Journal of Neural Engineering

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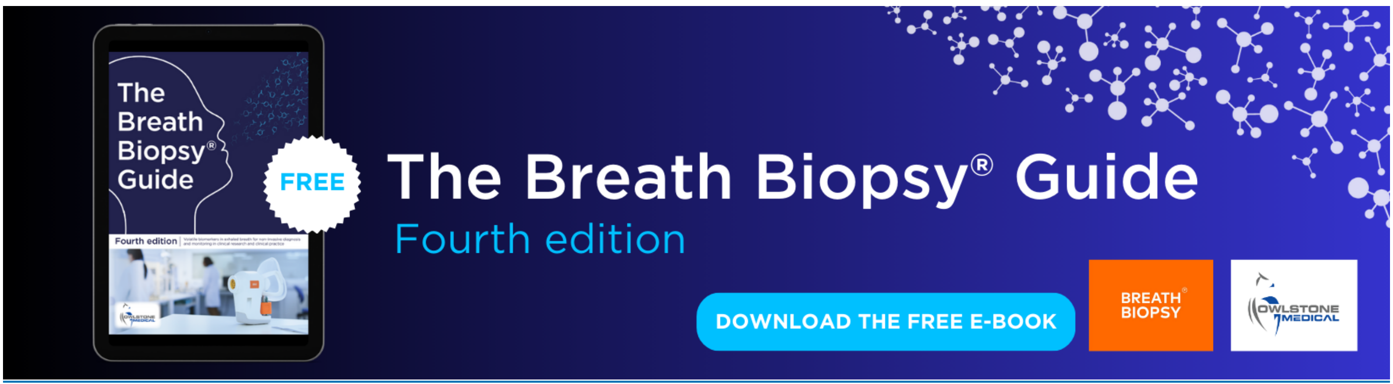
To cite this article: Khaled Aboumerhi *et al* 2023 *J. Neural Eng.* **20** 041004



IOP Publishing J. Neural Eng. 20 (2023) 041004 https://doi.org/10.1088/1741-2552/aceca3

Journal of Neural Engineering

OPEN ACCESS

RECEIVED
20 February 2023

REVISED
27 July 2023

ACCEPTED FOR PUBLICATION
2 August 2023

PUBLISHED
22 August 2023

TOPICAL REVIEW

Neuromorphic applications in medicine

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Keywords: medicine, neuromorphic engineering, neuromodulation, neuroprostheses, medical imaging

Abstract

In recent years, there has been a growing demand for miniaturization, low power consumption, quick treatments, and non-invasive clinical strategies in the healthcare industry. To meet these demands, healthcare professionals are seeking new technological paradigms that can improve diagnostic accuracy while ensuring patient compliance. Neuromorphic engineering, which uses neural models in hardware and software to replicate brain-like behaviors, can help usher in a new era of medicine by delivering low power, low latency, small footprint, and high bandwidth solutions. This paper provides an overview of recent neuromorphic advancements in medicine, including medical imaging and cancer diagnosis, processing of biosignals for diagnosis, and biomedical interfaces, such as motor, cognitive, and perception prostheses. For each section, we provide examples of how brain-inspired models can successfully compete with conventional artificial intelligence algorithms, demonstrating the potential of neuromorphic engineering to meet demands and improve patient outcomes. Lastly, we discuss current struggles in fitting neuromorphic hardware with non-neuromorphic technologies and propose potential solutions for future bottlenecks in hardware compatibility.

1. Introduction

Since the advent of cardiac defibrillators in 1930, medical technologies have played an increasingly vital role in patient care and diagnostics. The introduction of the pacemaker in 1958, followed by dialysis machines, insulin pumps, and advancements in miniaturization and imaging have made medical care and technological diagnostics more interdependent [1–4]. Prosthetics have similarly revolutionized patient care by assisting individuals with declining neurological functions due to neurodegenerative diseases, as well as people who have suffered injuries, such as amputees. Since the 1950s, the invention of cochlear and visual assistance implants has paved the way for neuromodulating devices that monitor, stimulate, and improve motor, auditory, visual, vestibular, and communicative functions. Neuroprosthetic devices have even restored function to entirely defunct neurological relays, thus enabling individuals to regain control over aspects of their lives that were once impossible [5–9].

Despite the significant advances in medical technologies, there are still many areas that require improvement. For instance, implantable devices face power requirements that often result in the need for extended battery life [10]. Fully implantable devices also suffer bandwidth issues which necessitate more frequent clinical visits to offload important neurological data. Moreover, typical tomography machines generate large images that require segmentation, classification, and recognition algorithms, which come at an extremely high computational cost [11, 12]. At a more fundamental level, bidirectional communication with the nervous system (i.e., neural recording and stimulation) remains largely asymmetric, as analog neuronal activity based on action potentials is generally translated into basic digital data, which limits our ability to comprehend and communicate with the brain.

To address these challenges, Carver Mead and Misha Mahowald pioneered the field of neuromorphic computing and engineering with their invention of the first neuromorphic silicon in 1989 [13]. Neuromorphic computing and engineering involve creating hardware and software models that emulate the structure of biological neural networks (BNNs), with a focus on developing designs that closely mimic the architecture of the human brain. Therefore, neuromorphic devices are designed to exploit the brain's efficiency in compression, communication, and the computational cost of hardware.

One significant advantage of neuromorphic approaches is their potential for low power consumption and extended battery life. Neuromorphic models are typically designed to be highly parallel, allowing them to perform computations using significantly less power than traditional computing systems [14]. This energy efficiency is particularly important in medically implanted devices, which frequently require or significantly benefit from long-lasting and reliable power sources. By leveraging neuromorphic computing, medical technologies can achieve higher performance and functionality while minimizing power consumption, leading to better patient outcomes and improved quality of life. Other advantages offered by neuromorphic devices are the ability to compress information to event-based data that can be manipulated easily into spikes [15, 16], minimize device sizes through novel complementary metal-oxide semiconductor (CMOS) technologies, improve computational speed, and reduce overall costs while mimicking the native computing architecture of the human brain [5, 17, 18].

Since the original conception by Mead and Mahowald's, engineers have developed a range of innovative devices, including silicon retinas, compressed event-based sensing schemes, olfactory systems, auditory systems, depression detection mechanisms, robotic limbs, on-chip disease detection devices [19], among others. Most of these inventions have demonstrated remarkable features such as low latency, low power, high bandwidth, and high dynamic range, all of which aim to achieve dramatic improvements in energy efficiency and overall performance [17, 20, 21].

This paper presents an overview of the potential of neuromorphic technologies in improving medical diagnostics and treatments. The examples discussed in this review cover a wide range of applications, including software and hardware, medical imaging and diagnosis [22], cell culture analysis, neuroprosthetic control, perception, and more, as shown in figure 1. To organize this content effectively, this paper is divided into six sections:

- A brief introduction to neuromorphic engineering.
- Neuromorphic approaches for diagnosis.
- Neuromorphic approaches for biosignal analysis.
- Neuromorphic approaches for neural interfaces.
- Advancements in neuromorphic tools for reverse engineering human biological senses.
- Difficulties in integrating neuromorphic engineering with medicine.

We conclude by discussing potential avenues for integrating neuromorphic engineering into traditional medicine to improve patient care and outcomes.

2. A brief introduction to neuromorphic engineering

Neuromorphic engineering aims to develop hardware and software systems that replicate the structure and function of BNNs. This brain-inspired approach has prompted researchers to investigate how the brain performs fundamental operations and apply those principles to both software and hardware designs.

However, it is important to note that both software and hardware approaches to neuromorphic engineering have their own advantages and challenges. Software approaches are often more flexible and easier to modify, but they may be less efficient than hardware approaches. Hardware approaches are often more efficient, but they can be more difficult to design and modify.

2.1. Neuromorphic hardware

Hardware neuromorphic engineering involves designing and building custom hardware that is optimized for performing the types of computations required by the aforementioned neural networks. Neuromorphic hardware typically consists of artificial neurons and synapses that are designed to mimic the behavior of biological neurons and synapses [23].

Compared to traditional computing systems, neuromorphic hardware has several advantages. Firstly, it functions similarly to the human brain, which is highly energy-efficient since it operates on the concept of in-memory computing and is not restricted by the von Neumann bottleneck [24]. This bottleneck is a limitation that arises in traditional computing systems and is named after the mathematician and computer scientist John von Neumann. In these systems, the central processing unit (CPU) and memory are separate components, and data must be transferred back and forth between them for processing. This data transfer creates processing speed restrictions and more energy usage.

Secondly, neuromorphic architectures perform parallel processing, which results in faster and more efficient computing [14]. Since the synapse and neurons are massively interconnected, computations can be performed simultaneously since each element can work independently.

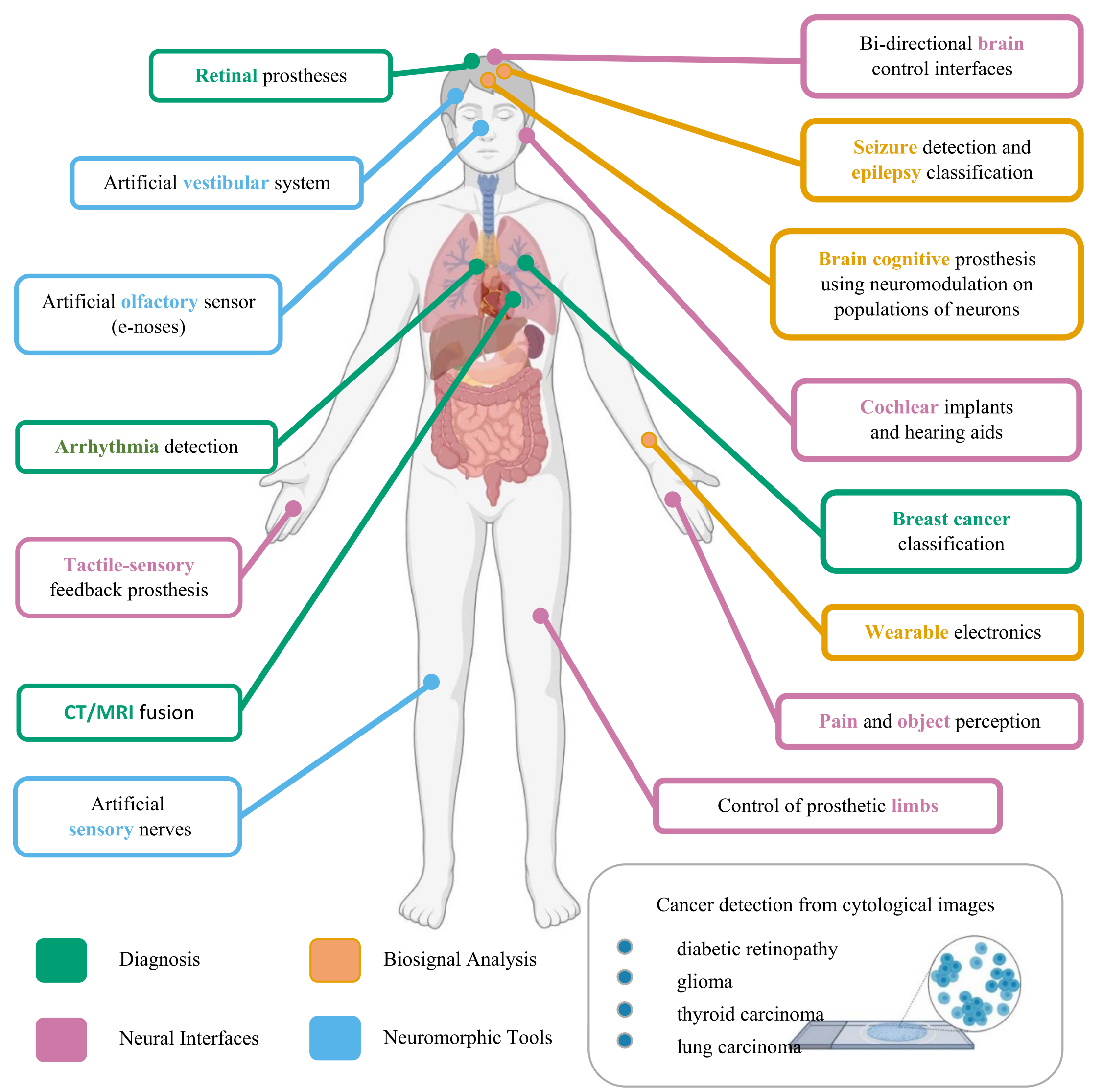

Figure 1. Neuromorphic computing has many applications and inspirations to-and-from medicine. Besides interfaces, neuromorphic detection algorithms also assist in diagnostic care (bottom-right).

Thirdly, it can adapt and learn from new inputs, making it well-suited for machine learning and artificial intelligence (AI) [25]. This concept is known as plasticity, where new information can easily be integrated. This makes neuromorphic hardware compatible with unsupervised learning, which naturally relies on the ability to change based on varying inputs.

Lastly, neuromorphic hardware is fault-tolerant, meaning it can function even if individual components fail [26–28]. In traditional computing systems, individual components, such as transistors, can fail causing large portions of the system to malfunction. However, in neuromorphic hardware, multiple artificial neurons and synapses are used to perform the same function [29]. This redundancy helps build resilience to systems failing. Additionally, neuromorphic hardware often employs distributed computation, which means that the processing is distributed across many computing elements rather than being centralized in a single processing unit. For a more detailed exploration of medical applications using neuromorphic circuitry, please see this review paper [30].

2.2. Neuromorphic software

Neuromorphic software often employs a variety of algorithms that are designed to mimic the functions of neurons and synapses in the brain. Some of the most popular algorithms used in neuromorphic software include spiking neural networks (SNNs) and spike-timing-dependent plasticity (STDP) [31].

SNNs model how biological neurons use spikes, or action potentials, to communicate between neurons, and store neuronal and synaptic states [31]. Therefore, unlike traditional artificial neural networks (ANNs), which use continuous values to represent information, SNNs use discrete pulses to communicate information. In addition, compared to ANNs which use non-biological activation functions like rectified linear units and hyperbolic tangents (tanh) [32], SNNs rely on implementing neural models, such as the leaky integrate-and-fire (LIF) neuron [33]. This makes them more biologically realistic and energy efficient. As a result, they are considered neuromorphic in nature because they are event-driven (e.g., discrete in value and continuous in time), biologically inspired, and can be deployed on compatible neuromorphic hardware. It is important to note that there are other methods the brain uses to encode/decode information, such as synaptic background noise [34], but the knowledge on action potentials is sufficient enough to make them more amenable to hardware implementations.

STDP is a learning algorithm that is used in SNNs to adjust the strength of the connections between neurons based on the timing of their spikes. The basic idea behind STDP is that when a presynaptic neuron consistently fires before a postsynaptic neuron, the connection between them is strengthened [31]. Conversely, when a presynaptic neuron consistently fires after a postsynaptic neuron, the connection between them is weakened. This type of learning can help SNNs adapt to new inputs and learn from experience.

Neuromorphic software has adapted conventional algorithms commonly used in traditional software to mimic the behavior of BNNs. These algorithms include deep learning convolutional neural networks (CNNs) [35], and recurrent neural networks (RNNs) [36]. Briefly, deep learning algorithms are capable of learning multiple levels of representation in data, making them a powerful machine learning tool. CNNs, which excel at recognizing spatial patterns in data, are often used in computer vision applications [37–39]. RNNs are well-suited for tasks involving sequential data, such as language translation and speech recognition.

While there will be instances that showcase the potential of hardware, most examples presented in this paper will concentrate on neuromorphic software. This is because software algorithms are not constrained by fabrication and hardware realization. Nonetheless, all the examples of neuromorphic applications will demonstrate that both brain-inspired hardware and software hold a promising future in healthcare.

3. Neuromorphic approaches for diagnosis

The use of medical imaging is particularly crucial in the detection of cancer, where early diagnosis can greatly improve a patient's chances of survival. Diagnostic imaging techniques enable doctors to identify tumors at their earliest stages. Therefore, there is a pressing need to develop intelligent, low-cost, portable, and low-power preliminary diagnostic hardware to facilitate early detection. Neuromorphic hardware has the potential to enable real-time data processing, significantly reducing power consumption, which is one of the major burdens of clinical applications.

This section provides an overview of how different neuromorphic hardware designs can be utilized in various stages of medical image processing. The focus is on specific clinical applications of cancer detection and diagnosis, where the benefits of neuromorphic hardware are particularly evident.

3.1. Imaging

Medical image processing refers to the process of digitizing data from an image and applying various mathematical operations to generate an enhanced image that is better suited for interpretation and analysis, especially for diagnostic purposes. However, diagnosing medical conditions based on images is a complicated task because diagnostic information is demonstrated differently by different imaging devices. Therefore, a combination of image sequences is often necessary to effectively interpret the clinical data.

Traditional image analysis methodologies involve segmentation, fusion, and contrast optimization (enhancement) to convert imaging data into meaningful biomarkers that provide insights into the physiology and pathophysiology of a tissue [40, 41]. More recently, the integration of high-performance computing and the accessibility of extensive medical imaging datasets have facilitated the deployment of sophisticated machine learning techniques and deep learning models, bringing analysis closer to the capabilities of the human brain. ANNs have demonstrated promising potential in image processing, speech recognition, pattern recognition, and medical diagnostics [42].

While ANNs are not inherently neuromorphic because they lack a biological basis for their operation, some have been adapted and reconfigured to be neuromorphic. A type of ANN that is highly relevant to image processing is the pulse-coupled neural network (PCNN). PCNNs are unsupervised neural models that are implemented to resemble the function of the visual cortex and therefore allow high-performance biomimetic image processing [43, 44]. Modeling the architecture of biological models is inherently neuromorphic in function and is an attempt to exploit energy-efficient and computationally intelligent mechanisms. Figure 2 illustrates the structure of the PCNNs. The functioning of the PCNN is based on a biological model that comprises a receptive field, modulation step to integrate convolutions, threshold detector, pulse generator, and binary output. The receptive field is equivalent to the dendritic part of a biological nerve network. Whether the pulse is generated depends on whether the internal activity term exceeds the dynamic threshold, and the threshold value is a function of the output state of

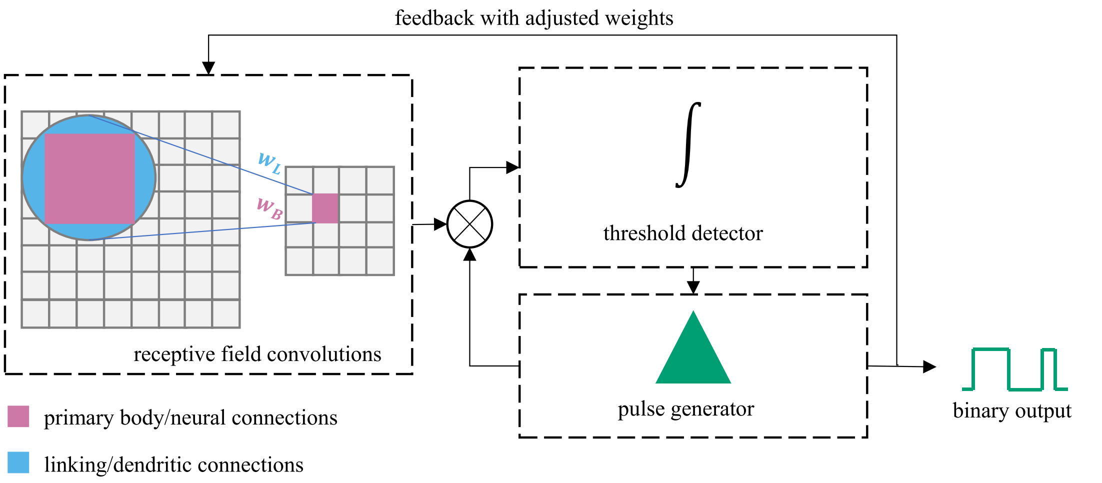

Figure 2. Pulse-coupled CNN. A typical convolution is performed using retinomorphic neural connectivity. Each pixel in the image (left) is connected to a neuron (body connections) and surrounding neurons (linking connections), both of which make-up the receptive field. Each connection has its own associated weights based on the distance from the computing pixel (e.g., linking radius). After pixel convolution, the outputs are passed through a threshold detector and pulse generator which fires a spike ('event' or 'pulse') based on whether the internal dynamics of the neurons have exceeded a limit.

the neuron. In summary, the PCNN model is a two-dimensional (2D), single-layered, horizontally linked neural network in which each pixel in the image (i, j) is connected to a unique neuron (i, j), and each neuron relates to the surrounding neurons within an arbitrary radius.

Another type of ANN, known as deep neural networks (DNNs), has emerged as a robust tool for biomedical image computing. DNNs are multilayer neural network algorithms that can learn complex features and create more abstract deep representations by combining low-level features, known as attribute classes or features [20]. Consequently, instead of relying on complicated image representation engineering, DNNs directly deal with raw image data and autonomously learn the representations for different tasks [21]. However, pre-processing raw images is often performed prior to feeding them into a DNN. This pre-processing may include standardizing the size of the images through resizing or cropping, normalizing the pixel values to have zero mean and unit variance, and applying data augmentation techniques like flipping, rotating, or introducing noise to the images to amplify the diversity of the training data [45–48]. These transformations serve to enhance the input data consistency and richness for the DNN, while also preventing overfitting by increasing the diversity and size of the training dataset. By applying these transformations, the DNN is better able to understand the underlying patterns and features in the data, potentially resulting in improved performance on tasks such as image classification, object detection, or segmentation. In addition, DNNs typically require a substantial quantity of training data, which may not be readily available.

Another obstacle for DNNs stems from their innate characteristic of high computational complexity, necessitating large amounts of memory for both the original data storage and temporary data processing. DNNs are incapable of handling shifts in input data distribution, a problem known as classification under covariate shift. Different strategies have been developed to mitigate the limitation of covariance shift, including importance weighted cross validation [49], discriminative learning through integrated optimization that does not explicitly model either the training or test distribution [50], and weighting the observed samples in maximize the log-likelihood function [51].

To overcome the limitations of DNNs and other ANN-based architectures, the latest research has explored the potential of bio-inspired neuromorphic hardware. Specifically, three neuromorphic designs, namely field programmable gate arrays (FPGAs), memristors or in-memory passive devices [52], and CMOS architectures, have been studied for their suitability in various stages of the medical image processing methodology. Finally, there has been an emergence of other neuromorphic models, such as SNNs (as depicted in figure 3), which are neural networks that much more closely resemble biology than typical ANNs, as discussed in the previous section. Specific examples of the use of each of these neuromorphic designs in different applications are presented in the following sections.

3.1.1. Image segmentation for medical diagnostics

Image segmentation is the process of dividing an image into multiple distinct regions or segments, each of which corresponds to a different object or part of the image. This technique is widely used in medical diagnostics, particularly in cytopathology and microscopic cellular imaging. The shape, size, and structure of nuclei observed in microscopic color

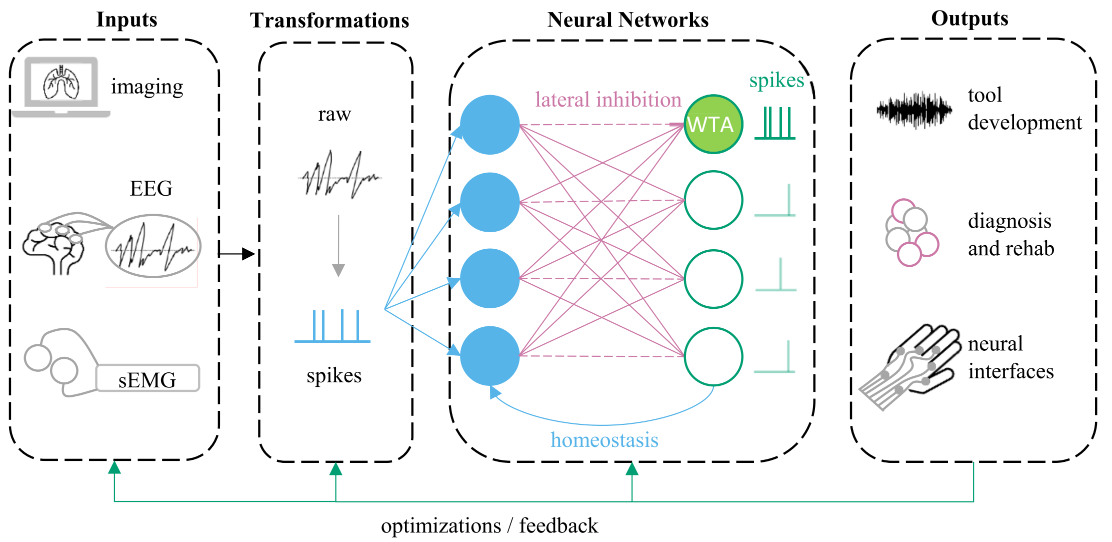

Figure 3. Examples of processing biosignals. Inputs (right) can come from images (MRIs, PET, calcium imaging), EEG measurements, sEMG recordings and more. Measurements that have a low-signal-to-noise ratio are often filtered, compressed, and/or sorted to pure-spikes for neuromorphic compatibility. In the case of learning, classification, and inference, different features are learned for control, perception, localizing patterns, and various feedback mechanisms. These feedback mechanisms then inform recording inputs and learning architectures for improved monitoring and accuracy. The outputs correspond different applications, where neuromorphic engineering is involved in tool development and engineering (replicating biosignals), diagnostics and rehab (i.e, cancer detection), and neural interfaces (prosthesis).

images provide crucial information to pathologists, assisting them in the identification of abnormal cellular changes that could indicate the presence of cancer [53]. Image segmentation can be achieved through various methods, including thresholding [54], region-based [55], edge detection [56], and clustering [57].

The technique most commonly used for segmentation is edge detection, which involves identifying points in an image where intensity changes sharply [56, 57]. In medical image processing, edge detection and extraction are particularly important for identifying clinical biomarkers and assessing tissue functionality and integrity. Edges can be broadly classified into two types: step edges, where there are sudden changes in pixel intensity values and roof edges, where the image intensity changes gradually and then returns to the starting value within a short distance, creating a 'roof shape' [58]. Memristive PCNNs (M-PCNNs) have been used to detect differences in gray scale values on edges to perform image edge detection of computed tomography (CT) images in grayscale [44]. The working principle of M-PCNN involves a corresponding neuron firing a pulse, which in turn excites the neighboring neurons it is connected to [44]. The stimulus on the connected network comprises the input pixel and the activation from the previous neuron. When the stimulus surpasses a threshold, the neuron will fire, leading to the propagation of the effect throughout the network based on the input image and the network connections. In areas with similar grayscale values, the spiking behavior of a single neuron will trigger a cluster of collective spiking activities [59]. The resulting output, therefore, provides information about the consistency of grayscale values in the images and their edges, as well as cell background, cytoplasm, and nuclei [60].

SNNs have proven to be an efficient tool for identifying objects in cell-stained images, which are colorized [61] Two SNN topologies are commonly used for unsupervised and supervised learning, both consisting of an input layer, hidden layer, and output layer [60, 62]. In unsupervised learning, the SNN learns directly from the pixels of an image, while supervised learning involves using a reference dataset. In previous work, the hidden layer of an SNN included radial basis functions with localized activation to transform red-green-blue (RGB) values into temporal values [61]. Once input data were segmented using an SNN, the activity of each output neuron was recorded, with a binary 1 indicating an active neuron and 0 indicating an inactive neuron for each input pixel [60]. These binary activation matrices were subsequently used to create binary images that show the edges detected by the neurons for each class. The final set of edges was obtained by fusing all images together.

3.1.2. Medical image (CT image and MRI) fusion

As mentioned earlier in this section, combining complementary information acquired from different imaging techniques can offer a more comprehensive understanding of pathological aspects for clinical diagnosis. CT provides the most detailed information on denser tissues with less distortion. On the other hand, magnetic resonance imaging (MRI) offers better information on soft tissues with more distortions. In clinical applications, multimodal medical images are readily available, and combining images from different modalities has become very important. As a result, medical image fusion has emerged as a promising new research field. Image fusion methods can be broadly categorized as spatial domain fusion and transform domain fusion. Spatial domain fusion involves directly processing the source images, such as using the weighted average method [63, 64]. However, this approach often leads to a reduction in the signal-to-noise ratio (SNR) and the spatial distortion can persist in the fused image.

On the other hand, the multiresolution image fusion technique, which is based on the wavelet transform [65], is the most commonly used approach for fusion in the transform domain. This technique involves decomposing the input images into multiple levels based on their transform coefficients, after which a fusion technique is employed [64] to produce a fusion decision map. Performing an inverse transformation of this decision map yields a fused image that includes all the details of the source images and reduces spatial distortion. However, this approach may also have some weaknesses, such as inadvertently reducing the SNR of the synthesized image being sensitive to various factors that can affect the fusion process. Yet, it is worth noting that many fusion techniques are based on the wavelet transform [66–68]. While the implementation of this wavelet fusion solely in software can be slow and computationally expensive, it can be combined with FPGA hardware to increase the computational speed [69, 70].

Consequently, a double-channel M-PCNN [44] can be a beneficial approach for image fusion. In this case, if a pixel in the fusion image is from image A and most adjacent pixels are from image B, then the pixels are replaced by image B's pixel in the original position, thereby improving the stability and continuity of the fused image. The double-channel M-PCNN's ability to input two images simultaneously enables it to consider both internal balance factors and nonlinear modulation characteristics, which are used to modulate the output of the initial fusion.

3.1.3. Medical image de-noising and enhancement

Pre-processing steps like medical image denoising and contrast enhancement are essential for subsequent medical image processing stages. M-PCNNs have also been utilized for image denoising, where each neuron is connected to its corresponding pixel and adjacent 3×3 neurons, as described in the previous section [44]. The output of a neuron is determined by whether its internal activity exceeds a certain threshold, resulting in either ignition or non-ignition. As a result, the output is significantly dependent on the pixel brightness and the correlation between them. In most cases, the brightness values of pixels affected by noise pollution are different from those of the surrounding pixels and have a weak correlation. Therefore, the output of these noisy pixels is different from that of the surrounding pixels. To summarize, M-PCNN is a useful approach for image denoising as it can differentiate the grayscale values of noise based on the firing of each neuron and its neighboring neurons. This ultimately results in adjustments to the brightness of the corresponding pixel values, leading to noise reduction and improved identification of biomarkers.

Another commonly used strategy for improving image quality is called Automated Transform by Manifold Approximation (AUTOMAP) [71]. This method relies on deep learning methods for reconstructing images from under-sampled or incomplete data, and is particularly useful in MRI applications. During the training process, AUTOMAP employs a dataset of pairs of sensor and image data generated using a known forward encoding model. By learning the spatial decoding transform between the sensor and image spaces, AUTOMAP can accurately reconstruct images from under-sampled or noisy data. The neural network architecture of AUTOMAP typically consists of multiple fully connected layers, followed by sparse convolutional layers. These layers operate between low-dimensional manifolds to improve the robustness of the reconstruction to noise and other artifacts. AUTOMAP has been shown to outperform other contemporary image-based denoising algorithms, such as a deep CNN Gaussian noise denoiser [67] and the block-matching and three-dimensional (3D) filtering denoising algorithm [72]. Additionally, AUTOMAP is effective in suppressing noise-like spike artifacts that may appear in the reconstructed images.

3.1.4. Feature extraction & classification in images

One of the more critical steps in the processing of medical images is efficient feature extraction clinical diagnosis decisions. In recent years, deep learning has become increasingly dependent in decision making based on medical images [73–75]. Firstly, deep learning enables data-driven automatic feature extraction, thereby reducing the workload and impact of the traditional manual feature extraction by clinicians. Secondly, the intrinsic deep structure of neural networks can represent the hierarchical interaction between features, revealing the relationship between high-dimensional features. Thirdly, optimizing the same deep structure an achieve extraction, selection, and classification simultaneously.

Consequently, deep learning has found broad applications in image recognition and classification tasks in the medical field. For example, CNNs, as well as a more complex versions such as deep CNNs, have been extensively used to classify pathological images. For instance, CNNs have been used to classify diabetic retinopathy [76, 77], colorectal polyps [78], gliomas [79], papillary thyroid carcinomas [80], and lung carcinomas [81] based on cytological images. In addition, CNNs have also been used to identify microaneurysms, exudates, and hemorrhages in fundus imaging [82].

Several deep CNN architectures demonstrated high-performance accuracy in ImageNet, a massive dataset of over 14 million images belonging to 1000 classes. Among them, AlexNet [83], VGGNet [84], ResNet [85], and InceptionNet [86] are the most commonly used. They can be efficiently run on CMOS chips such as the Eyeriss chip [87] and the LNPU chip [88], which make them well-suited as mobile diagnostic tools. These tools can be integrated into or complement medical imaging systems at the point of care for several medical imaging applications and cancer diagnosis [89].

SNNs have also shown promising results when trained on the Intel Loihi neuromorphic chip [90–92], where the spike count of output neurons was used for brain tumor image classification. This model consumes much less power while achieving reasonable accuracy by reducing model size [22], which enables efficient learning for edge computing.

In addition to CMOS-based technology, medical image classification implementation on FPGA is a well-researched topic, specifically to compare FPGA performance with CPU and GPU to explore the capabilities of FPGA in this field [76, 93, 94]. As an illustrative study, Ghani *et al* compared CPU and FPGA performances for image classification of fundus images in healthy subjects and glaucoma patients [94]. They used various preprocessing techniques based on adaptive thresholding, discrete wavelet transforms, and histograms to extract features that are then fed into a classifier made up of ANNs. They used a Nexy4 DDR FPGA and Intel i5-6200 CPU for comparison. They concluded that the FPGA surpassed the CPU in terms of both power efficiency and execution time.

Memristors are passive memory-holding devices that rely on electrical flow in a circuit. Three types of memristors include thin-film, spin/magnetic field-based, and three-terminal. Memristor crossbars, capable of carrying out multiply add operations in parallel in the analog domain, have also been implemented alone or coupled with CMOS systems for clustering and classification tasks. For example, memristor crossbars have been used in the binary classification of breast cancer (benign or malignant) using principal component analysis (PCA) [95, 96]. The typical process consists of two stages, which can be conducted in two layers of a memristor crossbar [96]. Firstly, an unsupervised algorithm is used to train the crossbar arrays of the memristors to learn and determine the principal components from the cancer data. The network learns the principal components by adjusting the memristor weights during training using Sanger's rule [97], also known as the generalized Hebbian algorithm, which is derived from Hebb's learning rule [98]. Secondly, the PCA stage effectively separates unlabeled data into clusters but does not classify them. To achieve classification, a conventional supervised learning process can be used to define a decision boundary and effectively classify tumors as malignant or benign. This is made possible by the memristor's intrinsic capacity to perform matrix operations, with the output vector determined by the dot product of the input vector and memristor weight matrix. In general, neuromorphic hardware is known for its low power consumption and is safe for use in low-cost portable microscopes and scanners [76]. This is of remarkable importance because DNNs have been reported to be the most effective method for nucleus/cell detection [99]. In summary, combining state-of-the-art imaging hardware with ANNs and DNNs implemented on low-power neuromorphic hardware can strongly augment the quality of screening and analysis, enabling the required early diagnosis.

4. Neuromorphic approaches for biosignal analysis

To understand the underlying mechanisms of health issues, scientists have assessed the body's function by capturing biosignals in many forms such as electroencephalograms (EEGs), electrocorticograms, electrocardiograms (ECGs), electro-oculography, surface electromyogram (sEMG), galvanic skin response, local field potentials, and respiration, as illustrated in figure 3. Different technologies are required for various scenarios that involve the analysis of biosignals. There are other biosignals such as bioimpedance and biomagnetic signals, but they are not often used because of their measurement complexity and implementation [100]. Biosignals originating from various internal or external sites such as the skin, heart, chest, skull, and skeletal muscles are easier to implement and process since they result from a sum of action potentials. However, their diverse characteristics require different extraction methods [100].

For example, one-dimensional signals, such as those related to heart conditions, can be detected using ECGs which detect changes associated with heart muscle contraction. 2D signals requiring spatial representations can be measured using functional MRIs (fMRIs) which monitor brain activity in relation to blood flow [101, 102]. Finally, 3D signals require medical ultrasound equipment to measure changes in sound waves across the internal tissue. Madan *et al* have also innovated on imaging by producing a 'glass brain' from fMRIs that can provide 3D renderings to visualize activation clusters that are both cortical and subcortical [103]. Each of these instances has different raw signal characteristics, including amplitudes, noise, variability, dimensionality, and frequencies. For example, electromyogram (EMG) signals typically range from 0 to 10 mV (+5 to −5) at 6–30 Hz [104], while ECGs, traditionally collected by electrodes placed on the chest, arm, and legs, are characterized between 0.1 and 2 mV at 0.6–50 Hz [105].

4.1. Primary cortex

Researchers have used intelligent neuromorphic paradigms to develop real-time detection for epileptic seizures using neuromorphic technology. There is a growing literature that uses typical brain-related biosignals to separate, identify, and even classify seizure-related markers [106–109]. We hereby include some representative examples to illustrate the capabilities and potential of these systems. The similarity of SNNs and the behavior of biological neurons in the brain, along with their high efficiency in tasks requiring temporal processing [110], has made them popular models for identifying seizures. Zarrin *et al* designed a deep SNN to classify three types of epileptic signals, namely seizure (ictal), pre-seizure (preictal), and seizure-free (interictal) signals. The SNN consists of an input layer that converts analog intracranial EEG spectrograms into spikes, two hidden convolutional layers, and a softmax activation function leading to the seizure and seizure-free categories [111].

Researchers have also designed a two-layer SNN that uses LIF neurons and synapses with biologically realistic temporal dynamics to detect high-frequency oscillations (HFOs) correlated with epilepsy. They collected EEG data from 11 patients and, by exploiting SNNs, were able to identify the occurrence of HFOs correlated with epileptic episodes with an accuracy of 80% [112, 113].

4.2. Cardiac anomalies and chest conditions

Real-time detection of arrhythmia has become increasingly important in monitoring cardiac anomalies to aid medical professionals to best treat patients. Neuromorphic devices, with their low power and low latency features, can assist in classifying the five beat types necessary for detection. An instance of this would be a hardware implementation of a feedforward neural network, composed of a memristive crossbar array with dimensions of 300 × 210 × 5, where the first layer has 300 neurons, the second has 210 neurons, and the last layer has five neurons. This network can achieve 96.17% accuracy without feature manipulation, such as wavelet transforms or spectral correlation [114].

Accurate detection of ECG anomalies has also been a top priority for scientists to prevent future cardiac arrest episodes. Due to the high cost and time it takes to diagnose humans in real-time, neuromorphic chips have been used to detect various pathologies by leveraging SNNs' quick and low-power classification capabilities. By using several analog ECG traces encoded as asynchronous streams of binary events, Moradi *et al* and their group have been able to identify pathologies such as paced beats and atrial premature beats using an event-driven neuron output layer to generate a binary trigger signal, indicating the presence or absence of a pattern. This technique was validated on the dynamic neuromorphic asynchronous processor chip (DYNAP) chip [120], further confirming the usefulness of neuromorphic chips in biomedical applications.

Not limited to direct neural interfaces involving nerves or cortical neurons, efficient processing-enabled neuromorphic designs have been found in various real-time biomedical interfaces. For example, a DYNAP chip was used to implement an SNN for arrhythmia detection [121]. The network was trained on labeled ECG data from ambulatory recordings, and the output spike trains of the neuromorphic chip were used for prediction. The results showed that the system achieved a 91% true-positive rate with only a 2.4% false-positive rate for detecting anomalous ECG readings. By leveraging the real-time processing capabilities of the neuromorphic chip, the system can timely warnings or preliminary diagnoses.

In addition, the novel coronavirus pandemic has called for methods to quickly and accurately detect chest anomalies associated with COVID-19. One promising method is the use of deep-convolutional SNNs, which can be integrated into neuromorphic chips due to their biological compatibility [122]. Firstly, Garain *et al* process chest CT scans through Gabor filters and translate them into spikes using intensity-to-latency encoding. Then, the resulting spikes are propagated through convolutional and pooling layers before being fed into a classifier to provide a diagnosis. The technique resulted in a remarkably high accuracy of 99% when classifying COVID-10 vs non-COVID-19 diagnoses.

4.3. Wearable devices

The demand for edge computing in wearables has increased dramatically, and devices must now incorporate low power and low latency characteristics to remain relevant and desirable. Therefore, it is obvious that wearable health monitoring systems should exploit neuromorphic technologies for their low latency, low power, small footprint, and data size [123]. In fact, the biological plausibility of neuromorphic hardware makes it more compatible with signal processing of biosignals while remaining secure from data breaches, a persistent problem in health-related instruments [124].

One promising example is from a team of scientists at the University of Chicago which has created an electrochemical transistor-based neuromorphic device that is intrinsically stretchable and ideal for accurately collecting health monitoring data such as heart rate and body temperature [125, 126]. They tested the device's signal acquisition and AI-based data analysis by using the Physionet's MIT-BIH Arrhythmia dataset and achieved an accuracy rate of 90% in classifying ECG signals. To ensure the device is suitable for the human skin's stretching and shifting properties, the researchers evaluated its performance under extremely strained conditions (0%–100% strain) and a strain-free state.

Cleary *et al* have also developed a wearable smart material called the microBrain (μBrain) [127]. The device is capable of event-driven SNN integrations in a fabric-based environment for applications in neurostimulating patients suffering from stroke or nerve compression dysfunctions that ultimately led to the loss of physical sensations. The key neuromorphic component of the μBrain is the artificial surface-mounted synapse resistors, which are capable of holding states while emulating a SNN. The artificial synapses and neurons are placed in a crossbar architecture which makes them easily configurable for a machine-learning task. To demonstrate compressional damage rejuvenation, the scientists proved the garment-based SNN can classify haptic sensing coming from artificial pressure sensors embedded into the garment's sleeve. This device holds a lot of potential as smart-wearables are becoming more popular, especially with the innovations in microfabrics.

Neuromorphic designs also offer great potential for virtual reality surgery, thanks to their quick, low-latency, low-power consumption, and high temporal resolution features [128, 129]. As neuromorphic hardware relies on events instead of continuous signals, it can handle the small details and quick reactions required for surgeries much more effectively than traditional circuits. We anticipate that future research will explore the combination of virtual reality headsets and neuromorphic hardware in surgical settings, as these brain-inspired circuits provide everything that surgeons need to perform their best.

4.4. Spintronics and magnetics

In addition to the expected applications of neuromorphic devices and algorithms, spintronics and magnetics have recently gleaned interest from many scientists. These two emerging fields can bring fast behaviors, low-power consumption, and retainable (non-volatile) memory—all features desirable in neuromorphic engineering. Before we mention neuromorphic applications, it is important to note that magnetic and spintronic applications have been used as neurostimulators in the form of highly tunable magnetic materials that are sometimes capable of remote stimulation [130], tools detecting magnetic signatures of the electric activity of the human heart [131], and as cellular-level neuromodulator using alternating ferromagnetic and anti-ferromagnetic structures to produce charge-current pulses suitable for affecting neuronal populations [132].

Because of these advancements, researchers have further investigated the potential for spintronic devices for neuromorphic computing. Kanno *et al* discusses how magnetic tunnel junctions can be adapted to behave similarly to neurons and synapses [133], and how differing magnetic textures, like those mentioned regarding tunable magnetic materials, can emulate functioning neurons [134, 135]. Scientists believe that the first integrations of spintronics in neuromorphic hardware will likely be the digital magnetic memories they can provide, which has a proven history in conventional circuit design.

5. Neuromorphic applications for neural interfaces

Advance technologies now allow us to combine machine learning algorithms with traditional neuromodulation techniques to enhance biomedical interfaces, which aim to modulate and decode biological signals to achieve immunotherapeutic or prosthetic outcomes [136]. Intensive real-time data processing is often necessary for these interfaces, which may require the transmission of data to an external computer with the computational power needed for processing [137, 138]. However, devices implanted in the human body face several limitations to avoid complications during use. In particular, the limited area of the human body available for interfaces, especially in the peripheral nervous system (PNS), and the regulatory guidelines and standards for implanted medical devices pose significant challenges. For instance, ISO14708-3 imposes restrictions on the outer surface temperature increase above body temperature (37 °C) for limited periods of time.

Given the constraints imposed on implanted biomedical interfaces, the emergence of neuromorphic hardware provides a promising alternative for processing data in real-time *in situ*. The structure of SNNs implemented on hardware makes it possible to perform complex parallel processing of large amounts of data [139–141]. *In-situ* processing would also improve the portability of the device, offering greater convenience and facilitating closer outpatient health monitoring [142]. Several research groups have developed neuromorphic hardware for a wide range of clinical applications, such as motor interfaces to interact with the environment, real-time health monitoring, sensory prostheses to restore lost biological senses, and cognitive prostheses to modulate brain activity or replace damaged brain circuitry [5, 123, 143, 144].

Circling back to the original inspiration from the brain, the most intuitive application of neuromorphic hardware lies in neural interfaces. Neuromorphic neural interfaces enable direct interaction with the central or peripheral nervous system by establishing

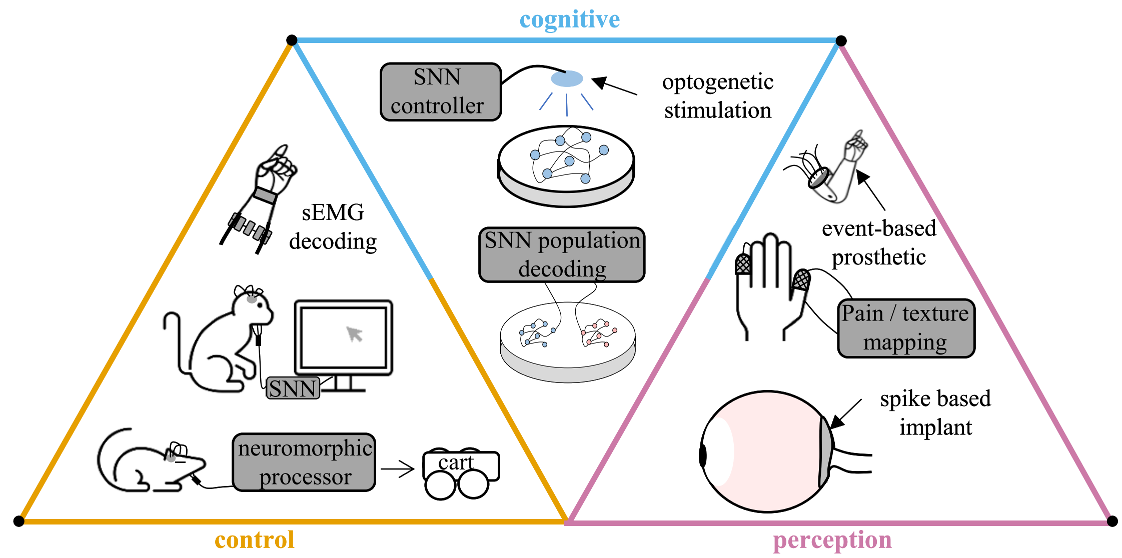

Figure 4. Neural interfaces can be categorized into three large components: perception, control, and cognitive. On the right, perception examples are illustrated where neuromorphic engineering has been used to create retinal implants [7], map texture and pain through fabricated materials [6], and relay perception from artificial limbs [115]. On the left, the opposite relay from the brain to the outside world has been demonstrated through controlling a cart [116], a computer cursor [117], and decode hand gestures for prosthetic control [118]. In the center, cognitive examples are given where neuromorphic engineering has been used to enhance disturbed neuron population communication [5] and stimulation [119] using optogenetics. The center is also highlighted as half blue half orange/purple since cognitive implementations often directly affect either perception or control.

a communication channel between artificial and biological neurons, providing a means to address impairments or physical disabilities [145]. In most scenarios, a bidirectional interface with a large biological neuron population is necessary [146, 147]. Consequently, multielectrode arrays (MEAs) are frequently used to record neuronal firing patterns, while a stimulator relays back information with pulses [148].

Many forms of neural interfaces exist, often falling into one or more of three categories: perception, control, and cognitive interfaces. Perception interfaces, such as retinal prostheses for the restoration of vision, aim to capture information about the outside world from an external device and relay it to the brain by stimulating sensory neurons [7]. This information flows in control interfaces, such as prostheses which enable users to control a computer cursor, and is reversed compared to perception interfaces. In cognitive interfaces, information flow is contained within the brain. For example, a neuromodulation implant designed to alter neuronal firing patterns may use the recorded activity from one population of neurons to determine stimulation parameters for modulating another population of neurons. Examples of each category are depicted in figure 4.

5.1. Perception interfaces

Neuromorphic interfaces for perception strive to establish direct connections with biological nerves through neural models to augment or entirely restore the senses in real-time. Researchers have developed sensors that mimic the highly sought-after features of biological sensing organs, such as sensory learning and spiking representations. When used in conjunction with neuromorphic processing techniques, these biomimetic sensors can be applied back to the human body and directly interfaced with biological sensory nerves.

A retinal prosthesis silicon-on-chip with 1225 channels exploited neuromorphic hardware to mimic the structure and processing performed by the biological retinal information network [7]. The system uses a 35 $\times$ 35 grid of neuromorphic pixels, each of which contains a spike-based photodiode sensor, neuromorphic image processor (NMIP), and stimulation generator. Similar to human receptive fields and their ability to detect contrast, each NMIP interacts with neighboring NMIPs to perform outline extraction of the incident light. Park *et al* have discovered that this outline extraction strategy can help preserve image integrity by protecting the image against current dispersion from retinal cells. To address the temperature limitation on implanted devices, a temperature regulation circuit was incorporated for every 5 $\times$ 5 pixel group, which disables the region if it exceeds the temperature threshold.

Scientists innovated another neuromorphic approach which involves the implementation of a real-time tactile sensory feedback interface. Researchers have invented an electronic-dermis (e-dermis) to serve as fingertips on upper-limb prostheses to enable the perception of touch and even pain [6]. Using Izhikevich models of mechanoreceptors and nociceptors [149], Osborn *et al* adjusted the measured pressure on tactile sensors to stimulation parameters for transcutaneous electrical nerve stimulation to elicit noxious and innoxious sensory feedback. The prosthesis used a linear discriminant analysis algorithm to distinguish between three objects with increasing sharpness, achieving a true positive rate of over 85% across all three objects. The reflex function was integrated by mimicking the PNS, enabling the prosthesis to automatically release its grip in the presence of a painful stimulus. A participant using the prosthesis demonstrated the ability to distinguish between the three objects with true-positive rate of over 87% and also experienced pain perception [115, 150, 151].

5.2. Control interfaces

In situations where individuals suffer from paralysis or loss of limb function, it is beneficial to have devices that can directly interface with the nervous system, such as an external prosthetic o supporting devices, to assist patients in navigating day-to-day tasks. Neuromorphic architectures are particularly attractive in these scenarios due to the need of high-fidelity signal recordings and real-time feedback for the development of a functional control system [152]. Although neuromorphic cortical control interfaces have not yet undergone clinical trials with human patients, several proof-of-concept models have been successfully tested in animals.

In one study, our team at Johns Hopkins University demonstrated the use of neuromorphic silicon integrate-and-fire neurons on a custom chip to control the motor output of paralyzed animals in real-time [153]. Using four neurons to represent four populations of neurons in the spinal cord (right hind limb flexor and extensor muscles) and the synaptic connections between them, the scientists were able to implement basic principles of forward locomotion similar to the normal gait of a cat. The silicon central pattern generating hardware was validated by using the chip to control three functionally paralyzed adult male cats through intramuscular electrode implantation, proving the design's ability to produce locomotion when provided with appropriate sensory inputs.

In a follow-up study, Mazurek *et al* expanded upon their earlier work by utilizing an integrated circuit to implement neuromorphic integrate-and-fire neurons as state-holding controls [154] to create a functional electrical stimulator (FES) through intraspinal microstimulation (ISMS). This innovative approach allowed for the integration of external sensory feedback, internal timing signals, and microstimulation to create a closed-loop solution for restoring locomotion. The custom chip controlled implanted electrodes, successfully activating flexion or extension movements in the lower limbs of a feline subject. The scientists eventually followed-up their work by improving long-distances of propulsive walking over the ground by ten times than the previous study by targeting the ventral horn and lamina IX bilaterally [155]. ISMS was able to achieve a distance of over 800 m without experiencing fatigue, which is a significant improvement compared to FES which only managed around 50 m. This application of ISMS ultimately proves the potential of neuromorphic engineering in mitigating spinal cord injuries and overall, huge benefits for the future of locomotion rejuvenation.

Dethier *et al* at Stanford University have also used an SNN implementation of a Kalman filter to control a computer cursor in monkeys [117]. They obtained cortical neural recordings using a 96-channel MEA. And then fitted the parameters of the Kalman filter to control the cursor based on arm kinematics. The researchers successfully mapped the filter to an offline SNN with 2000 neurons, achieving an RMS error of 6%. In an online closed-loop cursor control task, the system achieved a final success rate of over 94%. While the data processing side was not implemented in the hardware, the researchers demonstrated the potential use of a neuromorphic chip to enable *in situ* real-time control of a cursor using an SNN.

In another study, a neuromorphic neural interface was implanted in rats to drive a small mobile cart [116]. The rat's somatosensory cortex was stimulated, and the motor cortex activity was recorded using an MEA. To process the signal in real-time, researchers at the Italian Institute of Technology, ETH Zurich, and University of Zurich used a novel reconfigurable online learning spiking neuromorphic processor. The motor cortex's recorded activity was mapped onto 252 post-synaptic neurons on the processor, which weighed a force field using spike counts to drive a small mobile cart toward a target. The cart's position was then encoded and used to generate stimulation parameters back to the somatosensory cortex, creating a closed-loop control-perception interface. In the target-convergence task, the system achieved a 100% convergence rate in 100 trials. However, it is important to note that this study was performed on anesthetized rats, and the rats did not control the cart voluntarily. Nevertheless, this system demonstrates the feasibility of an implanted control neural interface running in real-time, using neuromorphic processing as the backbone.

Finally, exploring the potential application of neuromorphic computing to peripheral nerve recording and stimulation is currently limited in the literature, However, application of neuromorphic designs in this context holds promise for a real time sand seamless interface with nerves leading to low-consumption and high-efficient systems [156, 157]. For example, neuromorphic devices for pudendal nerve stimulation hold promise for advancing interventions aimed at improving urinary bladder control [158, 159]. Investigating this intersection could lead to innovative approaches that leverage the principles of neuromorphic computing to enhance the effectiveness and efficiency of these implants.

In addition to invasive neural interfaces, neuromorphic processing has also been applied to non-invasive neural interfaces, specifically in decoding sEMG recordings from motor neurons. In traditional EMG-controlled prosthetic limbs, nerve activity from the residual limb is used to control the device through gesture prediction or regression. However, integrating neuromorphic hardware into the signal decoding stage for online processing could potentially improve efficiency and reduce power consumption [160].

The neuromorphic DYNAP chip was also used to implement a hardware SNN for decoding sEMG recordings from a Myo band (Ctrl Labs, New York, NY, USA), which consists of eight surface electrodes. The recordings were converted into spike trains using a delta-modulator analog-to-digital converter (ADC) algorithm and input into the SNN. While the authors found the SNN to underperform other traditional classification algorithms, and the system was not implemented online, the study is a critical first step toward demonstrating the potential for ultralow-power neuromorphic hardware to replace more power-hungry processing pipelines [118].

5.3. Cognitive prostheses

Disruptions in neural circuitry or abnormal firing can often significantly impair the function of associated brain regions [161]. To address this issue, Buccelli *et al* at the Italia Institute of Technology have explored coupling the activity of a biological neuron population with neuromorphic hardware for real-time neuromodulation. A hardware-implemented SNN was utilized to establish bidirectional communication between two neuron populations via neuroprosthesis and was tested *in vitro* [5]. A BNN consisting of two neuron populations was grown on an MEA electrode and subjected to a simulated lesion using laser ablation. To restore communication between the two populations, an FPGA board with spiking neurons was used for real-time processing. If both neuron populations were intact, the detection of a network burst in one population would send a stimulation pulse sent to the other population. To consider scenarios where a neuron population was damaged, a hardware SNN with 100 Izhikevich neurons, consisting of 80 excitatory neurons and 20 inhibitory neurons, was employed to replace the biological neuron population. Both cases demonstrated an increased cross-correlation area of spike trains and a decreased probability of isolated network bursts in the lesion populations, indicating a partial restoration of synchronicity.

To enable one-way communication from an SNN to a BNN, a system was developed using optogenetic stimulation [119]. A neuronal culture expressing ChIEF-mCitrine, a genetically-encoded protein that can be expressed in neurons and can respond to blue light stimulation, was grown on an MEA to enable blue light responses. Similar to the previous study, an SNN composed of 100 Izhikevich neurons was implemented using an FPGA board. The SNN's spiking activity was used to stimulate the BNN via 8×8 pixels of blue LEDs. The experiment was repeated 12 times using four different sets of SNN parameters. Mosbacher *et al* measured the information transmission by analyzing the correlations between input similarity to the BNN and the corresponding output similarity of the corresponding output similarity from the BNN. The results showed a high correlation coefficient of 0.81, which was related to the intensity and frequency of the stimulus from the SNN. The degree of suppression of spontaneous network synchronization (NS), i.e., the ratio of NS's frequency in the BNN with and without the SNN, was found to be positively correlated with information transmission, indicating some success in establishing connectivity.

6. Neuromorphic perception

Neuromorphic sensors offer significant value in understanding the computational and memory efficiency of the nervous system. These brain-inspired sensors can provide insights into how biological machinery processes information and exploiting these observable features can lead to better medical interfaces.

Compared to current electromechanical sensors, biological sensing organs operate with much higher efficiency. For example, while a video camera continuously captures frame-by-frame data full of redundant information, the human retina uses numerous localized units that individually respond to incident light [21, 162]. The field of neuromorphic or biomimetic sensors, which aims to emulate biological sensing capabilities, has been extensively researched for several decades. Early work that introduced silicon retina, cochlea, and olfactory devices progressed with the introduction of improved architectures and novel materials [163–167].

The advancements of biomimetic sensors, alongside improvements in artificial sensing capabilities, offer various significant applications in the medical field. For example, spiking neuromorphic sensors can create more biologically faithful representations of external stimuli in neural prostheses to restore perception-related impairments (see section 5.1). In addition to enabling the restoration of perception-related impairments, more advanced biomimetic sensing models have the potential to drive innovations in health-monitoring devices and techniques, such as telepresence surgery [168]. Neuromorphic hardware has been used to replicate various senses, including sight, sound, olfaction, touch, and balance (vestibular mechanics). Many of these modern works have been largely directed toward reproducing the event-based representation of external stimuli and low-level signal processing that occurs in biological synapses [163, 165]. Advanced sensing applications can incorporate features such as learning through the use of devices like memristors or synaptic transistors.

6.1. Vision

The development of retina-inspired cameras has led to the creation and commercialization of event-based vision sensors. Similar to the retina, these devices use asynchronous spiking pixels that detect changes in light intensity rather than the intensity itself, as seen in the dynamic vision sensor. Further progress in this area has been made by several groups exploiting neuromorphic design to incorporate basic synaptic processing [162, 169]. With the integration of neuromorphic design and basic synaptic processing, these sensors hold great potential in detecting nuances and aiding in imaging, as well as detecting involuntary movements and paralysis in patients with conditions such as Parkinson's, stroke, Huntington's chorea, and more.

Neuromorphic phototransistors have been used to implement light sensors with memory characteristics. For example, a neuromorphic active pixel image sensor array (NAPISA) demonstrated synaptic plasticity [170]. Each pixel in the NAPISA contains a hybrid heterostructure phototransistor consisting of indium–gallium–zinc oxide and indium–zinc-oxide hybrid. By taking advantage of the charge trapping/de-trapping properties of the material, it was possible to achieve synaptic potentiation and depression in the photocurrent in response to light pulses. Another neuromorphic light-sensing array using the same charge-trapping concept also showed synaptic learning [171]. The device was constructed using carbon nanotubes and quantum dot phototransistors that exhibit short-term and long-term synaptic plasticity due to the dependency of the photoresponse on both light intensity and time. Gradual weight decay after a stimulus was used to emulate paired-pulse facilitation (PPF).

In similar cases, reinforcement learning has been demonstrated in phototransistors through long-term synaptic potentiation after repeated light pulses. The potential of neuromorphic phototransistors in medicine is vast, as they offer the ability to identify anomalies more quickly in screening results and help physicians localize issues. With the demonstrated synaptic learning and potentiation capabilities of these devices, they could be used in the future for advanced medical imaging techniques and even in the development of neural prostheses to restore perception-related impairments.

6.2. Touch

Many approaches to neuromorphic tactile sensors have been investigated for potential application in electronic skin (e-skin or e-dermis) [150, 151, 168, 172] as mentioned in section 5.1. These tactile systems mimic the structure of the somatosensory system by using resistive pressure sensors that output spike-encoded information to a synaptic device based on memristors or synaptic transistors. By utilizing this strategy, neuromorphic tactile systems are capable of integrating multiple stimuli over space and time and also exhibit synaptic learning and memory similar to those observed in biological systems.

Kim *et al* at Stanford University and Seoul National University have also created a biomimetic artificial sensory nerve for pressure-sensing using organic electronics [173]. The study utilized gold/carbon-nanotube hybrid resistive pressure sensors connected to ring oscillators, which converted stimuli into voltage spikes to be used as inputs to a synaptic transistor. The synaptic transistor's design allows it to integrate input pulses by connecting the gate electrode to multiple ring oscillators. In their study, the researchers used Braille letters as inputs and found incorporating synaptic transistors improved the distinguishability of different letters. Spiking sensors have also shown an inherent advantage of being naturally compatible with biological nerves. This was demonstrated by connecting a synaptic transistor to an efferent nerve on a roach leg, which successfully established a simple reflex arc with tactile stimuli.

The NeuTap neuromorphic tactile system uses a strategy similar to that of a synaptic transistor, connecting—resistive pressure-sensing to integrate isolated spatiotemporal stimuli [174]. Transistors made of polyvinyl alcohol, a biocompatible polymer that responds to changes in humidity, and indium–tungsten-oxide, a material commonly used in thin-film transistors, exhibited PPF, mentioned in section 5.1, when stimulated with two successive input spikes. Additionally, the dynamic changes in conductance resulting from stimuli and the subsequent conductance decay may mimic the memory and forgetting processes observed in biological synapses. Wan *et al* at Nanjing University demonstrated that the weights of the synaptic transistor could be used to distinguish simple tactile patterns when used as inputs to a supervised machine-learning model. This presents remarkable advantages in the field of prosthetics, where the ability to replicate memory and forgetting processes is essential for the perception of tactile sensations.

Memristors have also been used as synaptic devices for tactile neurons in some studies. For instance, a biomimetic e-skin using piezoresistive sensors was interfaced with a Pt/HfO_2/TiN memristor, a memory-holding device capable of high endurance and retention exhibiting a stable resistance state. Similarly, the application of pressure stimuli to the piezoresistive sensors induces conductance changes across the two terminals of memristors, resulting in the adjustment of artificial synaptic weights and thus enabling learning behaviors. These learning behaviors can be replicated in prosthetic devices, allowing patients to better interact with the world around them. The memristor's voltage response, which is equivalent to the excitatory post-synaptic current in neurons, was shown to increase with spike count, exhibiting plasticity behaviors similar to those seen in their biological counterparts. Kim *et al* at Seoul National University found that memristors can be utilized to store tactile memory in the form of conductance or synaptic weights, which can persist for a considerable amount of time after the stimuli [173], which is extremely advantageous for long-term prosthetic limbs.

The ability of neuromorphic tactile systems to mimic the somatosensory system and exhibit bio-like learning and memory, as demonstrated using synaptic transistors, holds great potential for their application in electronic skin and medical devices.

6.3. Hearing

Neuromorphic cochlear implants offer a promising approach to enhance auditory processing in individuals with severe to profound hearing loss. Drawing inspiration from the human nervous system, these implants strive to provide a more natural perception of sound while minimizing power consumption and optimizing the device's compactness.

One study by Jimenez-Fernandez *et al* introduced a novel neuromorphic binaural auditory sensor architecture implemented on an FPGA [175]. Unlike conventional digital cochlear implants, this design directly processes audio signals encoded as spikes using pulse frequency modulation. By employing address-event representation (AER), the system generates a frequency-decomposed audio representation, enabling researchers to investigate audio processing and learning activity in the brain. The implemented system demonstrated adjustable frequency range, maximum output event rate, power consumption, and slices requirements.

Marienborg also developed a processing unit for cochlear implants based on neuromorphic principles [176]. By leveraging nerve-cell modulation in microelectronics and drawing parallels with delta-sigma ADCs, the researchers proposed computationally efficient solutions with reduced power consumption. The work highlighted the potential of real-time signal processing in low-power electronics for cochlear implants.

Furthermore, Lande *et al* proposed a biologically inspired neuromorphic cochlear implant that incorporates spike-based signal processing [184]. This implant utilizes a single-chip micropower CMOS and digital control through neuromorphic coding and redundancy, allowing for scalability to a large number of channels. These studies contribute to the advancement of neuromorphic cochlear implants by integrating principles from neuroscience into microelectronics, ultimately leading to improved auditory processing.

6.4. Smell balance & others

Although neuromorphic synaptic processing has been primarily integrated into tactile and visual sensors, researchers have also explored the use of neuromorphic hardware for other senses. For example, there has been a growing interest in the development of artificial olfactory sensors, or e-noses, neuromorphic models for gas-sensing. Like the memory and learning exhibited in visual and touch sensors, an organic transistor-based nitrogen dioxide (NO_2) gas detector was implemented on several occasions, which showed synaptic plasticity and memory [185]. Detecting NO_2 is important for medical professionals since the harmful gas can cause respiratory problems and aggravate existing heart and lung diseases and is often found in air pollution. Researchers argue that the slow desorption rate of detected molecules allows for the accumulation of repeated and prolonged exposure. This could be leveraged as a memory system to simulate organ damage in health monitoring applications [186–188]. However, e-noses have not yet been fully exploited in medicine to detect disease and abnormality biomarkers, such as metabolic biomarkers for Parkinson's disease [189].

Another synaptic e-nose was developed by Han *et al* at the Korea Advanced Institute of Science and Technology by using a semiconductor metal-oxide gas sensor connected to a single metal-oxide semiconductor field-effect transistor neuron [190]. To enable firing at various frequencies, a parasitic capacitor was connected in parallel with the transistor. Different gases can elicit different spiking responses, and by adjusting the gate voltage of the transistor, inhibitory responses can also be achieved. Two sensing neurons were used as inputs to the simulated software SNN to classify four gases with an accuracy of 98.25% on 80 test samples. The authors also implemented a simple single-layer hardware SNN on a printed circuit board and tested its ability to classify the two wine brands. The SNN showed different output neuronal firing frequencies for each wine which can be used for accurate classification [191]. The ability to distinguish between odors has significant implications for olfactory dysfunction. Implementing these learning techniques on an olfactory interface could lead to precise regulation and smell dysfunction.

A neuromorphic model was also developed to mimic the vestibular system for potential applications in prosthetics and robotics [183, 191]. In humans, otolithic organs and semicircular canals provide a sense of acceleration and rotation, which supports natural balance and movement. This system models both otolith organs and semicircular canals using VLSI hardware. In this study, Corradi

Table 1. Applications and techniques of neuromorphic computing with potential in medicine.

References	Purpose	Techniques and tools	Results
		Imaging using hardware or software	
[88]	DNN accelerator	LNPU chip	Supports inference $\sim 2\times$ energy improvement
[87]	DNN accelerator	Eyeriss chip	200–300 mW consumption
[44]	Denoising/extraction on image fusion	M-PCNN	Edge extraction denoising
[22]	Breast cancer classification	Memristor crossbar SNN and Loihi	85.6% accuracy 3.4 mJ per inference
		Biosignal processing	
[19]	Seizure biosignal classification	DSNN	97.6% accuracy
[121]	Real-time ECG classification	SRNN and DYNAP	91% true positive rate 722.1 μW total power
[122]	COVID-19 diagnosis	DCSNN	99% accuracy
		Neural interfaces	
[7]	Retinal implant	Spiking photodiode sensors	2.7 mW consumption
[154, 155, 177]	Intramuscular/intraspinal stimulation in cats	Silicon central pattern generator	Controlled forward locomotion
[6]	Upper limb e-dermis	Izhikevich sensors	Classified fingers and objects perceived pain
[152]	Monkey computer cursor control	SNN	>94% success rate
[116]	Rat mobile cart control	SNN and ROLLs	100% convergence rate
[118]	sEMG and gesture prediction	SNN, DYNAP, and Myo	95% accuracy
[5]	Modulating and restoring network	SNN and FPGA	Bridged lesioned neurons
[119]	Modulation and restoring network	SNN optogenetic stimulation	Demonstrated network connectivity
		Biomimetic sensors	
[168]	Feedback for telepresence surgery	Spiking sensors	63% accuracy
[178]	Tactile sensor learning	Synaptic transistor	0.4% error rate
[179]	Photosensors emulating memory	Memristor	Memory retention post 1 week
[180]	Tactile sensor exhibiting learning	Organic synaptic transistor	Distinguished Braille
[172]	Tactile sensor memory	Spiking sensor w/ memristor	Demonstrated plasticity
[170]	Photosensors emulating memory	Synaptic phototransistor	Short/long-term potentiation
[181]	Gas sensor with memory	Organic synaptic transistor	Accumulated gas exposure
[181, 182]	Gas sensor with learning	SNN synaptic transistor	98.25% accuracy
[183]	Vestibular prosthesis	SNN and spiking sensors	IMU spike-encoded output

et al at the University of Zurich connected the spike-encoded output from a six-axis inertial measurement unit to a neuromorphic chip with 58 adaptive exponential integrate-and-fire neurons using the AER protocol [15, 16]. The AER is a neuromorphic approach that encodes the event's location, polarity (increase or decrease in measurement), and the time at which it occurs. In the implemented neuromorphic system, the otolith organs and semicircular canals were modeled separately. The neurons representing otolith organs were arranged in a grid on both the horizontal and vertical planes, with their positions indicating the preferred acceleration stimulus. For the semi-circular canals, the neurons were arranged in three planes of rotation and were encoded with four rotation neurons each, representing both clockwise and counterclockwise directions. An integrator network with additional memory and inhibitory neurons was used to develop a head direction by remembering the angular position. The response properties of the artificial neurons were found to align with biological vestibular afferent neurons, which validates their plausibility for use in prosthetics and robotics [180]. By mimicking the biological system, the use of neuromorphic hardware can offer a potentially more precise and natural sense of balance and movement, leading to improved outcomes for patients.

7. Challenges in integrating neuromorphic engineering with medicine

While this paper has demonstrated many potential applications of neuromorphic technology in medicine (see table 1), there are still limitations that make it challenging to incorporate traditional neuromorphic approaches.

One such limitation is the difficulty of recording neural signals and transmitting them off-chip [192, 193]. Neural signals typically have bandwidths of up to 10 kHz, which requires a sampling frequency of at least 20 kHz. With an MEA containing hundreds of recording sites, the resulting data can be on the order of megabytes per second, and using neuromorphic hardware for recording could exacerbate this issue by capturing even more data at a higher temporal acquisition rate. This can lead to challenges in data transfer and power consumption, potentially complicating medical decision-making.

Another challenge in integrating neuromorphic technology with medicine is the development of reliable and accurate algorithms for analyzing and interpreting the large amounts of data generated by neuromorphic devices. While traditional machine learning approaches are currently state-of-the-art, neuromorphic adaptations may not be suitable for processing data from devices that operate in varying environments and with varying data streams. For example, algorithms like SNNs can be difficult to train and are often dependent on specific datasets, which may limit their applicability to real-world situations [194, 195]. Besides dataset dependence, SNNs often require specialized learning rules and training algorithms that are not as well-established as those used for traditional neural networks. This added complexity can make it more challenging to fine-tune parameters for applications and may require more effort to optimize performance. Additionally, there is a need for standardized protocols for data collection and analysis to ensure consistency and reproducibility across different studies and devices, which is not currently offered by standard neuromorphic learning models.

The fabrication of neuromorphic hardware currently faces several limitations. The specialized components and architectures used in neuromorphic hardware can be different from those used in traditional computing hardware, resulting in increased costs and complexity. Additionally, as mentioned in section 2, analog architectures, which are often preferred due to their energy-efficient and computationally efficient solutions, can suffer from fabrication issues such as transistor–transistor mismatch. This natural variation in the electrical properties of devices can result in variations in behavior across the system, affecting accuracy and reliability [196, 197].

While the challenges listed above may present significant obstacles to development, researchers and healthcare practitioners can take an optimistic perspective from the strides that scientists have made in the many examples discussed throughout this review. These advancements demonstrate the potential for integrating neuromorphic technologies with medicine and motivate continued progress in the field.

8. Conclusion

Neuromorphic computing is a discipline intersecting engineering and neuroscience that exploits the brain's massively efficient mechanisms when performing everyday tasks. Following discoveries in biologically plausible learning mechanisms, miniaturization, emulative transistor design, and improved hardware tools, neuromorphic solutions have ushered their way into the application space. By mimicking the fundamental operations and architecture of our nervous system, scientists can begin to improve typical medical technology limitations by offering extremely low energy, low latency, high bandwidth, and biologically consistent solutions.

SNNs have emerged as contenders to typical machine learning methods, event-based processing has helped scientists reimagine communication protocols, and in-memory devices, like memristors, have disrupted von Neumann designs, challenging their dominance in the field of computing. These are a few of the improvements this paper has discussed when providing promising insight into potential medical technological improvements.

It is worth noting that neuromorphic engineering is still in its relative infancy when compared to conventional computing. Both software and hardware solutions have their restrictions simply because these novel brain-inspired approaches have not existed as long as their non-brain-inspired counterparts. Nevertheless, researchers have highlighted the potential of neuromorphic innovations to eventually complement or even replace the traditional problem-solving methods in medicine. We hope that this review has helped glean more interest in neuromorphic engineering and ultimately assist medical professionals in helping patients worldwide.

Data availability statement

Any data that support the findings of this study are included within the article.

Acknowledgments

Khaled Aboumerhi acknowledges the U.S. Fulbright Program for funding while at ETH Zürich in Switzerland. Aboumerhi also acknowledges and is grateful for the discussions had at the 2022 CapoCaccia Workshops Toward Neuromorphic Intelligence in Alghero, Sardinia, Italy. Amparo Güemes acknowledges funding support from the Royal Commission for the Exhibition of 1851. Francesco Tenore acknowledges funding from a Johns Hopkins University Applied Physics Laboratory sabbatical Grant.

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