample information of object shapes, weight and weight distributions. Note the dexterous information of hands during object graphing or other activities could be recorded by the sensing glove mentioned above (Figure 8f-h). Consequently, more realistic sensations through this epidermal VR interface are envisioned, along with further vibration excitations optimization beyond the intensity, frequency, pattern, and out-of-plane motion.

Thermal perception, a very common and essential skill of people’s daily lives, is expected to enable the improved thermal sensation of realism in virtual reality (VR) for users. Kim et al.[140] reported a thermal display glove integrated with piezoelectric sensors for hand motion sensing and flexible thermoelectric devices (TEDs) for bidirectional thermal stimulus (i.e., warm and cold) on the skin. Figure 9e displays the operation schematics of the physiological process and the interaction with a virtual object by wearing the thermal glove. Flexible TEDs are mounted on the front side of the thumb, index finger, middle finger, and upper part of the palm (Figure 9f). Thus, hot or cold feelings will be experienced by users through hands immediately when in contact with an object in the VR environment because of the fast temperature fluctuation ability of TEDs (10 °C within 0.5 s). As claimed by the authors, one advantage is the enhanced immersion in the VR environment for users because of the simultaneous haptic and thermal stimulations and the good wearability of gloves. Nonetheless, the thermal sensation is still limited by the number of TEDs used and the locations of TEDs attached. Thus, the temperature gradient of virtual objects might be ignored by the device. Another example was demonstrated by the same research group showing tactile and thermal responses (Figure 9g,h).[141] After transmitting the finger motions of the object grasping into the virtual environment, the user can readily experience the real tactile feedback on fingers of the virtual touch through the glove-integrated electrostatic force-based actuators. The haptic sensation in the current example might be ambiguous (i.e., just a simple compression feeling) with no object shape or weight information.[19,132] It should be noted that the tactile information among human-object interactions can be technically decoded using sensing gloves. Thus, combining the haptic and thermal interfaces into a unified sensing glove with the assistance of an ML algorithm could be one direction for the future “Meta Universe.” So that users can experience a more realistic sensation when grasping hot objects in a virtual environment. Nevertheless, coupling tactile and thermal sensations into one system, these VR interfaces would expand users’ interactions between reality and the virtual environment with much more realistic and immersive experiences along with visual, auditory, and haptic stimuli.

A recent advance of artificial multimodal sensations, including thermal and tactile stimuli, was also reported by You et al.[142] using a skin-like thin-film device with a multilayer structure (Figure 9i,j). Measurements on temperature and strain were realized simultaneously through analysis of the charge relaxation time and normalized capacitance change of the ion conductor. Figure 9k presents a few cases of the collected thermal and strain signals from two fingers stimulation, including pinch, spread, twist, and shear/touch. Such ability to monitor multimodal sensations would facilitate the learning process of human–environment interactions, enabling dedicated interactions when interfacing with virtual objects. One promising direction to enable high immersive VR and AR applications is to include as many sensations as possible, such as visual, auditory, tactile, thermal, and even gustatory and olfactory feelings.

The first challenge is to learn the detailed signatures of these sensations when one is interfacing with real environments. Such a learning process is currently in the very infant phase and will mature together with the advances in new materials and integrated devices and the broad deployment of intelligent algorithms for digesting a large quantity of sensing data. The second question relies on how to efficiently replicate the sensations from virtual interactions on real human bodies. Virtual interfaces of visual and auditory, and especially tactile sensations, have demonstrated some possibilities in the examples mentioned above with enhanced immersions. An additional requirement for smart VR/AR devices is to avoid any clumsy burden for wearing. For instance, epidermal VR/AR interfaces are desired to be theoretically undetectable when being used with at least no cumbersome wearability for users. Bulky external sources or rig structures would compromise some type of sensations, especially the tactile perception on hands with dexterous motions. Lee et al.[143] reported a pressure sensor consisting of gold nanomesh capable of monitoring finger pressure when manipulating external objects but with no detectable effects on human haptic sensing (Figure 9l). The imperceptibility of sensors, when worn on bodies or attached on skins with interference on human’s natural sensations, is essential for highly immersive VR/AR applications.

5. Conclusions and Perspectives

The trend of integrating ML techniques with the WSES has been promising for various application scenarios in the past few years. The seamless combination of these two technologies is expected to transform the conventional paradigms in many fields such as healthcare (vital signs monitoring and tracking, disease diagnosis and treatment), intelligent HMI, and multiple sensations-based VA/AR applications.[12,97,102,144–146] ML-assisted WSES
Figure 9. ML-assisted WSES for virtual and augmented reality applications. a–d) A wireless haptic electronic system capable of softly attaching on the skin and information communication via localized mechanical vibrations: a) schematic of the structure of the epidermal VR system; b) illustration of the pattern of “virtual touch process” and “sense of virtual touch”; c,d) the device produces a haptic pattern of sensation (“think and feel”) that reproduces the shape characteristics of objects (“feedback”) held in the robotic hand (“sensing”). Reproduced with permission. Copyright 2019, Springer Nature. e,f) A thermal display glove system capable of hand motion sensing and bidirectional thermal stimulus on skin: e) schematic of the operation of the thermal display glove linked to the virtual environment; f) the components of the thermal display glove. Reproduced under the terms of CC BY 4.0. Copyright 2020, the Authors. Published by Springer Nature. g,h) A soft virtual reality glove system capable of transmitting a virtual finger touch as tactile feedback to the real finger via pneumatic actuators; g) operation mechanism of the actuators; h) manipulating a virtual object by the movement of fingers in reality. Reproduced under the terms of CC BY 4.0. Copyright 2019, the Authors. Published by Springer Nature. i–k) A flexible multimodal ion-electronic skin (IE^M-skin) capable of differentiating thermal and mechanical stimuli without signal interference: i) photograph of the IE^M-skin attached to a dummy hand; j) structure of the IE^M-skin and k) its response to a shear force, including strain fields under multiple stress (digital images) along with temperature and strain profiles. Reproduced with permission. Copyright 2020, American Association for the Advancement of Science. l) A nanomesh pressure sensor with no detectable effects on human sensation when being attached on skins: 1) nanomesh sensor on the finger; 2) cross-section of the sensor; 3) grasping an object while nanomesh sensors measure the grip force via capacitance change; 4) measured grip force for six different objects. Reproduced with permission. Copyright 2020, American Association for the Advancement of Science.
brings many possibilities and fascinates the intelligent futures because of the improved capabilities on various aspects, such as accurate features classification and prediction of sensing data, efficient processing of high volume and dimension dataset, and capable of analyzing multimodal physiological signals. Despite such great efforts and achievements, challenges to the augmentation of algorithms or devices or both and obstacles to the large-scale employment of these ML-assisted WSES for practical applications remain goals. Here, we outline and highlight some of these challenges and obstacles.

5.1. Seamless Integration of Multiple Components

Applications of the WSES for healthcare or HMI generally require more than one vital sign or multiple body motions. Such demand can be met using an array of sensors with different functionalities or combining multiple individual devices into one system. These solutions might compromise the results of bio-monitoring or disease diagnosis due to unavoidable signal crosstalk interference. Additionally, external data acquisition equipment is still present for some reported studies on the WSES, making the miniaturization of devices at a system level still an issue. Furthermore, adding other components of a typical integrated device, such as power unit, data processing and transmission unit, and the wireless unit, into the WSES make the whole system wearable-friendly still a great challenge. These units are usually made of rigid materials and can be tailored to be soft and flexible by manipulating the device dimensions. Thus, this hybridization strategy of heterogeneous components within one system is widely deployed under the current material, and device paradigm and intensively studied for wearable applications. Nevertheless, interface issues between different components with a wide range of mechanical properties are still obstacles that usually bring about signal artifacts or data loss due to mechanical delamination.

5.2. Stable and Durable Performance

The requirement for capability for long-term use is indispensable when practical applications of the WSES become a reality. Useful information can be extracted from reliable and continuous monitoring data of a wearable device that might be affected by many factors from the devices themselves. For instance, most WSES are soft, flexible, and stretchable, making the stable and reliable output potential issues. Mechanical degradation after cyclic bending or stretching reduces the sensitivity of sensors, thus conceivably providing inaccurate information on health status and medical suggestions. Body motions induced artifacts for the WSES during daily use are also obstacles. ML algorithms show strength in extracting data features from the quality-compromised raw dataset, thus helping stabilize the performance of the WSES.

5.3. Advanced and Application-Tailored Algorithms

Although the advances of the WSES make the collected raw data of physiological signals available in large quantity and high quality, decoding these data into easy-understandable and direct-useful information that correlates with physiological activities or body movements is challenging. Most of the algorithms implemented in the WSES are supervised approaches that require data labeling. However, the variations of physiological signals from different individuals present great challenges for labeling new datasets with no compromised classification and prediction performance. A promising approach is to apply unsupervised ML algorithms to achieve comparable performance using unlabeled data for training. Or a hybrid approach of semi-supervised technique may present an alternative for both the labeled and unlabeled data. Another challenge relies on the optimization of matching ML-assisted WSES with expert knowledge for healthcare, thus providing supports to the existing clinical decision-making system. Additionally, utilizing ML algorithms for the early diagnosis of diseases may be undermined as hidden information of different diseases from the collected physiological data might be ignored by the algorithm. With the further development of new materials and device fabrication techniques, sensing data with different modalities can be obtained from different wearable sensors, such as strain sensors, ultrasound sensors, photoluminescence sensors, or others. Consequently, these multi-modal data could facilitate the performance improvement of using WSES for disease diagnosis. Meanwhile, developing an application-specific algorithm (i.e., corresponding to a specific modality of sensing data) is highly desired so that prediction and classification results are reliable sources for medical suggestions.

5.4. Power-Performance Consideration

For some cases, the sensing unit of the WSES can be designed to be self-powered. Nevertheless, the total energy consumption for WSES, including the sensing unit, data pre-processing units (i.e., amplifier, filters, and ADC), and Bluetooth transceiver etc., is usually substantial, especially when the on-site SoC (i.e., FPGA) is integrated for complex data processing by implementing machine learning algorithms (Figure 4h). One way is to deploy miniature-size units with low power consumption at the cost of compromised yet acceptable performance. Isolating the high-power-demand units from the WSES is another way to avoid the inclusion of bulky batteries. For instance, the computing unit with high power demand can be realized by benefiting the SoC capacity on a smart mobile phone. This design adds additional data transmission between the WSES and the computing unit (i.e., smartphone) via Bluetooth. Nonetheless, too frequent data movements in large amounts along the signal chain from the sensing unit to a computing unit may result in more energy consumption. Thus, edge computing capability within the WSES that demands less power is a promising trend to solve the power-performance dilemma further. [147]

In conclusion, exploring new materials and intelligent algorithms initiates the beginning of the WERE for potential applications in healthcare, medical treatment, HMI and VR/AR, etc. By tailoring algorithms, augmented sensing performance and operation quality of the WSES become possible, pushing a step forward to realize the practical deployments. Despite the challenges mentioned above, research groups worldwide are actively exploring new possibilities to tackle these obstacles.
We believe that ML-assisted WSES will enable many new possibilities in materials and algorithms development for broad applications.

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Conflict of Interest
The authors declare no conflict of interest.

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