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Artificial Intelligence in Healthcare: Review and Prediction Case Studies

Guoguang Rong [a,b], Arnaldo Mendez [c], Elie Bou Assi [c], Bo Zhao [d], Mohamad Sawan [a,b,c,*]

[a] School of Engineering, Westlake University, Hangzhou 310024, China
[b] Institute of Advanced Study, Westlake Institute for Advanced Study, Hangzhou 310024, China
[c] Polystim Neurotech Laboratory, Polytechnique Montréal, Montréal, QC H3T1J4, Canada
[d] Institute of VLSI Design, College of Information Science and Electronic Engineering, Zhejiang University, Hangzhou 310027, China

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ABSTRACT

Artificial intelligence (AI) has been developing rapidly in recent years in terms of software algorithms, hardware implementation, and applications in a vast number of areas. In this review, we summarize the latest developments of applications of AI in biomedicine, including disease diagnostics, living assistance, biomedical information processing, and biomedical research. The aim of this review is to keep track of new scientific accomplishments, to understand the availability of technologies, to appreciate the tremendous potential of AI in biomedicine, and to provide researchers in related fields with inspiration. It can be asserted that, just like AI itself, the application of AI in biomedicine is still in its early stage. New progress and breakthroughs will continue to push the frontier and widen the scope of AI application, and fast developments are envisioned in the near future. Two case studies are provided to illustrate the prediction of epileptic seizure occurrences and the filling of a dysfunctional urinary bladder.

1. Introduction

Artificial intelligence (AI) is defined as the intelligence of machines, as opposed to the intelligence of humans or other living species [1,2]. AI can also be defined as the study of "intelligent agents"—that is, any agent or device that can perceive and understand its surroundings and accordingly take appropriate action to maximize its chances of achieving its objectives [3]. AI also refers to situations wherein machines can simulate human minds in learning and analysis, and thus can work in problem solving. This kind of intelligence is also referred to as machine learning (ML) [4].

Typically, AI involves a system that consists of both software and hardware. From a software perspective, AI is particularly concerned with algorithms. An artificial neural network (ANN) is a conceptual framework for executing AI algorithms [5]. It is a mimic of the human brain—an interconnected network of neurons, in which there are weighted communication channels between neurons [6]. One neuron can react to multiple stimuli from neighboring neurons and the whole network can change its state according to different inputs from the environment [7]. As a result, the neural network (NN) can generate outputs as its responses to environmental stimuli—just as the human brain reacts to different environmental changes. NNs are typically layered structures of various configurations. Researchers have devised NNs that can do ① supervised learning, where the task is to infer a function that maps an input to an output based on example pairs of inputs and outputs; ② unsupervised learning, where the task is to learn from test data that has not been labeled, classified, or categorized, in order to identify common features in the data and, rather than responding to system feedback, to react based on the existence or inexistence of identified common features in new data; and ③ reinforced learning, where the task is to act within the given surroundings in order to maximize rewards and minimize penalties, both according to some form of accumulative nature [8]. With the advancement of computation power, NNs have become "deeper," meaning that more layers of neurons are involved in the network to mimic a human brain and carry out learning. In addition, more functions can be incorporated into the NN, such as merging feature extraction and classification functions into a single deep network—hence the technical term "deep learning" [9,10].

From a hardware perspective, AI is mainly concerned with the implementation of NN algorithms on a physical computation platform. The most straightforward approach is to implement

* Corresponding author.
E-mail address: sawan@westlake.edu.cn (M. Sawan).

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NN algorithm on a general-purpose central processing unit (CPU), in a multithread or multicore configuration [7]. Furthermore, graphical processing units (GPUs), which are good at convolutional computations, have been found to be advantageous over CPUs for large-scale NNs [11]. CPU and GPU co-processing has turned out to be more efficient than CPU alone, especially for spiking NNs [12,13]. Moreover, some programmable or customizable accelerator hardware platforms, such as field-programmable gate arrays (FPGAs) and application-specific integrated circuits (ASICs), can implement NNs toward a customized application in a more efficient way, in terms of computation capability, power efficiency, and form factor [14]. Compared with GPU and CPU, these platforms can be customized for a specific application and thus can be more power efficient and compact than GPU and CPU platforms. To deploy AI in edge devices, such as mobile phones in wireless networks or sensor nodes in the Internet of Things (IoT), further improvements in power efficiency and form factor are needed. Researchers have tried to implement AI algorithms using analog integrated circuits [15,16], spintronics [17], and memristors [18–20]. Some of these new platforms, such as memristor crossbar circuits [21], can merge computation with memory and thus avoid the problem of access to the "memory wall" of traditional von Neumann architectures. This access is mandatory in order to update needed parameters. Recently, researchers have tried to improve the efficiency of AI implementation by reducing the number of bits used for data representation. It turns out that the computation accuracy can be maintained when the data representation goes from 32 or 16 bits down to 8 bits. The advantage is faster computation, less power, and smaller form factor [22]. However, the "memory wall" limits remain. On the other hand, the adoption of appropriate training methods (e.g., deep training instead of surface-level training [23] or using pre-training techniques [24]) and the use of balanced datasets [25], sufficient amounts of data [26], and constant availability [27] of datasets are important factors to consider in order to achieve satisfactory performance of ANNs.

Due to the rapid development of AI software and hardware technologies, AI has been applied in various technical fields, such as the IoT [28], machine vision [29], autonomous driving [30,31], natural language processing [32,33], and robotics [34]. Most interestingly, researchers in the biomedical fields have been actively trying to apply AI to help improve analysis and treatment outcomes and, consequently, increase the efficacy of the overall healthcare industry [35–37]. Fig. 1 shows the number of publications in this area in the last 20 years, from 1999 to 2018. The growth of interest is obvious, especially in the last five years, and continued growth in future can be forecast. The benefits that AI can offer to biomedicine were envisioned a couple of decades earlier [38]. In fact, reviews have been published on the role of AI in biomedical engineering [36,37]. More recently, new progress has been made in AI and its applications in biomedicine.

This paper reviews recent breakthroughs in the application of AI in biomedicine, covering the main areas in biomedical engineering and healthcare.

The goal for healthcare is to become more personal, predictive, preventative, and participatory, and AI can make major contributions in these directions. From an overview of the progress made, we estimate that AI will continue its momentum to develop and mature as a powerful tool for biomedicine. The remainder of this paper is oriented toward the main AI applications. Section 2 includes a description of information processing and algorithm implementation, while Section 3 focuses on disease diagnostics and prediction. Case studies of the prediction of two medical diseases are reported in Section 4. Finally, conclusions are summarized in Section 5.

2. Information processing and algorithm implementation

The main applications of AI in biomedicine can be divided into four categories. The first three categories described in this section are intended to efficiently treat big data and provide quick access to data in order to solve issues related to healthcare. These applications deal with living assistance for elderly and disabled people, natural language processing techniques, and fundamental research activities. The last category of AI applications concerns the diagnosis and prediction of diseases and will be analyzed in Section 3.

2.1. AI for living assistance

In the area of assisted living for elderly and disabled people, AI applications using corresponding smart robotic systems are paving the way for improvements in life quality. An overview of smart

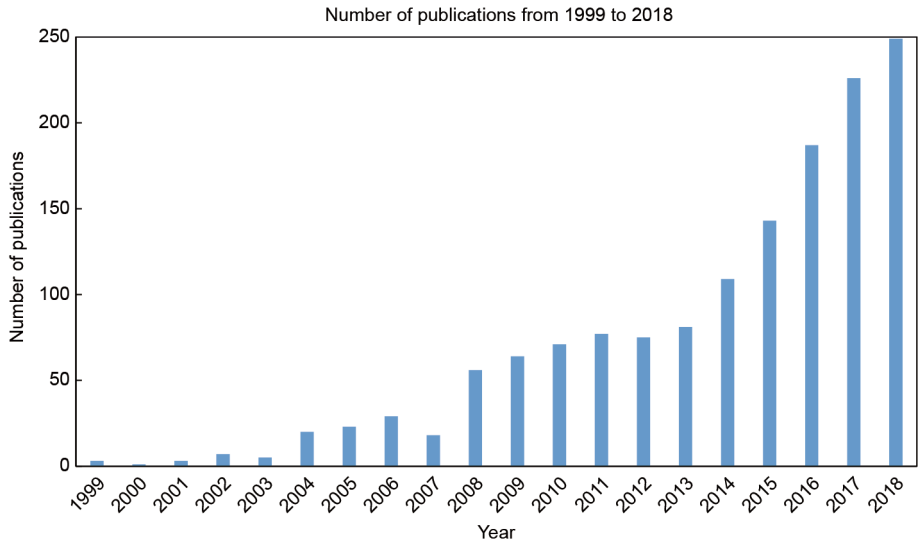

Fig. 1. Growing research interest in the application of AI in biomedicine, as demonstrated by the number of publications on this topic during the last 20 years. The literature search was done using the Web of Science with the topic of "AI" or "ML" and the topic of biomedicine" or "biomedical."

home functions and tools offered for people with loss of autonomy (PLA), and intelligent solution models based on wireless sensor networks, data mining, and AI was published recently [39]. NNs can be trained with specific image-processing steps to recognize human facial expressions as commands. Furthermore, human–machine interfaces (HMIs) based on facial expression analysis allow people with disabilities to control wheelchairs and robot assistance vehicles without a joystick or sensors attached to the body [40].

An "ambient intelligent system" called RUDO can help people who are blind to live together with sighted people and work in specialized fields such as informatics and electronics [41]. People who are blind can make use of multiple functions of this intelligent assistant through a single user interface. A "smart assistant" based on AI can help pregnant women with dietary and other necessary advice during crucial stages of maternity. It is capable of providing suggestions at "an advanced level" through its own intelligence, combined with "cloud-based communication media between all people concerned" [42].

A fall-detection system based on radar Doppler time–frequency signatures and a sparse Bayesian classifier can reduce fall risks and complications for seniors [43]. In fact, "smart communication architecture" systems for "ambient assisted living" (AAL) have been developed to allow AI processing information to be gathered from different communication channels or technologies, and thus to determine the occurrences of events in the network environment and the assistance needs of elderly people [44]. The "ambient intelligence" of smart homes can provide activity awareness and ensued activity assistance to elderly people such that AAL environments allow "aging in place"—that is, aging at home. For example, the activity-aware screening of activity limitation and safety awareness (SALSA) intelligent agent can help elders with daily medication activities [45]. ML in motion analysis and gait study can raise an alarm at hazardous actions and activate preventative measures [46,47]. Fig. 2 [39] shows the model for AAL.

In this scenario, sensors collect data about the ambient environment and human behavior, which is then analyzed by cloud computing or edge intelligence. A decision is then made regarding what actions are necessary, and this decision is used to activate alarms or preventative measures. An expert system based on AI, in conjunction with mobile devices and personal digital assistants (PDAs), can help persons with lasting memory damage by enhancing their memory capabilities so as to achieve independent daily living [48]. This is a significant extension of the expert system for memory rehabilitation (ES-MR) for "non-expert" users.

2.2. AI in biomedical information processing

Breakthroughs have been made in natural language processing for biomedical applications. In the area of biomedical question answering (BioQA), the aim is to find fast and accurate answers to user-formulated questions from a reservoir of documents and datasets. Therefore, natural language-processing techniques can be expected to search for informative answers [49]. To begin with, the biomedical questions must be classified into different categories in order to extract appropriate information from the answer. ML can categorize biomedical questions into four basic types with an accuracy of nearly 90% [50]. Next, an intelligent biomedical document retrieval system can efficiently retrieve sections of the documents that are most likely to contain the answers to the biomedical questions [51]. One novel scheme for processing one of the four basic types of BioQA—the yes-or-no answer generator, which originates from word sentiment analysis—can work effectively toward information extraction from binary answers [52].

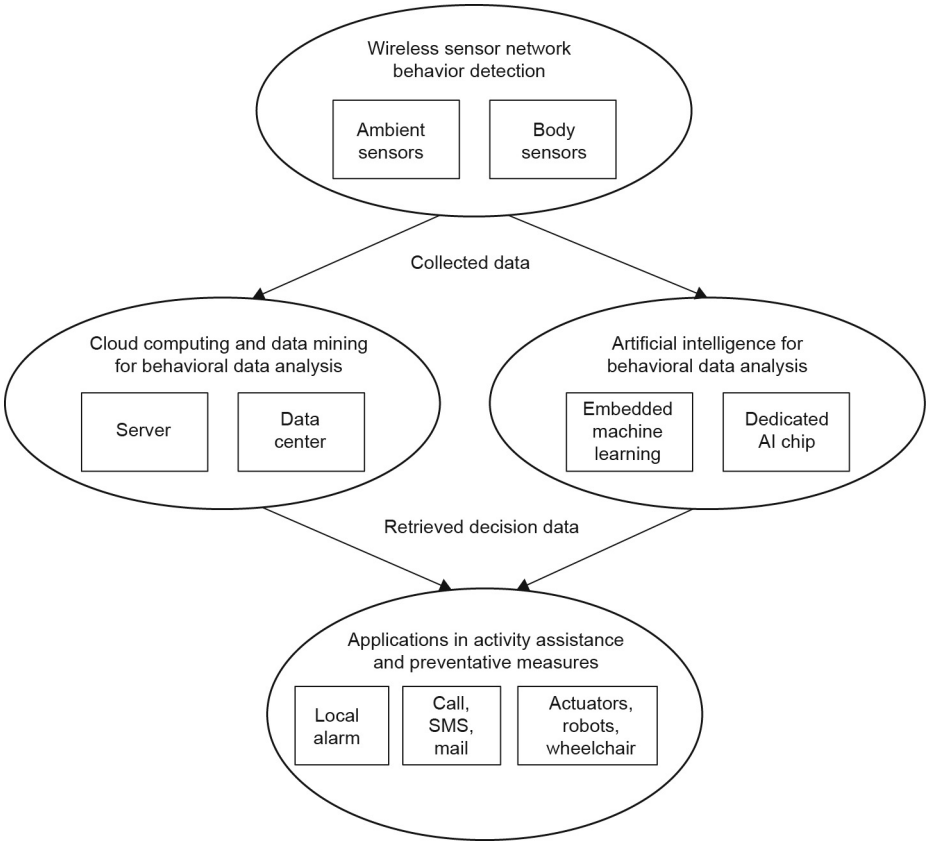

Fig. 2. The proposed model of AAL for "aging in place" [39]. SMS: short message service.

For biomedical information collected from different sources over an elongated period of time, many important tasks can dominate; these are clinical information merging, comparison, and conflict resolution [53]. These have long been time-consuming, labor-intensive, and unsatisfying tasks performed by humans. To improve efficiency and accuracy, AI has been demonstrated to be capable of performing these tasks with results as accurate as professional evaluator can do [54]. Also, natural language processing of medical narrative data is needed to free humans from the challenging task of keeping track of temporal events while simultaneously maintaining structures and reasons [55]. ML can be used to process high-complexity clinical information (e.g., text and various kinds of linked biomedical data), incorporate logic reasoning into the dataset, and utilize the learned knowledge for a myriad of purposes [56].

2.3. AI in biomedical research

In addition to being able to act as an "eDoctor" for disease diagnosis, management, and prognosis, AI has unexplored usage as a powerful tool in biomedical research [57]. On a global scale, AI can accelerate the screening and indexing of academic literature in biomedical research and innovation activities [58,59]. In this direction, the latest research topics include tumor-suppressor mechanisms [60], protein–protein interaction information extraction [61], the generation of genetic association of the human genome to assist in transferring genome discoveries to healthcare practices [62], and so forth. Furthermore, biomedical researchers can efficiently accomplish the demanding task of summarizing the literature on a given topic of interest with the help of a semantic graph-based AI approach [63]. Moreover, AI can help biomedical researchers to not only search but also rank the literature of interest when the number of research papers is beyond readability. This allows researchers to formulate and test to-the-point scientific hypotheses, which are a very important part of biomedical research. For example, researchers can screen and rank figures of interest in the increasing volume of literature [64] with the help of an AI to formulate and test hypotheses.

Some intelligent medical devices are becoming increasingly "conscious" [65,66], and this consciousness can be explored in biomedical research. An intelligent agent called the computational modeling assistant (CMA) can help biomedical researchers to construct "executable" simulation models from the conceptual models they have in mind [67]. Fig. 3 [67] shows a general view of the process flow and interactions between a CMA and human researchers. The CMA is provided with various knowledge, methods, and databases. The researcher hypothesis is expressed in the form of biological models, which are supplied as input to the CMA. The intelligence of the CMA allows it to integrate all this knowledge and these models, and it transforms the hypothesis of the researchers into concrete simulation models. The researcher then reviews and selects the best models and the CMA generates simulation codes for the selected models. In this way, the CMA enables a significantly accelerated research process and enhanced productivity. In addition, some intuitive machines could guide scientific research in fields such as biomedical imaging, oral surgery, and plastic surgery [68,69]. Human and machine consciousness and its relevance to biomedical engineering have been discussed in order to better understand the impact of this development [70].

3. Disease diagnostics and prediction

The most urgent need for AI in biomedicine is in the diagnostics of diseases. A number of interesting breakthroughs have been made in this area. AI allows health professionals to give earlier and more accurate diagnostics for many kinds of diseases [71]. One major class of diagnosis is based on *in vitro* diagnostics using biosensors or biochips. For example, gene expression, which is a

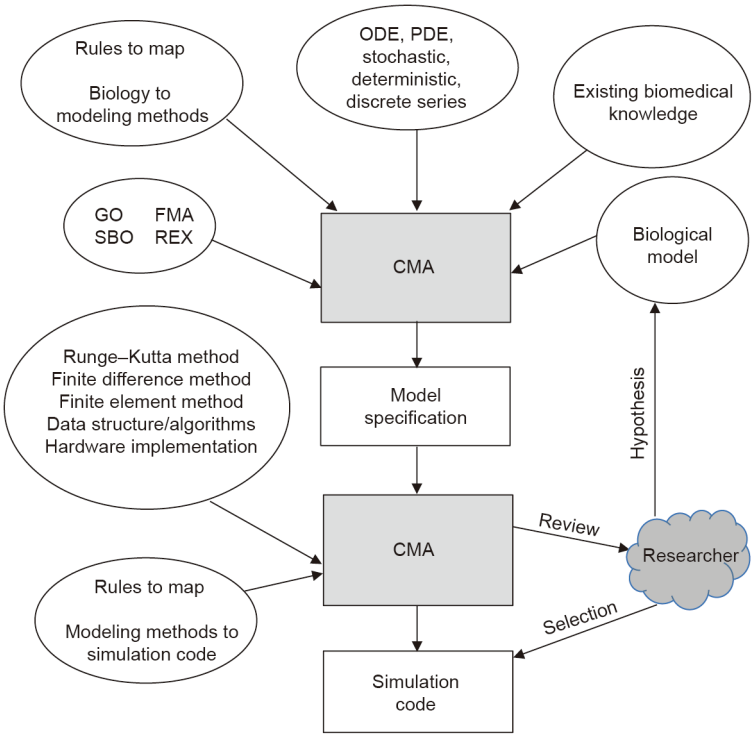

Fig. 3. A general perspective of process flow and interactions between a CMA and human researchers in view of various ontologies and knowledge databases [68]. ODE: ordinary differential equation; PDE: partial differential equation; GO: gene oncology; FMA: foundational model of anatomy ontology; SBO: systems biology ontology; REX: physicochemical process ontology.

very important diagnostic tool, can be analyzed by ML, in which AI interprets microarray data to classify and detect abnormalities [72,73]. One new application is to classify cancer microarray data for cancer diagnosis [74].

With integrated AI, biosensors and related point-of-care testing (POCT) systems can diagnose cardiovascular diseases in the early stage [75]. In addition to diagnosis, AI can help to predict the survival rates of cancer patients, such as colon cancer patients [76]. Researchers have also identified some limitations of ML in biomedical diagnosis and have suggested steps to minimize the effects of these drawbacks [77]. Thus, there is still much potential for AI in diagnostics and prognostics.

Another important class of disease diagnostic is based on medical imaging (two-dimensional) and signal (one-dimensional) processing. Such techniques have been employed in the diagnosis, management, and prediction of illnesses. For one-dimensional signal processing, AI has been applied to biomedical signal feature extraction [78], such as electroencephalography (EEG) [79], electromyography (EMG) [80], and electrocardiography (ECG) [81]. An important application of EEG is epileptic seizure prediction. It is very important to predict seizures so as to minimize their impact on patients [82]. In recent years, AI has been recognized as one of the key elements of an accurate and reliable prediction system [83,84]. It is now possible to predict by means of deep learning [85], and the prediction platform can be deployed in a mobile system [86]. AI can also play an important role in diagnosis based on biomedical image processing [87]. AI has been utilized in image segmentation [88], multidimensional imaging [89], and thermal imaging [90] to improve image quality and analysis efficiency. AI can also be deployed in portable ultrasonic devices, so that untrained personal can use ultrasound as a powerful tool to diagnose many kinds of illnesses in undeveloped regions [91].

In addition to the above applications, AI can assist standard decision support systems (DSSs) [92,93] to improve diagnostic accuracy and facilitate disease management in order to reduce the burden on personnel. For example, AI has been used in the integrated management of cancer [94], to support the diagnosis and management of tropical diseases [95] and cardiovascular diseases [96], and to support the decision-making process of diagnostics [92]. These applications demonstrate that AI can be a powerful tool for early and accurate diagnostics, management, and even prediction of diseases and patient conditions. Two case studies are illustrated below.

4. Healthcare

AI is now covering a wide range of healthcare applications [97]. In particular, it has been used for signal and image processing, and for predictions of function changes such as in urinary bladder control [98], epileptic seizures [99], and stroke predictions [100]. Below, we describe two typical case studies: bladder volume prediction and epileptic seizure prediction.

4.1. Bladder volume prediction

When the storage and urination functions of the bladder fail as a result of spinal cord injury or because of other neurological diseases, health status, or aging, various complications occur in the patient's health conditions. Nowadays, partial restoration of bladder function in drug-refractory patients can be achieved using implantable neural stimulators. To improve the efficiency and safety of neuroprostheses through conditional neurostimulation [101], a bladder sensor that detects stored urine is required as a feedback device that applies electrical stimulation only when needed. The sensor can also be used to notify patients with impaired sensations in a timely manner when the bladder needs to be emptied or when an abnormally high residual post-micturition volume remains after an incomplete voiding.

We have proposed new methods [102] and developed a dedicated digital signal processor (DSP) [103] for sensing both the pressure and its fullness in urine by using afferent neural activities from the regular neural roots of the bladder (i.e., mechanoreceptors), which depicts the changes during filling.

Smart neuroprostheses are typically composed of two units: an internal unit implanted in the patient and an external unit, which is usually carried as a wearable device. Both units are typically connected by a wireless link that conveys data and provides power to the implant. The internal unit performs several functions: neural signal recording; on-chip processing (to a variable extent, depending on the application) of the signals conveying sensory information; neurostimulation of appropriated nerves using functional electrical stimulation (FES) techniques; logical control of the implanted unit functions; and communication with the external unit. When additional signal processing is needed to execute more complex algorithms that require extra computing capabilities, which are not suitable for implantation due to the size, power consumption, temperature rise, electromagnetic emission, and so forth, the internal unit sends the recorded signal to the external unit, which executes more complex algorithms and sends back appropriated neurostimulation commands. The external base station integrates the implant–user interface and the implant–computer interface for greater flexibility.

The work presented in this section is aimed at the design of an effective implantable volume and pressure sensor for the urinary bladder that is capable of providing the necessary feedback to the neuroprosthesis. This sensor can eventually be used for either implementing a conditional neurostimulation approach to restore bladder functions or for bladder-fullness sensing in patients with impaired sensations due to the several diseases and conditions mentioned above. To better meet patients' needs regarding bladder neuroprosthetic devices, we chose to implement within the implantable unit an optimized DSP capable of decoding in real time the bladder pressure and volume. This approach greatly influenced the choice of the most suitable prediction methods, which are described below.

Qualitative and quantitative monitoring methods based on ML algorithms were proposed to decode the afferent neural activity produced by the bladder natural sensors (i.e., mechanoreceptors responding to bladder wall stretching). To implement these methods, the neural activity recorded by the implantable unit must be detected, discriminated (i.e., classified), and then decoded in real time. The proposed qualitative method decodes the bladder fullness into just three levels (i.e., low, medium, and high). This method significantly reduces the number of operations, using fewer hardware resources, so that the power consumption is minimized. The quantitative method needs more complex algorithms to compute the bladder volume or pressure to feedback the closed-loop system for the neurostimulation, but it is optimized to run in the implanted unit with minimum power consumption, thanks to customized hardware.

The monitoring algorithms used for the qualitative and quantitative methods first perform an offline learning phase (also known as a training phase) in real time. During this phase, the sensor learns or identifies the parameters intended for real-time monitoring. For the learning phase, we can choose the best algorithms, regardless of their complexity and execution time, because they are executed offline in a computer connected to the implant through the external unit. Thanks to the learning phase, we can shift the complexity and hardware burden to offline processing, allowing the real-time monitoring phase to be implemented with lower complexity yet effective prediction algorithms and optimized power consumption. The learning phase includes:

(1) Digital data conditioning, which involves band-pass filtering with a non-causal linear-phase finite impulse response (FIR) filter;

(2) Identification of the afferent neural activity with the best correlation with bladder volume and/or pressure (Unit 1 in the example shown in Fig. 4). The Spearman's rank correlation coefficient (ρ) was used instead of the Pearson (linear) correlation coefficient because the former assesses a monotonic dependence, which is not necessarily linear, which improves the robustness of our estimation method. Eq. (1) was used to compute the Spearman's rank correlation coefficient:

$$\rho_k = \frac{\sum_{i=1}^{n}(\mathrm{FR}_{i,k} - \overline{\mathrm{FR}}_k)(V_{i,k} - \overline{V}_k)}{\sqrt{\sum_{i=1}^{n}(\mathrm{FR}_{i,k} - \overline{\mathrm{FR}}_k)^2 \sum_{i=1}^{n}(V_{i,k} - \overline{V}_k)^2}} \quad (1)$$

where ρ_k is the Spearman's coefficient of the class k unit; k is the number of classes detected; i is the counter of timeframes; n is the number of the timeframes used along the recorded signals, henceforward referred to as bins; $\mathrm{FR}_{i,k}$ is the used values of the units' firing rate (FR) per second; $V_{i,k}$ is the mean volume for the same bin; $\overline{\mathrm{FR}}_k$ and $\overline{V}_k$ are the means of all FRs and volume bins relative to class k, respectively;

(3) Computing the background neural activity, where the background baseline is computed by the averaging of the neural FR for 60 s before the bladder is filled with saline;

(4) Volume curve quantization using bins, which results in a finite number of bins with a properly chosen width, henceforward defined as the bin width (BW);

(5) FR integration, which involves computing of the FR within the bins (i.e., the number of spikes detected within the bin for the selected unit), henceforward called the bin-integrated rate (BIR);

(6) Volume or pressure prediction, for which, as mentioned above, we used two algorithms for bladder volume or pressure prediction: a qualitative one to predict three levels of bladder fullness and another to quantify it. A short description of both algorithms is presented below.

The qualitative volume or pressure prediction algorithm predicts three levels representing bladder fullness (low, medium, and high): low volume (a comfortable level), the need-to-void medium volume level (within some predefined time), and the urge-to-void high volume (where there is a risk of urine leaking). The programmed thresholds correspond to 0.25, 0.5, and 1.0 times the full capacity of the bladder volume. By using linear-regression-based algorithms in the learning phase, we computed the BIR for these three degrees of fullness: $\mathrm{BIR}_{0.25}$, $\mathrm{BIR}_{0.5}$, and $\mathrm{BIR}_{1.0}$. Finally, the qualitative volume or pressure prediction was realized by finding the minimum distance within the real-time computed BIR and the stored reference values ($\mathrm{BIR}_{0.25}$, $\mathrm{BIR}_{0.5}$, and $\mathrm{BIR}_{1.0}$). Based on this method, each bin was assigned to one of the three fullness levels. To find the optimal bin length, the BW was swept using different intervals and the length yielding the best (i.e., lowest) qualitative estimation error (E_{qual}) was adopted using Eq. (2). To compute E_{qual} in Eq. (2), we calculated the overall success rate (OSR) [104], which is the ratio of all good classifications of the states over all performed classifications. The OSR is evaluated by adding B_i, the number of bins for which the estimated state matches the actual one, and dividing by the total number of bins (n).

$$E_{\mathrm{qual}} = 1 - \mathrm{OSR} = 1 - \frac{\sum_{i=1}^{n} B_i}{n} \quad (2)$$

To implement the quantitative volume and pressure estimation using a frugal amount of hardware resources, a regression method model was used, as shown in Eq. (3):

$$\hat{V} = \sum_{i=0}^{N}(c_i \times \mathrm{BIR}_i) \quad (3)$$

where $\hat{V}$ is the estimated volume, c_i represents the regression model coefficients. We used the bisquare robust fitting method to compute c_i and minimize the impact of the outlier values [105]. The optimal order (N) for the regression model, shown in Eq. (3), was found by running simulations (trials) with real neural recordings from animal models. By running several simulation trials, we selected the minimal N and the shortest BW, which yielded the lowest estimation error.

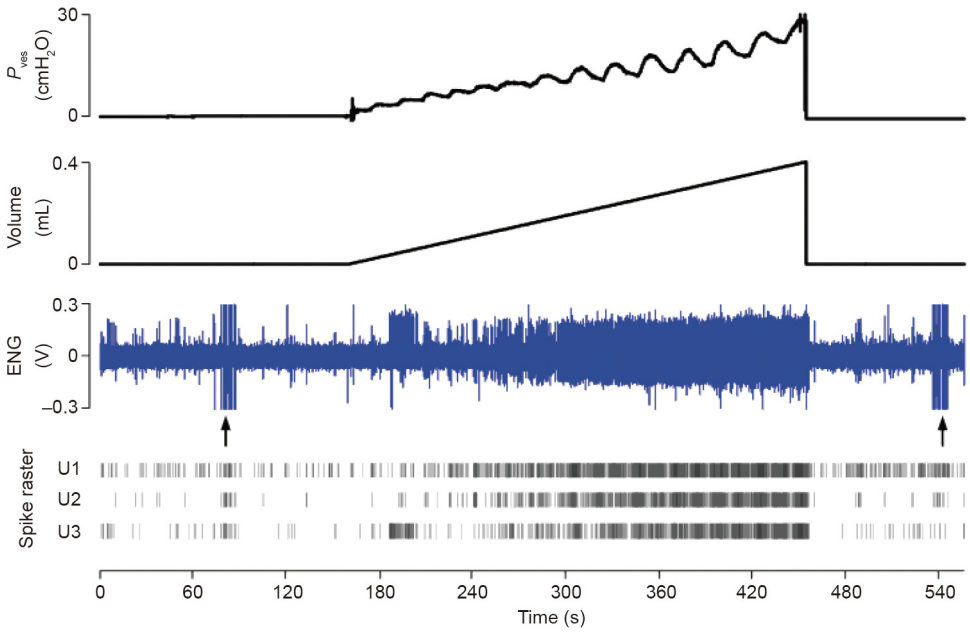

Fig. 4. Bladder afferent neural activity recordings (ENG) during a slow filling. The spike's raster of three units identified is shown. Unit 1 activity exhibited the best correlation with the bladder volume in this example. ENG: electroneurogram; P_{ves}: vesical pressure; U1: Unit 1; U2: Unit 2; U3: Unit 3; 1 cmH_2O = 98.0655 Pa.

Eq. (3) can also be used to estimate the pressure by substituting $\hat{V}$ by $\hat{P}$. The parameters needed for pressure estimation can also be computed during the learning phase.

We used the root mean square error (RMSE), which is computed using Eq. (4), for the validation of the algorithms in real-time-like test runs. In Eq. (4), V_i is the present volume (or pressure, V_P) of the bin i, $\hat{V}_i$ (or $\hat{P}_i$) is the estimated bin of the volume (or pressure) value computed using Eq. (3) for the same bin i, and n is the total number of bins.

$$\mathrm{RMSE} = \sqrt{\frac{\sum_{i=1}^{n}\left(V_i - \hat{V}_i\right)^2}{n}} \tag{4}$$

The real-time monitoring phase runs the following steps: ① digital non-causal filtering; ② on-the-fly spike classification; ③ BIR computing using the optimal BW; ④ comparing the BIR to the baseline and setting the volume to 0 for lower values; and, if the BIR is higher, ⑤ proceeding to compute the bladder volume or pressure using Eq. (3). Several test runs were executed to test and validate our algorithms, as shown in the example in Fig. 5 [106].

Finally, all the proposed algorithms were validated using data recorded from anesthetized rats during acute experiments. More details about these experiments and prediction algorithms are given in Ref. [102].

We succeeded in qualitatively predicting the three states of bladder fullness in 100% of the trials when the recorded afferent neural activities exhibited a Spearman's correlation coefficient of 0.6 or better. We also succeeded in quantitatively predicting the bladder volume and pressure employing time windows of appropriately chosen durations.

We implemented a dedicated DSP, shown in Fig. 6 [106], to monitor the bladder volume or pressure, running the algorithms described above. The DSP runs the on-the-fly spike sorting and sensory decoding of the afferent neural activity of the bladder in real time to predict the volume or pressure value, as described in this section. The dedicated DSP was validated using synthetic data (with known *a priori* ground truth), and with signals recorded from acute experiments from the bladder afferent nerves.

The on-the-fly spike-sorting algorithm runs on the dedicated DSP and compares advantageously with other works reported in the literature [103]. We achieved a higher accuracy (92%) even when using difficult synthetic signals composed of highly correlated spike waveforms and low signal-to-noise ratios. The volume or pressure prediction module showed an accuracy of 94% and 97% for quantitative and qualitative estimations, respectively.

4.2. Epileptic seizure prediction

Epilepsy, a neurodegenerative disease, is one of the most common neurological conditions and is characterized by spontaneous, unpredictable, and recurrent seizures [107,108]. While first lines of treatment consist of long-term medications-based therapy, more than one third of patients are refractory.

On the other hand, recourse to epilepsy surgery is still relatively low due to very modest success rates and fear of complications. An interesting research direction is to explore the possibility of predicting seizures, which, if made possible, could result in the development of alternative interventional strategies [83]. Although early seizure-forecasting investigations date back to the 1970s [109], the limited number of seizure events, the paucity of intracranial electroencephalography (iEEG) recordings, and the limited extent of interictal epochs have been major hurdles toward an adequate evaluation of seizure prediction performances.

Interestingly, iEEG signals acquired from naturally epileptic canines implanted with the ambulatory monitoring device (NeuroVista) have been made accessible through the ieeg.org online portal [110]. However, the seizure onset zone was not disclosed/available. Our group investigated the possibility of forecasting seizures using the aforementioned canine data. Subsequently, we performed a directed transfer function (DTF)-based, quantitative identification of electrodes located within the epileptic network [111]. A genetic algorithm was employed to select the features most discriminative of the preictal state. We proposed a new fitness function that is insensitive to skewed data distributions. An average sensitivity of 84.82% at a time-in-warning of 10% was reported on the held-out dataset, improving previous seizure prediction performances [111].

Trying to find new opportunities for seizure prediction, we also explored novel features to track the preictal state based on higher order spectral analysis. Extracted features were then used as inputs to a multilayer perceptron for classification. Our preliminary findings revealed significant differences between interictal and preictal states using each of three bispectrum-extracted characteristics ($p < 0.05$). Test accuracies of 73.26%, 72.64%, and 78.11% were achieved for the mean of magnitudes, normalized bispectral entropy, and normalized squared entropy, respectively. In addition, we demonstrated the existence of consistent differences between the epileptic preictal and interictal states in mean phase–amplitude coupling on the same bilateral canine iEEG recordings [112].

In contrast, we also explored the possibility of using quantitative effective connectivity measures to determine the network of

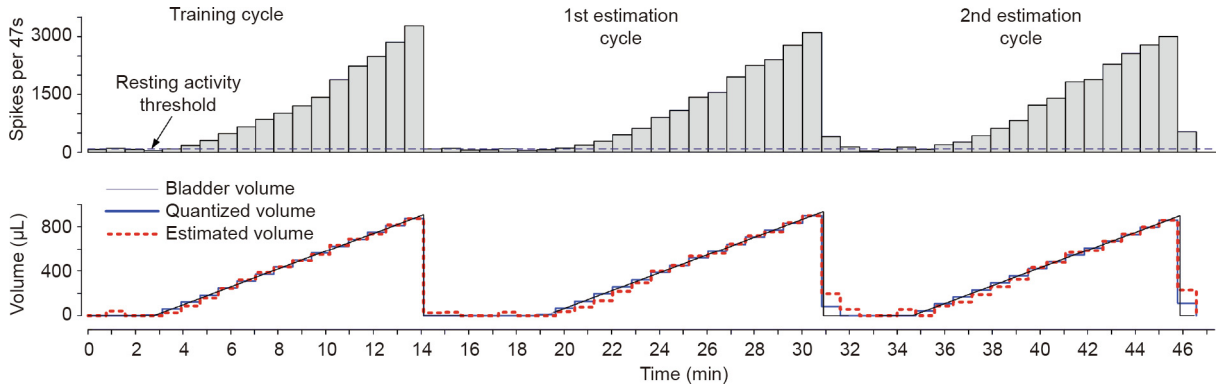

Fig. 5. Quantitative volume estimation in simulated real-time data-processing experiments [106]. The first measurement cycle was used as a training phase, followed by two consecutive cycles where the volume was computed from the training phase. The optimal BW for this fiber was 47 s, using a regression model of order six. The fitting error of the first cycle and the estimation errors of the following two cycles were very low, as shown by the $\mathrm{RMSE}_{\mathrm{all}}$ of each cycle: 2%, 3.9%, and 4.1%, respectively.

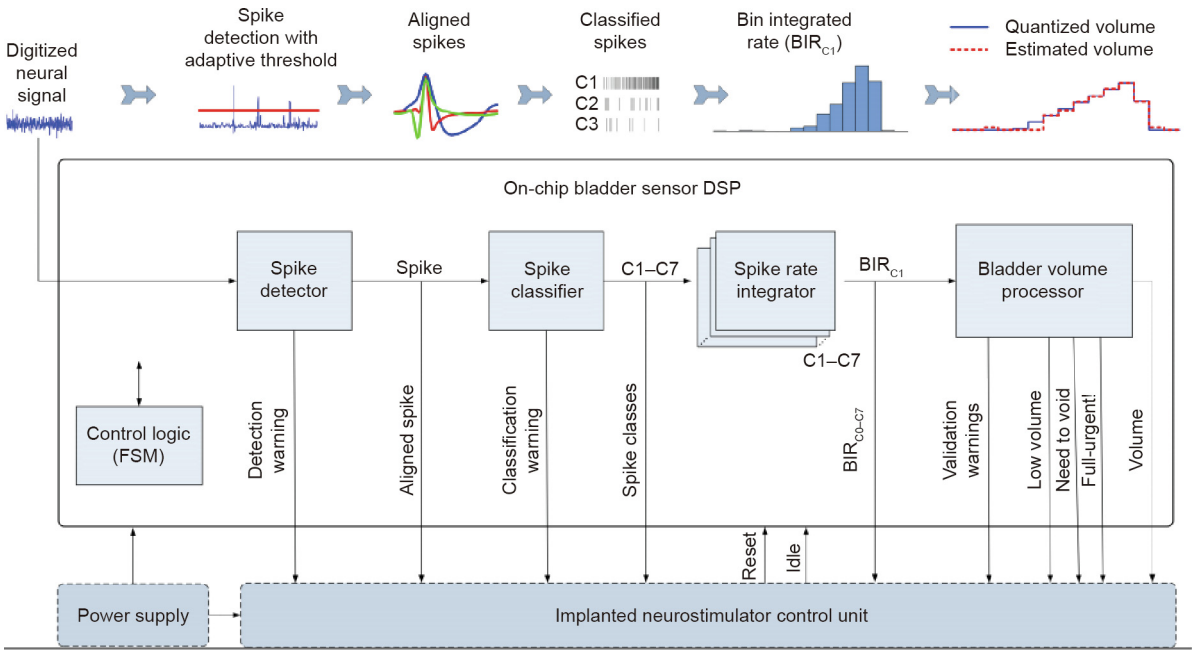

Fig. 6. Dedicated DSP intended for bladder volume or pressure monitoring [106]. FSM: finite state machine; C1–C7: clusters of data classifications.

seizure activity in high-density recordings. The ability of the DTF to quantify causal relations between iEEG recordings has been previously validated. However, quasi-stationarity of the analyzed signals remains a must to avoid spurious connections between iEEG contacts [113]. Although the identification of stationary epochs is possible when dealing with a relatively small number of contacts, it becomes more challenging when analyzing high-density iEEG signals. Recently, a time-varying version of the DTF was proposed: the spectrum-weighted adaptive directed transfer function (swADTF). The swADTF is able to cope with non-stationarity issues and automatically identify frequency ranges of interest [113]. Subsequently, we validated the possibility of finding seizure activity generators and sinks by employing the swADTF on high-density recordings [114]. The database consisted of patients with refractory epilepsy admitted for pre-surgical evaluation at the University of Montreal Hospital Center. Interestingly, the identified seizure activity sources were within the epileptic focus and resected volume for patients who went seizure-free after surgical resection. In contrast, additional or different generators were identified in non-seizure-free patients. Our findings highlighted the feasibility of accurately identifying seizure generators and sinks using the swADTF. Electrode selection methods based on effective connectivity measures are thus recommended in future seizure-forecasting investigations.

Recent findings highlight the feasibility of predicting seizures using iEEG recordings; the transition from interictal into ictal states consists of a "buildup" that can be tracked using advanced feature extraction and AI techniques. Nevertheless, before current approaches can be translated into actual clinical devices, further research is needed on feature extraction, electrode selection, hardware implementation, and deep learning algorithm.

5. Conclusion

In this paper, we reviewed the latest developments in the application of AI in biomedicine, including disease diagnostics and prediction, living assistance, biomedical information processing, and biomedical research. AI has interesting applications in many other biomedical areas as well. It can be seen that AI plays an increasingly important role in biomedicine, not only because of the continuous progress of AI itself, but also because of the innate complex nature of biomedical problems and the suitability of AI to solve such problems. New AI capabilities provide novel solutions for biomedicine, and the development of biomedicine demands new levels of capability from AI. This match of supply and demand and coupled developments will enable both fields to advance significantly in the foreseeable future, which will ultimately benefit the quality of life of people in need.

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Compliance with ethics guidelines

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Nomenclature

AAL	ambient assisted living
AI	artificial intelligence
AN	artificial neural network
ASIC	application-specific integrated circuits
BioQA	biomedical question answering
BIR	bin-integrated rate
CMA	computational modeling assistant
DSP	digital signal processor
DSS	decision support system

DTF	directed transfer function
ECG	electrocardiography
EEG	electroencephalography
EMG	electromyography
ES-MR	expert system for memory rehabilitation
CPU	central processing unit
GPU	graphical processing unit
FES	functional electrical stimulation
FIR	finite impulse response
FPGA	field-programmable gate array
HMI	human–machine interface
iEEG	intracranial electroencephalography
IoT	Internet of Things
ML	machine learning
NN	neural network
PDA	personal digital assistant
PLA	people with loss of autonomy
POCT	point-of-care testing
RMSE	root mean square error
SALSA	screening of activity limitation and safety awareness
swADTF	spectrum-weighted adaptive directed transfer function
FR	firing rate
BW	bin width
OSR	overall success rate

References

[1] Minsky M. Steps toward artificial intelligence. Proc IRE 1961;49(1):8–30.
[2] Weng J, McClelland J, Pentland A, Sporns O, Stockman I, Sur M, et al. Autonomous mental development by robots and animals. Science 2001;291(5504):599–600.
[3] Wooldridge M, Jennings NR. Intelligent agents: theory and practice. Knowl Eng Rev 1995;10(2):115–52.
[4] Huang G, Huang GB, Song S, You K. Trends in extreme learning machines: a review. Neural Netw 2015;61:32–48.
[5] Hopfield JJ. Neural networks and physical systems with emergent collective computational abilities. Proc Natl Acad Sci USA 1982;79(8):2554–8.
[6] Watts DJ, Strogatz SH. Collective dynamics of 'small-world' networks. Nature 1998;393(6684):440–2.
[7] Zucker RS, Regehr WG. Short-term synaptic plasticity. Annu Rev Physiol 2002;64:355–405.
[8] Schmidhuber J. Deep learning in neural networks: an overview. Neural Netw 2015;61:85–117.
[9] LeCun Y, Bengio Y, Hinton G. Deep learning. Nature 2015;521(7553):436–44.
[10] Arel I, Rose DC, Karnowski TP. Deep machine learning—a new frontier in artificial intelligence research. IEEE Comput Intell Mag 2010;5(4):13–8.
[11] Dinkelbach HU, Vitay J, Beuth F, Hamker FH. Comparison of GPU- and CPU-implementations of mean-firing rate neural networks on parallel hardware. Network Comput Neural Syst 2012;23(4):212–36.
[12] Naveros F, Garrido JA, Carrillo RR, Ros E, Luque NR. Corrigendum: event- and time-driven techniques using parallel CPU–GPU co-processing for spiking neural networks. Front Neuroinform 2018;12:24.
[13] Naveros F, Luque NR, Garrido JA, Carrillo RR, Anguita M, Ros E. A spiking neural simulator integrating event-driven and time-driven computation schemes using parallel CPU–GPU co-processing: a case study. IEEE Trans Neural Netw Learn Syst 2015;26(7):1567–74.
[14] Nurvitadhi E, Sheffield D, Sim J, Mishra A, Venkatesh G, Marr D. Accelerating binarized neural networks: comparison of FPGA, CPU, GPU, and ASIC. In: Proceedings of 2016 International Conference on Field-Programmable Technology; 2016 Dec 7–9; Xi'an, China; 2016. p. 77–84.
[15] Bartolozzi C, Indiveri G. Synaptic dynamics in analog VLSI. Neural Comput 2007;19(10):2581–603.
[16] Kwon MW, Baek MH, Hwang S, Park K, Jang T, Kim T, et al. Integrate-and-fire neuron circuit using positive feedback field effect transistor for low power operation. J Appl Phys 2018;124(15):152107.
[17] Grollier J, Querlioz D, Stiles MD. Spintronic nanodevices for bioinspired computing. Proc IEEE 2016;104(10):2024–39.
[18] Jeong H, Shi L. Memristor devices for neural networks. J Phys D Appl Phys 2018;52(2):023003.
[19] Prezioso M, Merrikh-Bayat F, Hoskins BD, Adam GC, Likharev KK, Strukov DB. Training and operation of an integrated neuromorphic network based on metal-oxide memristors. Nature 2015;521(7550):61–4.
[20] Wen S, Huang T, Zeng Z, Chen Y, Li P. Circuit design and exponential stabilization of memristive neural networks. Neural Netw 2015;63:48–56.
[21] Zhang X, Huang A, Hu Q, Xiao Z, Chu PK. Neuromorphic computing with memristor crossbar. Phys Status Solidi A 2018;215(13):1700875.
[22] Yoshida J. IBM guns for 8-bit AI breakthroughs [Internet]. Cambridge: EE Times; 2018 Dec 3 [cited 2019 Jan 17]. Available from: https://www.eetimes.com/document.asp?doc_id=1334029&utm_source=eetimes&utm_medium=networksearch.
[23] Marshall RC, Freed DB, Karow CM. Learning of subordinate category names by aphasic subjects: a comparison of deep and surface-level training methods. Aphasiology 2001;15(6):585–98.
[24] Erhan D, Bengio Y, Courville A, Manzagol PA, Vincent P, Bengio S. Why does unsupervised pre-training help deep learning? J Mach Learn Res 2010;11:625–60.
[25] Yuan X, Xie L, Abouelenien M. A regularized ensemble framework of deep learning for cancer detection from multi-class, imbalanced training data. Pattern Recognit 2018;77:160–72.
[26] Rodríguez-Pérez R, Bajorath J. Prediction of compound profiling matrices, part II: relative performance of multitask deep learning and random forest classification on the basis of varying amounts of training data. ACS Omega 2018;3(9):12033–40.
[27] Dudek-Dyduch E, Tadeusiewicz R, Horzyk A. Neural network adaptation process effectiveness dependent of constant training data availability. Neurocomputing 2009;72(13–15):3138–49.
[28] Chiang M, Zhang T. Fog and IoT: an overview of research opportunities. IEEE Internet Things J 2016;3(6):854–64.
[29] Guo Y, Liu Y, Oerlemans A, Lao S, Wu S, Lew MS. Deep learning for visual understanding: a review. Neurocomputing 2016;187:27–48.
[30] Nguyen H, Kieu LM, Wen T, Cai C. Deep learning methods in transportation domain: a review. IET Intell Transp Syst 2018;12(9):998–1004.
[31] Yang D, Jiang K, Zhao D, Yu C, Cao Z, Xie S, et al. Intelligent and connected vehicles: current status and future perspectives. Sci China Technol Sci 2018;61(10):1446–71.
[32] Alshahrani S, Kapetanios E. Are deep learning approaches suitable for natural language processing? In: Métais E, Meziane F, Saraee M, Sugumaran V, Vadera S, editors. Natural language processing and information systems. Cham: Springer; 2016. p. 343–9.
[33] Kim TH. Emerging approach of natural language processing in opinion mining: a review. In: Tomar GS, Grosky WI, Kim TH, Mohammed S, Saha SK, editors. Ubiquitous computing and multimedia applications. Berlin: Springer; 2010. p. 121–8.
[34] Schaal S. Is imitation learning the route to humanoid robots? Trends Cogn Sci 1999;3(6):233–42.
[35] Yu KH, Beam AL, Kohane IS. Artificial intelligence in healthcare. Nat Biomed Eng 2018;2(10):719–31.
[36] Mamoshina P, Vieira A, Putin E, Zhavoronkov A. Applications of deep learning in biomedicine. Mol Pharm 2016;13(5):1445–54.
[37] Peng Y, Zhang Y, Wang L. Artificial intelligence in biomedical engineering and informatics: an introduction and review. Artif Intell Med 2010;48(2–3):71–3.
[38] Dahal N, Nandagopal N, Nafalski A. Nedic Z. Modeling of cognition using EEG: a review and a new approach. In: Proceedings of 2011 IEEE Region 10 Conference; 2011 Nov 21–24; Bali, Indonesia; 2011. p. 1045–9.
[39] Dahmani K, Tahiri A, Habert O, Elmeftouhi Y. An intelligent model of home support for people with loss of autonomy: a novel approach. In: Proceedings of 2016 International Conference on Control, Decision and Information Technologies; 2016 Apr 6–8; St. Julian's, Malta; 2016. p. 182–5.
[40] Rabhi Y, Mrabet M, Fnaiech F. A facial expression controlled wheelchair for people with disabilities. Comput Methods Programs Biomed 2018;165:89–105.
[41] Hudec M, Smutny Z. RUDO: a home ambient intelligence system for blind people. Sensors 2017;17(8):1926.
[42] Tumpa SN, Islam AB, Ankon MTM. Smart care: an intelligent assistant for pregnant mothers. In: Proceedings of 2017 4th International Conference on Advances in Electrical Engineering; 2017 Sep 28–30; Dhaka, Bangladesh; 2017. p. 754–9.
[43] Wu Q, Zhang YD, Tao W, Amin MG. Radar-based fall detection based on Doppler time–frequency signatures for assisted living. IET Radar Sonar Navig 2015;9(2):164–72.
[44] Lloret J, Canovas A, Sendra S, Parra L. A smart communication architecture for ambient assisted living. IEEE Commun Mag 2015;53(1):26–33.
[45] García-Vázquez JP, Rodríguez MD, Tentori ME, Saldaña D, Andrade ÁG, Espinoza AN. An agent-based architecture for developing activity-aware systems for assisting elderly. J Univers Comput Sci 2010;16(12):1500–20.
[46] Lai DTH, Begg RK, Palaniswami M. Computational intelligence in gait research: a perspective on current applications and future challenges. IEEE Trans Inf Technol Biomed 2009;13(5):687–702.
[47] Chin LC, Basah SN, Yaacob S, Juan YE, Kadir AKAB. Camera systems in human motion analysis for biomedical applications. In: Proceedings of International Conference on Mathematics, Engineering and Industrial Applications 2014; 2014 May 28–30; Penang, Malaysia; 2014. p. 090006.
[48] Man DWK, Tam SF, Hui-Chan CWY. Learning to live independently with expert systems in memory rehabilitation. NeuroRehabilitation 2003;18(1):21–9.
[49] Ben Abacha A, Zweigenbaum P. MEANS: a medical question-answering system combining NLP techniques and semantic Web technologies. Inf Process Manage 2015;51(5):570–94.

[50] Sarrouti M, Ouatik El Alaoui S. A machine learning-based method for question type classification in biomedical question answering. Methods Inf Med 2017;56(3):209–16.
[51] Sarrouti M, El Alaoui SO. A generic document retrieval framework based on UMLS similarity for biomedical question answering system. In: Proceedings of the 8th KES International Conference on Intelligent Decision Technologies; 2016 Jun 15–17; Puerto de la Cruz, Spain; 2016. p. 207–16.
[52] Sarrouti M, El Alaoui SO. A yes/no answer generator based on sentiment-word scores in biomedical question answering. Int J Healthc Inf Syst Inform 2017;12(3):62–74.
[53] Shahar Y. Timing is everything: temporal reasoning and temporal data maintenance in medicine. In: Horn W, Shahar Y, Lindberg G, Andreassen S, Wyatt J, editors. Artificial intelligence in medicine. Berlin: Springer; 1999. p. 30–46.
[54] Rodriguez-Esteban R, Iossifov I, Rzhetsky A. Imitating manual curation of text-mined facts in biomedicine. PLoS Comput Biol 2006;2(9):e118.
[55] Zhou L, Hripcsak G. Temporal reasoning with medical data—a review with emphasis on medical natural language processing. J Biomed Inform 2007;40(2):183–202.
[56] Athenikos SJ, Han H. Biomedical question answering: a survey. Comput Methods Programs Biomed 2010;99(1):1–24.
[57] Handelman GS, Kok HK, Chandra RV, Razavi AH, Lee MJ, Asadi H. eDoctor: machine learning and the future of medicine. J Intern Med 2018;284(6):603–19.
[58] Almeida H, Meurs MJ, Kosseim L, Tsang A. Data sampling and supervised learning for HIV literature screening. IEEE Trans Nanobioscience 2016;15(4):354–61.
[59] Névéol A, Shooshan SE, Humphrey SM, Mork JG, Aronson AR. A recent advance in the automatic indexing of the biomedical literature. J Biomed Inform 2009;42(5):814–23.
[60] Choi BK, Dayaram T, Parikh N, Wilkins AD, Nagarajan M, Novikov IB, et al. Literature-based automated discovery of tumor suppressor p53 phosphorylation and inhibition by NEK2. Proc Natl Acad Sci USA 2018;115(42):10666–71.
[61] Yang Z, Tang N, Zhang X, Lin H, Li Y, Yang Z. Multiple kernel learning in protein–protein interaction extraction from biomedical literature. Artif Intell Med 2011;51(3):163–73.
[62] Yu W, Clyne M, Dolan SM, Yesupriya A, Wulf A, Liu T, et al. GAPscreener: an automatic tool for screening human genetic association literature in PubMed using the support vector machine technique. BMC Bioinf 2008;9(1):205.
[63] Plaza L, Díaz A, Gervás P. A semantic graph-based approach to biomedical summarisation. Artif Intell Med 2011;53(1):1–14.
[64] Liu F, Yu H. Learning to rank figures within a biomedical article. PLoS One 2014;9(3):e61567.
[65] Ruffini G. An algorithmic information theory of consciousness. Neurosci Conscious 2017;3(1):nix019.
[66] Arsiwalla XD, Herreros I, Verschure P. On three categories of conscious machines. In: Lepora NF, Mura A, Mangan M, Verschure PFMJ, Desmulliez M, Prescott TJ, editors. Biomimetic and biohybrid systems. Cham: Springer; 2016. p. 389–92.
[67] Christley S, An G. A proposal for augmenting biological model construction with a semi-intelligent computational modeling assistant. Comput Math Organ Theory 2012;18(4):380–403.
[68] Almog DM, Heisler EM. Computer intuition: guiding scientific research in imaging and oral implantology. J Dent Res 1997;76(10):1684–8.
[69] Kanevsky J, Corban J, Gaster R, Kanevsky A, Lin S, Gilardino M. Big data and machine learning in plastic surgery: a new frontier in surgical innovation. Plast Reconstr Surg 2016;137(5):890e–7e.
[70] Negoescu R. Conscience and consciousness in biomedical engineering science and practice. In: Proceedings of International Conference on Advancements of Medicine and Health Care through Technology; 2009 Sep 23–26; Cluj-Napoca, Romania; 2009. p. 209–14.
[71] Sajda P. Machine learning for detection and diagnosis of disease. Annu Rev Biomed Eng 2006;8:537–65.
[72] Molla M, Waddell M, Page D, Shavlik J. Using machine learning to design and interpret gene-expression microarrays. AI Mag 2004;25(1):23–44.
[73] Pham TD, Wells C, Crane DI. Analysis of microarray gene expression data. Curr Bioinform 2006;1(1):37–53.
[74] Shi TW, Kah WS, Mohamad MS, Moorthy K, Deris S, Sjaugi MF, et al. A review of gene selection tools in classifying cancer microarray data. Curr Bioinform 2017;12(3):202–12.
[75] Vashistha R, Dangi AK, Kumar A, Chhabra D, Shukla P. Futuristic biosensors for cardiac health care: an artificial intelligence approach. 3. Biotech 2018;8(8):358.
[76] Ahmed FE. Artificial neural networks for diagnosis and survival prediction in colon cancer. Mol Cancer 2005;4(1):29.
[77] Foster KR, Koprowski R, Skufca JD. Machine learning, medical diagnosis, and biomedical engineering research–commentary. BioMed Eng Online 2014;13:94.
[78] Krishnan S, Athavale Y. Trends in biomedical signal feature extraction. Biomed Signal Process Control 2018;43:41–63.
[79] Hamada M, Zaidan BB, Zaidan AA. A systematic review for human EEG brain signals based emotion classification, feature extraction, brain condition, group comparison. J Med Syst 2018;42(9):162.
[80] Kehri V, Ingle R, Awale R, Oimbe S. Techniques of EMG signal analysis and classification of neuromuscular diseases. In: Proceedings of the International Conference on Communication and Signal Processing 2016; 2016 Dec 26–27; Lonere, India; 2016. p. 485–91.
[81] Rai HM, Chatterjee K. A unique feature extraction using MRDWT for automatic classification of abnormal heartbeat from ECG big data with multilayered probabilistic neural network classifier. Appl Soft Comput 2018;72:596–608.
[82] Cook MJ, O'Brien TJ, Berkovic SF, Murphy M, Morokoff A, Fabinyi G, et al. Prediction of seizure likelihood with a long-term, implanted seizure advisory system in patients with drug-resistant epilepsy: a first-in-man study. Lancet Neurol 2013;12(6):563–71.
[83] Bou Assi E, Nguyen DK, Rihana S, Sawan M. Towards accurate prediction of epileptic seizures: a review. Biomed Signal Process Control 2017;34:144–57.
[84] Fergus P, Hignett D, Hussain A, Al-Jumeily D, Abdel-Aziz K. Automatic epileptic seizure detection using scalp EEG and advanced artificial intelligence techniques. BioMed Res Int 2015;2015:986736.
[85] Stacey WC. Seizure prediction is possible—now let's make it practical. EBioMedicine 2018;27:3–4.
[86] Kiral-Kornek I, Roy S, Nurse E, Mashford B, Karoly P, Carroll T, et al. Epileptic seizure prediction using big data and deep learning: toward a mobile system. EBioMedicine 2018;27:103–11.
[87] Stoitsis J, Valavanis I, Mougiakakou SG, Golemati S, Nikita A, Nikita KS. Computer aided diagnosis based on medical image processing and artificial intelligence methods. Nucl Instrum Methods Phys Res A 2006;569(2):591–5.
[88] Fasihi MS, Mikhael WB. Overview of current biomedical image segmentation methods. In: Proceedings of 2016 International Conference on Computational Science and Computational Intelligence; 2016 Dec 15–17; Las Vegas, NV, USA; 2016. p. 803–8.
[89] Jo Y, Cho H, Lee SY, Choi G, Kim G, Min HS, et al. Quantitative phase imaging and artificial intelligence: a review. IEEE J Sel Top Quantum Electron 2019;25(1):6800914.
[90] Ghafarpour A, Zare I, Zadeh HG, Haddadnia J, Zadeh FJS, Zadeh ZE, et al. A review of the dedicated studies to breast cancer diagnosis by thermal imaging in the fields of medical and artificial intelligence sciences. Biomed Res 2016;27(2):543–52.
[91] Personal ultrasound [Internet]. New York: Butterfly Network; c2019 [cited 2019 Jan 17]. Available from: https://english.butterflynetwork.com/.
[92] Elkin PL, Schlegel DR, Anderson M, Komm J, Ficheur G, Bisson L. Artificial intelligence: bayesian versus heuristic method for diagnostic decision support. Appl Clin Inform 2018;9(2):432–9.
[93] Safdar S, Zafar S, Zafar N, Khan NF. Machine learning based decision support systems (DSS) for heart disease diagnosis: a review. Artif Intell Rev 2018;50(4):597–623.
[94] Haque S, Mital D, Srinivasan S. Advances in biomedical informatics for the management of cancer. Ann NY Acad Sci 2002;980(1):287–97.
[95] Ibrahim F, Thio THG, Faisal T, Neuman M. The application of biomedical engineering techniques to the diagnosis and management of tropical diseases: a review. Sensors 2015;15(3):6947–95.
[96] López-Fernández H, Reboiro-Jato M, Pérez Rodríguez JA, Fdez-Riverola F, Glez-Peña D. The artificial intelligence workbench: a retrospective review. ADCAIJ 2016;5(1):73–85.
[97] Tran BX, Vu GT, Ha GH, Vuong QH, Ho MT, Vuong TT, et al. Global evolution of research in artificial intelligence in health and medicine: a bibliometric study. J Clin Med 2019;8(3):360.
[98] Tantin A, Bou Assi E, van Asselt E, Hached S, Sawan M. Predicting urinary bladder voiding by means of a linear discriminant analysis: validation in rats. Biomed Signal Proces Control 2020;55:101667.
[99] Bou Assi E, Gagliano L, Rihana S, Nguyen DK, Sawan M. Bispectrum features and multilayer perceptron classifier to enhance seizure prediction. Sci Rep 2018;8(1):15491.
[100] Sakai K, Yamada K. Machine learning studies on major brain diseases: 5-year trends of 2014–2018. Jpn J Radiol 2019;37(1):34–72.
[101] Martens FMJ, van Kuppevelt HJM, Beekman JAC, Rijkhoff NJM, Heesakkers JPFA. Limited value of bladder sensation as a trigger for conditional neurostimulation in spinal cord injury patients. Neurourol Urodyn 2010;29(3):395–400.
[102] Mendez A, Sawan M, Minagawa T, Wyndaele JJ. Estimation of bladder volume from afferent neural activity. IEEE Trans Neural Syst Rehabil Eng 2013;21(5):704–15.
[103] Mendez A, Belghith A, Sawan M. A DSP for sensing the bladder volume through afferent neural pathways. IEEE Trans Biomed Circuits Syst 2014;8(4):552–64.
[104] Witten IH, Frank E. Data mining: practical machine learning tools and techniques. 2nd ed. San Fransisco: Morgan Kaufmann; 2005.
[105] Motulsky H, Christopoulos A. Fitting models to biological data using linear and nonlinear regression: a practical guide to curve fitting. New York: Oxford University Press; 2004.
[106] Mendez A. Bladder volume decoding from afferent neural activity [dissertation]. Montreal: Polytechnique Montreal; 2013.
[107] Wiebe S, Eliasziw M, Bellhouse DR, Fallahay C. Burden of epilepsy: the Ontario health survey. Can J Neurol Sci 1999;26(4):263–70.
[108] Fisher RS, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, et al. Epileptic seizures and epilepsy: definitions proposed by the international league against epilepsy (ILAE) and the international bureau for epilepsy (IBE). Epilepsia 2005;46(4):470–2.
[109] Mormann F, Andrzejak RG, Elger CE, Lehnertz K. Seizure prediction: the long and winding road. Brain 2007;130(2):314–33.

[110] Howbert JJ, Patterson EE, Stead SM, Brinkmann B, Vasoli V, Crepeau D, et al. Forecasting seizures in dogs with naturally occurring epilepsy. PLoS One 2014;9(1):e81920.
[111] Bou Assi E, Nguyen DK, Rihana S, Sawan M. A functional-genetic scheme for seizure forecasting in canine epilepsy. IEEE Trans Biomed Eng 2018;65(6):1339–48.
[112] Gagliano L, Bou Assi E, Nguyen DK, Rihana S, Sawan M. Bilateral preictal signature of phase–amplitude coupling in canine epilepsy. Epilepsy Res 2018;139:123–8.
[113] van Mierlo P, Carrette E, Hallez H, Raedt R, Meurs A, Vandenberghe S, et al. Ictal-onset localization through connectivity analysis of intracranial EEG signals in patients with refractory epilepsy. Epilepsia 2013;54(8):1409–18.
[114] Bou Assi E, Rihana S, Nguyen DK, Sawan M. Effective connectivity analysis of iEEG and accurate localization of the epileptogenic focus at the onset of operculo-insular seizures. Epilepsy Res 2019;152:42–51.