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Review article

Biomedical applications of wearable biosensors

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ABSTRACT

Over the last decade, both scientific and commercial communities have focused on developing wearable sensors for biomedical use. These sensors monitor vital signs in various individuals, including patients, athletes, infants, and the elderly. They contribute to mobile health technologies, offering real-time health recommendations and management. Wearable and implantable devices are reshaping healthcare, driven by sensor advancements. Biosensors, known for their simplicity and adaptability, hold significant potential. This review focuses on categorizing wearable biosensors, including classifying biological elements, nanomaterials, and transducers. It also examines the various types of wearable sensors, specialized sensor designs, applications in textile materials, wearable medical devices, and the advantages of biosensors in medicine. Comprehensive analysis of the various applications of wearable biotechnology while addressing the challenges and possible remedies associated with wearable technology were reviewed.

1. Introduction

Medicine, biology, and biotechnology heavily rely on biological and biochemical mechanisms. Biosensors play a pivotal role in converting these signals, helping to surmount the challenge of directly translating biological data into electrical signals [1–4]. Recent advancements in methods and tools have broadened the utilization of these devices [2,5,6]. A biosensor is an analytical instrument responsible for assessing modifications induced by biological processes and transducing them into electrical signals. Any biological constituent or substance, encompassing enzymes, tissues, microorganisms, cells, acids, and the like, can be harnessed in a biological process. The resultant output from the transducer may manifest as current or voltage, contingent on the specific enzyme and components incorporated within the biological entity (electrical form) [7–11].

Biosensors, which may characterize and quantify biomolecules, have significantly advanced in biology, medicine, and veterinary science over the past two decades. As previously indicated, a biosensor is a composite entity comprising several integral components: an analyte recognition element, a bioreceptor, a transducer, electronic components, and a reader interface [12–17]. The associated electronics or signal processing components are conventionally linked to the reader interface of the biosensor, facilitating the presentation of outcomes. These reader interfaces are often meticulously crafted to align with diverse operational principles inherent to various biosensors [18–22]. Notably, the expense of developing such reader interfaces can at times be the most substantial aspect of sensor development. During assessment, as the biosensor evaluates the target substance in reaction to distinct stimuli, the transducer adeptly captures the ensuing data and converts the signal into an electrical manifestation, which is subsequently quantified and relayed as output data [23–26]. Biosensors emerge from an ever-expanding domain that intricately amalgamates fundamental research in biology, chemistry, and physics with engineering, computer science, and assorted other disciplines [27]. The necessity is the driving force behind this convergence, which aims to accommodate various application domains. Within the purview of this study, we shall view attributes such as specificity, storage capability, operational efficiency, and environmental robustness, among others, all of which collectively influence the choice of biological material [28–31].

2. Classification of wearable biosensors

The term "biosensor" is defined by the International Union of Pure and Applied Chemistry as "a device employing specific biochemical alterations facilitated by isolated enzymes, immune systems, tissues, organelles, or whole cells to identify chemical compounds, typically through electrical, thermal, or optical signals." In line with this definition, a biosensor comprises three core constituents, each of which will be

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expounded upon in this chapter: i. A bioreceptor, a molecular entity (such as an enzyme, cell, or antibody) that recognizes the target analyte, ii. A transducer, a component that translates the biorecognition event into a measurable signal, iii. Electronics, encompass a signal-processing system that converts the transduced signal into a discernible display. By this framework, biosensors are categorized based on three fundamental factors: I) the type of biological component employed, II) the type of nanomaterials integrated, and III) the type of transducer implemented [32,33].

2.1. Type of biological element used

Biosensors have been developed employing an assortment of biological recognition constituents, including cofactors, enzymes, antibodies, microorganisms, organelles, tissues, and cells sourced from more complex organisms.

2.1.1. Enzyme-based

Enzyme-based chemical biosensors derive their foundation from biological principles [34–36]. These biosensors hinge upon enzymes that necessitate stability within the customary operational conditions of the biosensor, alongside their capability to induce specific biological reactions. An intricate grasp of the target analyte and the intricacies of the surrounding matrix in which the analyte is to be quantified are pivotal considerations in the design of biosensors. Amperometric enzyme-based biosensors come with a range of challenging limitations. These encompass the risk of signal degradation due to fouling agents and susceptibility to interference from compounds inherent to the sample matrix. In order to gain deeper insights into the functionality of enzyme biosensors, this chapter scrutinizes their analytical performance throughout various periods and explores methodologies implemented to enhance their efficacy. Additionally, the interplay between biosensing and the composition of biological fluids is addressed, shedding light on their reciprocal interaction.

Castillo et al. [37] outlined the subsequent applications of enzyme-based amperometric biosensors:

1. Offline Analytical Equipment: These biosensors facilitate the extraction of biological samples, which are then subjected to analysis for target analytes in a detached manner. An illustrative example is the availability of commercially procurable instruments used to gauge blood glucose levels.
2. In Vivo Sensing: Implantable biosensors continuously monitor alterations in target analyte concentrations in extracellular environments within the body. Notably, these implantable devices are primarily restricted to preclinical investigations conducted on animal models due to their invasive nature.
3. Online Integration: This category involves the fusion of biosensors with sampling apparatuses embedded within biological substrates or the body. An instance of this concept is the coupling of flow-through detectors containing biosensor components with implanted microdialysis probes. This synergistic approach enables real-time analysis.

Amperometric enzyme-based biosensors can encounter interference from chemicals present within the solid matrix [37–39]. This predicament is particularly pronounced in biological samples where small molecule metabolites, proteins, macromolecules, cells, and electrochemical confounders coexist. Intricate metabolic processes, such as blood coagulation, amplify the complexity of these fluids. Various pathological states, ranging from inflammation to tumorigenesis, can alter specific fluid parameters' chemical composition and pH, thereby influencing enzyme activity and subsequently impacting biosensor efficacy. To navigate these challenges, extraction, preconcentration, filtration, and derivatization strategies can be employed as pretreatments to alleviate matrix-induced interference. Nonetheless, the preferable course of action involves employing biosensors directly in the unaltered matrix, evading the need for preparatory interventions. This approach aligns with the desire to maintain the authenticity of the sample matrix while capitalizing on the direct application of biosensors. Amperometric enzyme biosensors are classified into three fundamental generations based on the electron transfer mechanism employed to measure the biochemical reaction or the separation level of biosensor components (including transducers, enzymes, mediators, and cofactors). In all cases, the presence of an enzyme is essential, thereby rendering sensor functionality contingent upon several variables, such as operational pH, temperature, and related factors.

2.1.1.1. First generation biosensors. The number of analytes and/or enzymatic reaction byproducts that diffuse toward the transducer surface and produce an electrical response is measured by first generation biosensors (Fig. 1.**A**). Additionally, they are known as mediatorless amperometry biosensors [40–43].

This family of biosensors takes advantage of an enzyme's ability to convert a substrate into an electroactive, quantifiable byproduct by immobilizing it on the transducer surface. These biosensors depend on two classes of enzymes: oxidases and dehydrogenases. Coenzymes (such as NAD+, NADP+, NADH, NADPH, ATP FAD, and FADH) are needed for oxidases and dehydrogenases to catalyze reactions, and these coenzymes must be replenished for the enzyme to catalyze subsequent processes. For instance, the following reactions take place when oxidase enzymes are engaged Eqs. (1) and (2):

$$\text{S+E-FAD} \rightarrow \text{E-FAD-S} \rightarrow \text{E-FADH}_2\text{+P} \tag{1}$$

$$\text{E-FADH}_2\text{+O}_2 \rightarrow \text{E-FAD +H}_2\text{O}_2 \tag{2}$$

First generations biosensors are extremely sensitive and have very short response times, usually in the order of one second. First generation biosensors frequently need electrode pretreatment to produce repeatable surfaces and sensor response, and matrix effects linked to interference adjustments are frequently required. Additionally, repeated use of amperometric biosensors, particularly in undiluted samples or complex biological matrices, frequently causes the transducer surfaces to foul, affecting the biosensor response [44–47].

2.1.1.2. Second generation biosensors. The mediators that operate as oxidizing agents in second generation biosensors, also known as mediator amperometric biosensors, serve as electron carriers. This method makes working at low potentials achievable while reducing O_2 dependence and the effects of interfering molecules. Although methylene blue, phenazines, methyl violet, alizarin yellow, Prussian blue, thionin, azure A and C, toluidine blue, and inorganic redox ions are also frequently utilized, ferricyanide and ferrocene are the most popular and well-known mediators. Replace oxygen with an acceptor that can transfer electrons from the enzyme's redox center (E) to the electrode to achieve even more significan gains (Fig. 1.**B**).

The following scheme explains how the reaction happens:

$$\text{S + E(ox)} \quad \rightarrow \quad \text{P + E(red)} \tag{5}$$

$$\text{E(red) + 2MOX} \quad \rightarrow \quad \text{E(ox) + 2MRED + 2 H}^+ \tag{6}$$

$$\text{2MRED} \quad \rightarrow \quad \text{2MOX + 2e}^- \tag{7}$$

Media may be immobilized on the electrode surface or added to the sample. In order to define the biosensor performance over time for immobilized mediators, it is crucial that the mediator is trapped near the enzyme and that, if the mediator is lost, the duration of loss is understood. A suitable mediator is stable throughout the reaction while it is occurring and does not participate in the electron transfer. Additionally, the mediator ought to have a lower redox potential compared to other electroactive chemicals in the sample. Since second generation biosensors typically have low stability because of the immobilized mediators, they are less frequently used than first generation biosensors.

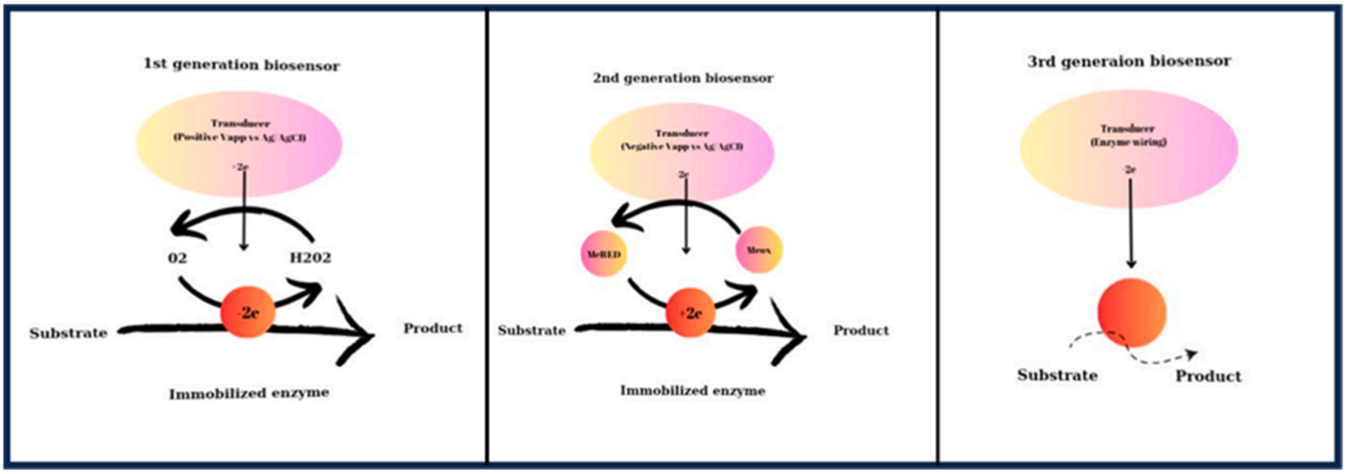

Fig. 1. Enzyme-based biosensors; A. first, B. second, and C. third (adapted from Rocchitta et al.) [274].

2.1.1.3. Third generation biosensors. Third generation biosensors rely on bio electrocatalysis, in which an enzyme and electrode directly transfer electrons **(**Fig. 1**.C)**. Three components comprise a third generation biosensor: an electrode as the entrapping surface, a redox polymer (or nano-scale wiring element) to ensure signal propagation, and an enzyme as the bio-recognition element. Performance is enhanced by "wiring" the redox center of the detecting enzyme to the electrode surface using a redox polymer. Although still in development, third-generation biosensors are only sometimes employed for analysis. Third generation biosensors, however, are hopeful due to advancements in polymer science and nanotechnology since the sensors are predicted to have rapid response times and be primarily unaffected by oxygen/cofactor concentrations.

2.1.2. Biological matrices

2.1.2.1. Saliva. Saliva is appealing for noninvasive health monitoring since it is simple to retrieve on demand and has a composition that changes with body health and status [48,49]. The average salivary production rate can be greater than 1 L per day, and levels of metabolites, enzymes, hormones, and proteins can change in response to physical activity, dietary choices, chronic conditions including diabetes and pancreatitis, stress and depression, and cancer [50]. Salivary flow rate can also be telling because it varies with hydration, drugs, and circadian rhythms and further influences the levels of biomarkers. It is essential to ensure that the analytes being tested represent the secretions from salivary glands and not leftover food or drink because saliva is prone to contamination. It converts complicated sugars into simple sugars; hence, its activity might interfere with the precise detection of analytes, such as glucose [49,51]. The pH of normal saliva, influenced by oral hygiene and saliva buffers (bicarbonate), ranges from 6.5 to 7.4 [52,53].

2.1.2.2. Urine. Nearly all the cations found in urine are Na^+, K^+, Ca^{+2}, Mg^{+2}, and NH_4^+, whereas around 80% of the anions are chloride, sulphate, phosphate, and bicarbonate. Proteins and cells are insignificant. The pH of urine typically ranges from 4.6 to 8, which is influenced by food and general health [54].

2.1.2.3. Tears. Tears are appealing for continuous health monitoring because they are readily available, on demand, and frequently produced at rates of over 1 L per minute. The lachrymal glands secrete tears, which can be an intriguing fluid for minimally invasive monitoring. Insignificant amounts of protein can be found in tears. The pH range should be between 6.5 and 7.6 [51].

2.1.2.4. Sweat. Sweat contains urea, uric acid, sugar, lactic acid, amino acids, and ammonia, with individual quantities varying wildly. Sweat typically has a pH of about 5.5 [55,56].

2.1.2.5. Blood, plasma and serum. White blood cells, red blood cells, platelets, and plasma, the liquid component of blood, are all mixed in intricate ways. Plasma is roughly 55% of blood volume and is 90% water. Blood plasma without fibrinogen is called serum. Numerous water-soluble substances, including nutrients, hormones, and electrolytes, are in serum and plasma. Drugs and proteins may also be found, including globulins (containing antibodies), fibrinogen (a blood clotting factor), albumin (an essential protein component), and other clotting factors. Immunoglobulins, albumin, lipoproteins, haptoglobin, and transferrin are a few of the up to 10,000 proteins in serum. Blood has a strong buffering capacity, and its pH typically ranges from 7.35 to 7.45 [57,58].

2.1.2.6. Extracellular fluid and brain extracellular fluid. The majority of the components of ECF are ions (Na^+, Cl, and Ca2 +), glucose, amino acids, and ATP, with very little protein [59,60]. Amperometric biosensors are used for various purposes, including implanting these devices in specific brain regions where they touch brain extracellular fluid (bECF). The composition of the bECF could be thoroughly characterized by in vivo microdialysis. Notably, the ionic makeup of bECF (NaCl 147 mM, KCl 2.7 mM, $CaCl_2$ 1.2 mM, $MgCl_2$ 0.85 mM) is well known [61,62]. There are also electroactive compounds, including ascorbic acid (AA). AA is one of the most potent antioxidants and conducts a variety of tasks at the neuronal level. Additionally, catecholamines such as dopamine and noradrenaline, as well as their primary metabolites, are present. These include 3,4-dihydroxyphenylacetic acid, 3-methoxytyramine, and homovanillic acid (HVA). In addition to 5-hydroxy-tryptamine (serotonin) and its metabolite 5-hydroxyindoleacetic, uric acid produced by the breakdown of purines can be found in bECF. In addition to these chemicals, bECF contains many others that can be identified using amperometric biosensors, including glucose, lactate, glutamate, acetylcholine, and choline [63,64].

2.1.3. Antibody-based

Specific biomolecules are naturally chosen by antibodies [65,66]. They are y-shaped proteins that plasma cells, an essential component of the immune system, manufacture. By specifically attaching to their membrane, antibodies recognize infections and direct the immune system's attention to them. Each antibody has a specific substrate to which it will only bind. Even though antibodies come in many forms, they are all molecules bound specifically. The detection threshold and sensitivity of the biosensor may change depending on how the antibodies are bound to the transducer. The four approaches are random non-covalent, random covalent, oriented via the binding site, and oriented via an extra binding molecule. The origin of the antibodies employed in biosensors has an impact on the biosensor's results as well. There are three main categories of antibodies: monoclonal, recombinant, and polyclonal. Purification of polyclonal antibodies involves screening them with an antiserum directed against the target. Non-homogeneous antibodies are the result of this [67].

When homogenous antibodies are required, monoclonal antibodies are created by fusing antibody-producing plasma cells with immortal myeloma cells. These are examined to identify any cells making the required antibody, and then they are cloned until every cell makes the desired antibody. Recombinant antibodies, however, are created differently. They come from engineered microbes and are purified. Many of these recombinant antibodies need to be refolded after being purified in bulk. Recombinant antibodies, on the other hand, give the producer of the antibody more control over the final product (Fig. 2**.A)**. As a result, amino acids that interact with metals in the sensor framework can be included in the design of the antibody tail [69,70].

2.1.4. *Biological tissue-based*

Hormones, medications, and poisons can all be detected and measured using biosensors that are based on the tissue architecture of living animals [71,72]. Tissue-based biosensors have the potential to be used in a variety of biomedical sciences, including physiology, pharmacology, and biodefense. Tissue-based biosensors can typically be created from genetically altered cells or through direct genetic alteration that introduces biosensor proteins into animal tissue. The concentration of the molecule becoming detected is converted by biosensor cells into a physical signal that can be precisely quantified. The most adaptable foundation for tissue-based biosensors is provided by biophotonics [73,74]. Fluorescence or bioluminescence are the two types of light that biosensor cells can produce. Of the two, bioluminescence does not need a light source for input and has a better signal-to-noise ratio in living organisms than fluorescence. Using fusion proteins that can produce resonance energy transfer, protein-protein interactions can detect almost any chemical [75–77].

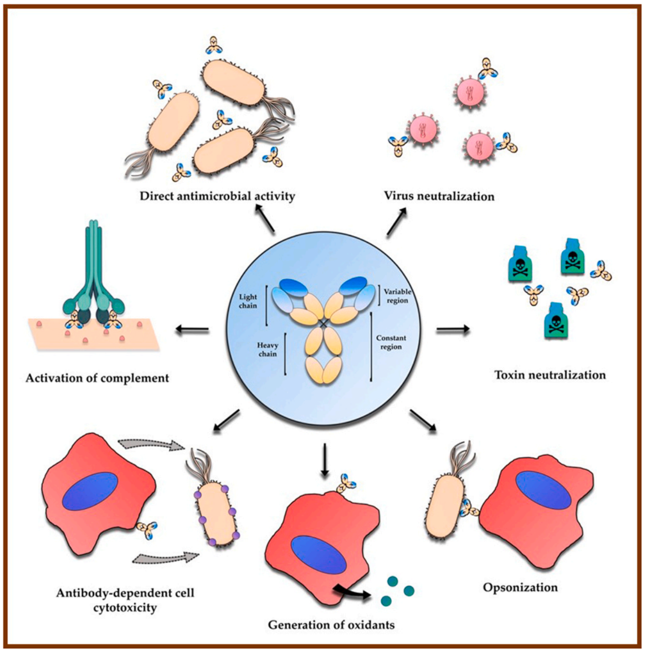

Fig. 2. A. Antibody-based (adapted by Seixas et al.) [68].

2.1.5. *Microorganism-based*

An analytical tool known as a microbial biosensor combines microorganisms with a physical transducer to produce a quantifiable signal proportional to the concentrations of analytes. Numerous microbial biosensors have recently been created for environmental, culinary, and medicinal applications [78,79].

Algae, bacteria, and yeast are a few examples of microbes that provide an alternative for making biosensors because cell culture allows for the large-scale production of these organisms. Additionally, microbial cells are more accessible to manipulate and have superior survival and stability in vitro than other cells from higher species like plants, animals, and humans, which can substantially simplify the fabrication process and improve the performance of biosensors. The ability of microbes to respond to various compounds, which can be utilized as the signal for sensing purposes, can be compared to a "factory" made up of multiple enzymes and cofactors/coenzymes. Even though microorganisms' metabolisms are non-specific, selectively microbial biosensors may be possible if undesirable metabolic pathways are blocked or desired ones are stimulated and if the microorganisms are adapted to the proper substrate of interest (target) through careful cultivation conditions [80,81].

The microbial cells, which act as the biosensor's recognition element, must be closely linked to the transducer to convert the biochemical reaction into a physical signal efficiently. Consequently, immobilizing microbes on transducers is crucial in creating microbial biosensors. Upon adding analytes to the immobilized microorganisms, various analytical techniques using appropriate transducers can detect the interaction between the bacteria and the target molecules. The analyte concentration and the observed signal can be linked. The most popular sensing methods employed in creating microbial biosensors are electrochemical and optical methods, which will be discussed in this review [82–84].

2.1.6. *Cell-based*

Bioreceptors encompass viable microbial cells that have undergone genetic modification to produce measurable signals in response to specific chemical or physical stimuli present in their surroundings [85–87]. Bioreporters, a subset of bioreceptors, encompass two pivotal genetic constituents: a promoter gene and a reporter gene. The promoter gene becomes activated (transcribed) upon the presence of the target stimulus within the cellular environment. In a conventional bacterial cell, the promoter gene is interlinked with other genes, which subsequently undergo transcription and translation, culminating in synthesizing proteins instrumental in the cell's response or adaptation to the encountered stimulus. In the context of bioreporters, the relevant genes or fragments thereof are replaced by a reporter gene. When the reporter gene becomes activated, it prompts the production of reporter proteins, which generate a discernible signal. Consequently, the presence of this signal signifies that the bioreporter has detected a specific target stimulus within its environment. Initially devised for fundamental investigations into factors influencing gene expression, this framework has extended its utility to various applications [88–90].

2.1.7. *Nucleotide-based*

The increasing amount of sequencing data supports an increasing number of potential single nucleotide polymorphisms (SNPs) (Fig. 3**.A)**, which are thought to disclose the genetic foundation of a person's vulnerability to disease and the variety of treatment responses. Therefore, there is a pressing need to create a sensitive, quick, user-friendly, and economical SNP identification technique. In the past two decades, biosensing methods have been created by fusing the distinct specificity of biological processes with the sensitivity of physical sensors, which has significantly improved the ability to identify SNPs [91,92].

Single nucleotide polymorphism (SNP), which is a single nucleotide variation in a specific and defined genetic site and occurs in the human genome at a frequency of about 1 in every 1000 bases, is one of the most

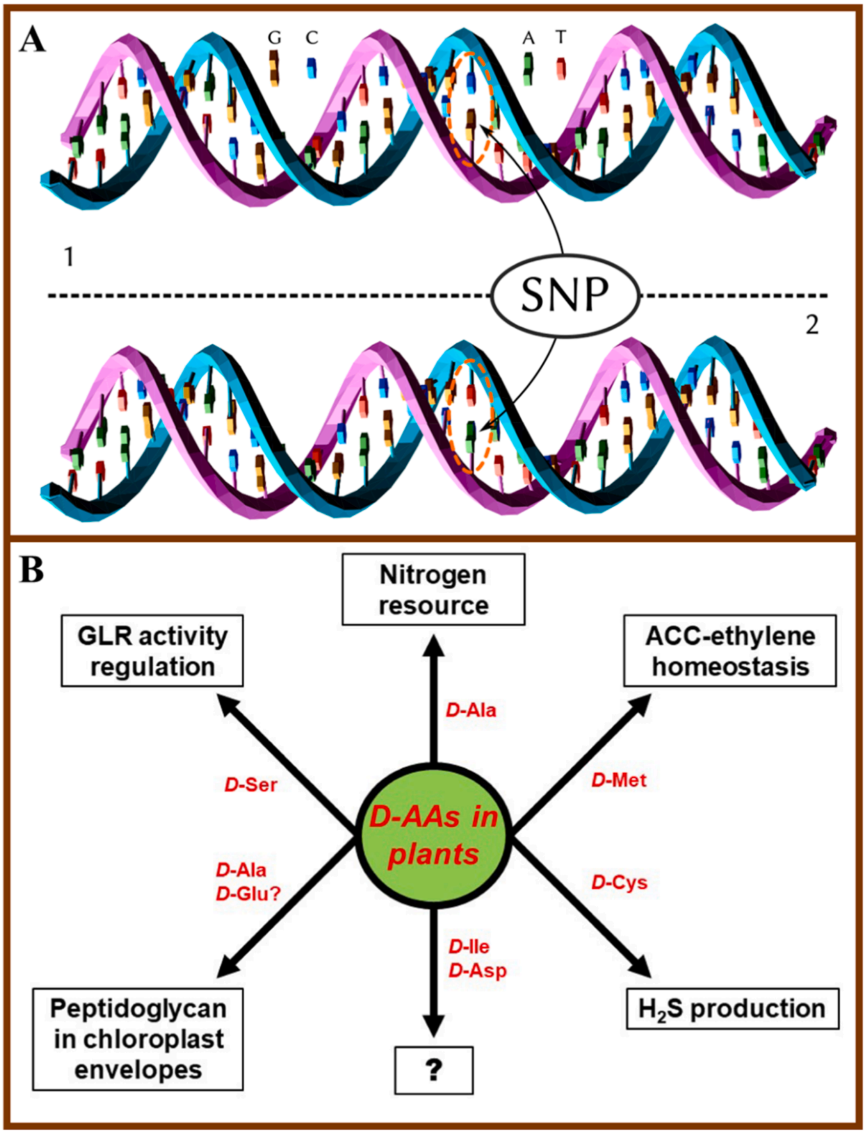

Fig. 3. A. Nucleotide-based: Single nucleotide polymorphism (SNP), B. Amino acid-based graphical abstract (reprinted from Kolukisaoglu) [272].

prevalent types of genetic variation [93–96]. Approximately 1.42 million SNPs have currently been found by the SNP collaboration. SNPs are broadly dispersed and highly conserved throughout the genome, making the map of SNPs a high-resolution genetic marker. Additionally, even harmless sequence changes in gene coding areas may change the amino acid sequence, affecting how well the related protein functions. SNP genotyping methods have recently been published using a variety of methods. The discovery of novel and unidentified SNPs could be accomplished via conventional techniques such as DNA sequencing. However, direct sequencing is not ideal due to its complicated processes and lengthy operating durations. Changes in conformation are among the alternate strategies. These methods could identify SNP-containing regions specifically to avoid complex DNA sequencing. However, their use is constrained due to inherent flaws, including low throughput and specificity. DNA microarray and denaturing high-performance liquid chromatography have recently been proposed for quick, effective, and extensive SNP analysis. However, both techniques demand pricey infrastructure and radioactive/fluorescent tags. Rapid, fundamental, and focused technology is critically required in this high throughput SNP testing situation for basic science and clinical diagnosis [97,98].

2.1.8. *Sensory receptor-based*

The development of biosensors was sped up by the identification and characterization of the multigene family coding the sensory receptors in various vertebrate or invertebrate models [99–102]. The structure, signaling mechanisms, and functions of sensory receptors differ amongst organisms. As a result, the operation and design of the biosensor device determine the creature that will serve as the sensory receptors. Dog olfactory receptors, for instance, are employed to detect drugs, humans, and explosive goods. On the other hand, because of their size and low cell density, Drosophila sensory receptors are considered promising biosensing candidates in clinical diagnostics. Drosophila cells can be grown at room temperature and are generally straightforward. Additionally, the Fundamentals of genetics, molecular biology, and neurology of Drosophila's gustatory and olfactory systems have been thoroughly studied and described. This might clarify how the Drosophila sensing systems are used in biosensing applications [103–105].

2.1.9. *Amino acid-based*

Amino acids (AAs) have garnered substantial attention across a spectrum of research endeavors in the chemistry and biology fields [106–109]. Their pivotal roles within cellular pathology and physiological processes have rendered AAs and their derivatives a focal point in the drug development landscape. As fundamental constituents for many proteins, hydrophobic and hydrophilic AAs exhibit remarkable properties, spanning aspects such as reverse cross-linking, chirality, and charge density. Traditionally, AAs have been dichotomized into nutritionally essential and nonessential categories for humans. Reports have surfaced indicating the utilization of AAs as adjunct therapies for various ailments. However, the clinical utility of AAs remains limited due to their modest molecular weight and suboptimal pharmacokinetics, presenting a pragmatic hurdle that necessitates resolution. The significance of AA analysis is perpetually on the rise across diverse domains, including biochemistry, clinical chemistry, nutrition, and pharmaceutical formulation. Numerous samples exhibit an array of AA contents, chemical compositions, and sample matrices (ranging from food to biological fluids or protein hydrolysates). AAs generate essential biomolecules like hormones, neurotransmitters, antibodies, and signaling molecules (Fig. 3. B). Assessing AA concentrations within biological fluids is pivotal for the early detection of various ailments, given that AAs function as precursors for numerous biomarkers. Studies have implicated numerous AAs in the etiology of disorders such as phenylketonuria, citrullinemia, and homocystinuria [109–111].

2.2. *Type of nanomaterials*

2.2.1. *Carbon-based nano-biosensor*

This chapter encompasses a variety of carbon-based nanomaterials (CNMs), including lattice structures resembling honeycombs, such as carbon nanotubes (CNTs), graphene (comprising graphene oxide (GO) and reduced graphene oxide (rGO), along with other related materials), and graphite. Carbon-based nanomaterials possess remarkable attributes, including low toxicity, high thermal and chemical stability, exceptional electrical conductivity, and impressive mechanical properties [112–116]. Their exceptional characteristics have garnered significant attention, particularly in wearable electronics. One noteworthy innovation described in this chapter involves a high elasticity strain gauge that employs capacitive sensing via parallel electrodes constructed from carbon nanotubes separated by a stretchable dielectric material. This device exploits the Poisson effect to induce strain, bringing the two transmitting electrodes closer. The capacitance of the sensor remained constant over 3000 cycles of testing at a 3% strain. Additionally, the chapter explores a sensor design reminiscent of crumpled/wrinkled skin, utilizing graphene for noninvasive real-time pulsing. Manipulating the stiffness of the substrate material (Polydimethylsiloxane or PDMS) allows for practical radial pulse measurements across various age groups and before/after movement, achieving an optimal equilibrium between sensitivity and linearity. Another notable innovation involves a strain sensor resembling fish scales crafted using elastic tape and a graphene layer. This design enables graphene layers to overlap by employing reversible slip, thereby modifying contact resistance. This sensor detects stretching and bending deformations due to its fish-scale-like structure, demonstrating high sensitivity, wide deformation range, reliability, and stability. Production involves stretching/exhausting a composite film composed of rGO and elastic tape, a simple, cost-effective, energy-efficient, and scalable technique. Furthermore, the chapter discusses a strain sensor predicated on highly aligned CNT fibers characterized by exceptional elasticity. This device, featuring a flexible substrate, rapid responsiveness, endurance, and the capacity to measure strains surpassing 900% with superior sensitivity, holds promise for applications spanning from soft robotics to conventional strain gauge applications (Fig. 4**.**) [113,117,118].

2.2.2. *Polymer-based*

Polymer conductors and semiconductors are pivotal constituents in the assembly of wearable sensors, owing to their cost-effectiveness, solution-processability, and facile chemical modification. These materials serve as foundational components for wearable sensor construction. Leveraging the inherent flexibility and stretchability of these materials offers benefits, including scalable and economical production, high-density integration of devices, and noteworthy tolerance to strain [123–127].

The fabrication of highly stretchable sensors and transistors centers around using conductive and composite semiconducting materials that exhibit innate stretchability. Typically, these materials encompass three key components: Stretchable Conductor, consisting of polydimethylsiloxane (PDMS) infused with a combination of gold

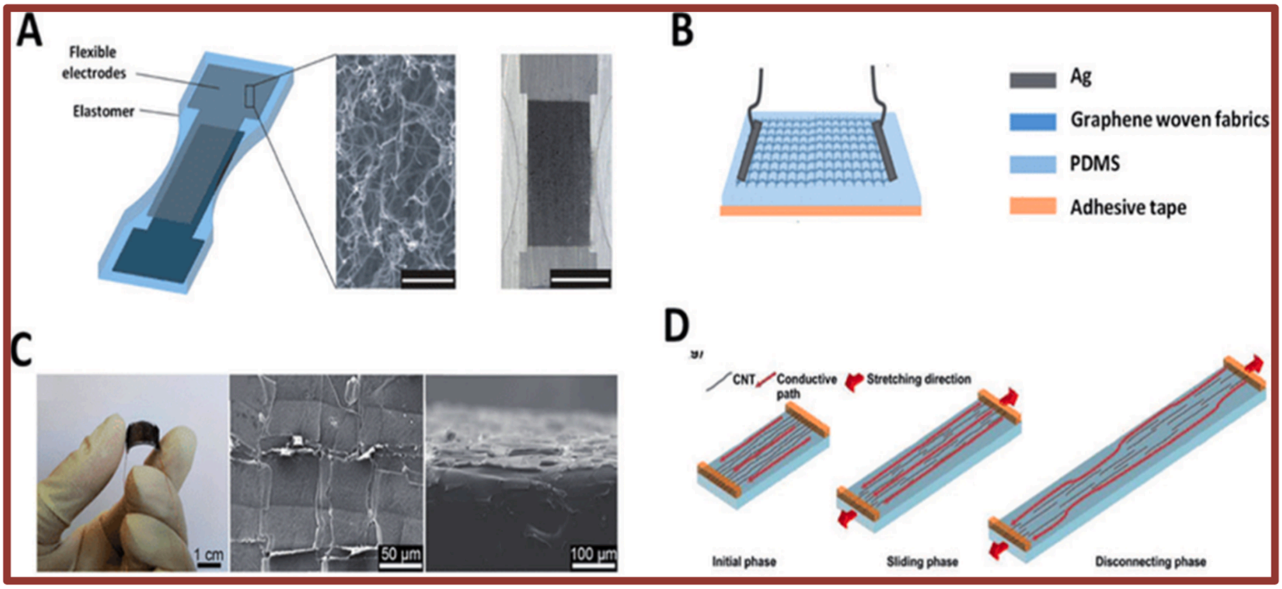

Fig. 4. Carbon nanomaterial-based wearable biosensors; A. Poisson Capacitor Design. The left-to-right Diagram illustrates the geometry of the device. The scale bar is 500 nm: SEM data shows CNT percolation inside the electrode—a close-up shot of the device's sensing area (Reprinted (adapted) with permission from [119] Copyright 2023 American Chemical Society). B. Illustration of the pulse sensor's schematic in (Reprinted (adapted) with permission from [120] Copyright 2023 American Chemical Society). C. Strain sensors made of graphene that resemble fish scales (FSG). The left-to-right Photograph. SEM images in top and cross-sectional views (Reprinted (adapted) with permission from [121] Copyright 2023 American Chemical Society). D. Schematic illustration with a scale bar of 0.75 cm that depicts the shape of a CNT fiber under strain (Reprinted (adapted) with permission from [122] Copyright 2023 American Chemical Society).

nanoparticles (AuNP) and silver nanowires (AgNW). Stretchable Semiconductor: Comprising nanofibrils of poly(3-hexylthiophene) (P3HT-NF) and similar materials [128–130]. Ion Gel: Employed as a stretchable gate dielectric. The resulting electronic structures are pliable, adaptable, and resistant to human movement. Applying electronic ink onto the designated surfaces culminates in a firm bond upon drying, thus ensuring ultra-conformity. This approach, termed Drawn-on-Skin (DoS) electronics, leverages straightforward assembly procedures to avoid reliance on specialized equipment. Moreover, these electronic devices can be stacked atop other layers of electronic composites, facilitating versatility across diverse surfaces. A novel sensor utilizing Electronic textile technology was presented in literature studies. The sensor accurately tracks respiration rates in real time, explicitly focusing on wireless health monitoring. The process of drop-casting silver nanoparticle ink manufactures the sensor. The addition of a PDMS encapsulating layer enhances flexibility. The sensor is incorporated into a chest strap and precisely captures respiration rate data, which is subsequently relayed wirelessly to a smartphone via Bluetooth. This study introduces a promising breakthrough in wearable sensor technology monitoring respiratory activity [131].

2.2.3. Organic and inorganic nanomaterial

Conventional silicon-based devices play a pivotal role in real-time data processing and communication. However, these devices are frequently constructed on rigid chips, which can be limiting. To address this concern, one approach involves modifying the materials through minor or substantial structural adjustments to enable the integration of electronic components onto rigid chips. This strategy facilitates the creation of wearable devices that offer greater flexibility. Viscoelastic polymers and elastomers constitute another essential component in wearable sensors due to their combined characteristics of viscosity and elasticity. Elastomers exhibit weak intermolecular forces, generally possess a low Young's modulus, and exhibit high failure strain. Creating conductive elastomers primarily involves combining elastic materials with metallic nanoparticles [132–136]. This synergy imbues the resulting material with conductivity and stretchability, enabling the fabrication of stretchable conductors. Developing stretchable conductors with exceptional conductivity and stretchability involves optimizing multiple factors. These include the design of the materials, the ratio of elastomer to metallic nanomaterial, and the fabrication techniques employed for the metallic nanocomposites. Finely tuning these variables makes it possible to engineer stretchable conductors that exhibit high conductivity and exceptional stretchability, a feat achieved through meticulous consideration of material composition and fabrication methods [137–139].

2.3. Type of transducer

2.3.1. Electrochemical biosensor

Electrochemical biosensors are primarily used to detect various substances such as hybridized DNA, DNA-binding agents, and glucose content [16,140–142]. These biosensors can be classified into three categories based on the electrical parameters they utilize for measurement: conductimetric, amperometric, and potentiometric. Conductimetric, amperometric, and potentiometric electrochemical biosensors each leverage specific electrical characteristics to perform their analyses (Fig. 5. A). The domain of electrochemistry provides the advantage of enabling investigations with turbid materials and entails lower equipment capital costs compared to optical methodologies. However, in contrast to their optical counterparts, electrochemical approaches may exhibit slightly reduced levels of selectivity and sensitivity. Despite this, electrochemical biosensors remain valuable tools for a range of applications due to their unique attributes and cost-effectiveness [143–145].

2.3.1.1. Conductimetric biosensors. The parameter under scrutiny in electrochemical biosensors involves the measurement of the electrical conductance or resistance of the solution. As electrochemical reactions generate ions or electrons, the overall conductivity or resistivity of the solution undergoes fluctuations. These variations are quantified and appropriately calibrated. However, it is essential to note that conductance measurements are not exceedingly sensitive and may entail limitations in their precision and responsiveness [146–148].

2.3.1.2. Amperometric biosensors. Undoubtedly, one of the most prevalent electrochemical detection techniques employed in biosensors is the amperometric method. This remarkably sensitive biosensing approach excels in identifying electroactive species present within biological samples. The fundamental principle underlying amperometric biosensors is that the generated current is directly proportional to the concentration of the targeted chemical compound. The Clark Oxygen electrode is a typical example of an amperometric biosensor, frequently utilized for oxygen detection and measurement [149–151].

2.3.1.3. Potentiometric biosensors. In this particular type of sensor, the parameter under observation is an electrochemical process's oxidation or reduction potential. Although less common compared to other biosensors, this category can still encompass a variety of techniques. The fundamental principle revolves around the understanding that when a voltage is applied to an electrode immersed in a solution, electrochemical reactions enable the passage of current. The voltage at which these reactions occur unveils distinct reactions and specific species,

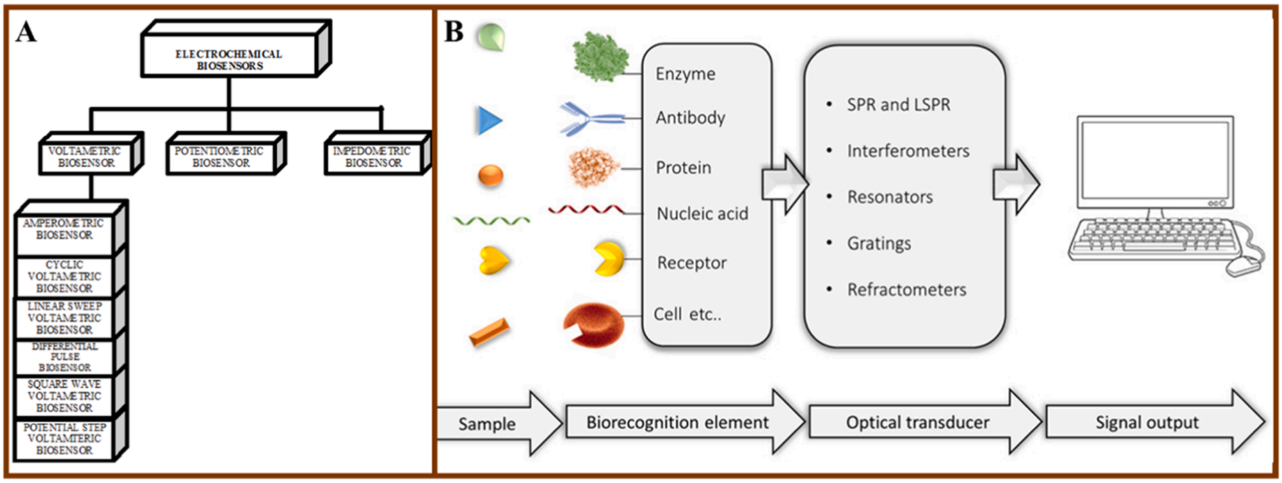

Fig. 5. Type of transducer: A. Electrochemical biosensor (reprinted from Bhardwaj) [273], B. Optical biosensor. (reprinted with permission from) [159].

providing insight into the underlying biochemical interactions [152–154].

2.3.2. Optical biosensor

In this type of biosensor, the measurable output signal is light. The biosensor can be constructed using electrochemiluminescence or optical diffraction[155–158]. Optical transducers (Fig. 5.**B**) hold significant appeal for direct (label-free) bacterial detection. When bacterial cells interact with receptors immobilized on the transducer surface, minute refractive index or thickness alterations occur, which these sensors can detect. These sensors connect subtle modifications in light properties and changes in molecules' concentration, mass, or quantity. Various optical techniques, including ellipsometry, mono-mode dielectric waveguides, resonant mirrors, and interferometers, have been documented to detect bacterial infections. These methods harness changes in light behavior to provide insights into bacterial interactions and infections, offering a versatile and sensitive approach to biosensing applications.

2.3.2.1. Surface plasmon resonance biosensor. The optical sensor operates on the principle of an evanescent field and employs a thin gold layer for sensing purposes [160–162]. By detecting reflection minima on arrays of photodetectors, this sensor facilitates the exploration of interactions between an analyte that flows over an immobilized interacting substance on a gold surface. This technology is known as Surface Plasmon Resonance (SPR), which has proven effective in identifying pathogenic microorganisms through immunoreactions. SPR exploits the changes in the refractive index near the sensor surface to deduce molecular interactions, making it a powerful tool in biosensing and diagnostic applications.

2.3.2.2. Piezoelectric biosensors. The piezoelectric (PZ) biosensor offers real-time output, affordability, and user-friendly operation. The fundamental idea involves applying a selective coating, such as antibodies targeting bacteria, onto the surface of the PZ sensor [163–166]. This coated sensor is then immersed in a bacterial solution. As bacteria adhere to the antibodies, the mass of the crystal increases. Consequently, the resonance frequency of the oscillation in the crystal decreases, providing a quantifiable indication of the bacterial binding event. PZ biosensors present a direct and efficient approach to detecting bacterial interactions and can be applied in various fields, including diagnostics, environmental monitoring, and biotechnology.

2.3.3. Heat and temperature depended biosensor

In demanding weather conditions, such as extreme heat or cold, monitoring body temperature can be a valuable defense against potential heat-related illnesses [167–169]. Standard methods like rectal and oesophageal probes for measuring core body temperature are invasive, uncomfortable for the individual, and unsuitable for continuous monitoring. Thermistors are solid temperature sensors that exhibit changes in electrical resistance in response to temperature fluctuations. They possess delicacy, high sensitivity, and remarkable repeatability in their resistance-temperature characteristics. An example of wearable e-textile thermistors is the LilyPad Arduino, developed by Leah Buechley and SparkFun [170–172]. These devices are designed to be integrated into clothing and are even washable. They come with various input, output, power, and sensor boards to accommodate diverse applications and needs. These wearable thermistors offer a practical and non-intrusive means of continuously monitoring body temperature, making them particularly suitable for individuals working in extreme climates.

2.3.4. Magnetic biosensor

Magnetic materials possess distinct attributes that can be leveraged to craft biosensors capable of rapid measurements directly at the testing location [173–176]. By detecting alterations in magnetic traits or magnetically induced effects like changes in coil inductance, resistance, or magneto-optical properties, magnetic biosensors employ paramagnetic or superparamagnetic particles, as well as crystals, as a mechanism for detecting biological interactions. These particles utilized in magnetic biosensors exhibit diameters ranging from nanometers to microns and are coated with bio-receptors such as antibodies or nucleic acid strands. When these particles interact with the targeted molecules, their physical characteristics undergo modifications that could involve changes in size or movement. Detection technologies in magnetic biosensors encompass coils, Giant Magnetoresistive (GMR) devices, Hall Effect devices, and optical and imaging techniques [177–179]. A noteworthy feature of magnetic biosensors is their capacity to manipulate paramagnetic particles within a magnetic field, guiding them to the sensor surface where biological interactions occur. This capability accelerates the binding interactions, enabling swift detection of the target. The distinctive properties of magnetic materials and the array of techniques employed make magnetic biosensors highly effective tools for swiftly detecting various biological interactions. These biosensors hold substantial potential for diagnostics, biotechnology, and beyond applications.

2.3.5. Thermal detection biosensor

This specific type of biosensor capitalizes on a fundamental characteristic of biological reactions: the absorption or generation of heat, leading to temperature changes within the reaction medium. These biosensors are designed by combining temperature sensors with immobilized enzyme molecules. The heat generated by the enzyme's activity is measured and correlated with the concentration of the target analyte upon the interaction between the analyte and the enzyme. This type of biosensor is commonly employed to detect harmful microorganisms and chemicals. By monitoring heat changes during these interactions, these biosensors offer a reliable and sensitive means of identifying and quantifying specific substances of interest [72, 180–182].

2.3.6. Ion-sensitive biosensor

Supercapacitive inotropic pressure sensors convert input pressure into a consistent change in capacitance output. This type of pressure sensor operates by capitalizing on generating an electron double layer (EDL) at the junction of the electrode and the dielectric layer, enhancing the compression effect. To elaborate, an ionic gel is confined between the electrodes, comprising many positive and negative ions [183–186]. As voltage is applied, positive and negative ions are drawn toward their respective oppositely charged electrodes, forming two distinct EDLs. The behavior of this sensor hinges on alterations within the region between the electrode and the active material. Under specific pressures, the expansion of the contact surface induces positive or negative ions, leading to increased capacitance values. In essence, changes in pressure influence the distribution and alignment of ions, consequently influencing the system's capacitance. Supercapacitive inotropic pressure sensors provide a mechanism to translate pressure variations into measurable capacitance changes, making them valuable for applications requiring precise pressure detection and monitoring [187,188].

3. Considerations and requirements for wearable sensors

Skin-mounted biosensors have gained significant attention from industry and scientific communities, fueled by the advancement of device manufacturing technologies. These innovations cater to various applications, including electronic skin (e-skin), health monitoring, underwater sensing, and human-machine interfaces. In the following section, we delve into the forefront of manufacturing techniques utilized for creating wearable sensors. These techniques play a crucial role in enabling the development and deployment of skin-mounted biosensors for various practical and groundbreaking uses [189–191].

3.1. Cost

Their ease of manufacturing will influence the cost and eventual accessibility of wearable health-monitoring devices. The shift towards decentralized healthcare at home has the potential to lead to reduced costs for both the healthcare system and the users/patients. This transition could result in fewer hospital visits, shorter hospital stays, and decreased travel expenses for users/patients. The cost-effectiveness of these technologies will hinge on various factors, including initial investment, training, and maintenance. This will play a pivotal role in determining the seamless integration of these technologies into healthcare systems. Ultimately, the extent to which wearable health-monitoring devices can provide value for money while delivering improved healthcare outcomes will determine their adoption and future prominence in the healthcare landscape [190,192].

3.2. Usability

The functionality of a wearable sensor must align with specific clinical needs, addressing crucial health factors for individuals [193, 194]. It is essential to consider the intended purpose of data collection; some devices may require an immediate response in cases like a myocardial infarction (MI) or a fall, while others may gather more gradual data over time, such as activity levels or temperature variations. Irrespective of the purpose, the collection and sharing of such data must adhere to established standards to ensure the effectiveness of any system [195–197]. A user-friendly interface that is easily understandable, regardless of a person's prior knowledge, is paramount. The ease of use is a pivotal aspect.

Moreover, the system should be able to offer intelligent insights and sense contextual cues. Ideally, signal processing and data exchange would occur seamlessly within the system without requiring additional intervention from the user/patient. Privacy and security concerns have come to the forefront with transmitting medical data from these devices to users, caregivers, or healthcare professionals. Standards address these issues and establish a foundation for future device interoperability, which is anticipated to foster market competition and contribute to reduced device costs. In pursuing successful wearable sensors, considering clinical relevance, user-friendliness, intelligent processing, privacy, security, and interoperability standards are crucial.

3.3. Wearability

Wearable devices should possess compactness, lightweight design, and low associated noise levels. Intrusiveness in the user's or patient's daily life should be minimized, prioritizing their comfort and discretion (Fig. 6). The importance of wearability depends on the device's intended usage. For example, devices utilized for continuous monitoring necessitate more careful consideration than those employed sporadically for data collection. Factors such as sensor size, power supply requirements, and the on-body hardware play significant roles in determining the wearability of devices. These considerations can currently limit wearability. However, as discussed in a later section, this challenge may be addressed by integrating these components into e-textiles. By exploring innovative solutions like e-textiles, the constraints of wearable device wearability could be mitigated, leading to enhanced user experiences and greater acceptance of these technologies [198–200].

Fig. 6. Considerations and requirements for wearable sensors: Wearability (reprinted from Francés-Morcillo et al.) [201].

3.4. Performance

Assessing a wearable device's dependability and practicality in real-life scenarios is paramount. The device's performance should withstand typical user/patient activities, accounting for factors like mobility and environmental changes, by its intended function. Such considerations enhance system reliability by identifying issues and preventing erroneous data collection. Power consumption poses a significant challenge when designing wearable sensors, as they require long-term, maintenance-free operation. Wireless technologies, such as Bluetooth, demand around 50–100 mW of power and may also face challenges from connection failures or interference from other transmissions within the industrial, scientific, and medical (ISM) spectrum. Integrating low-power semiconductor circuitry and energy-harvesting devices can potentiate these power limitations. Ultimately, achieving a balance between performance, affordability, functionality, and dependability is crucial to facilitating the integration and adoption of wearable technologies into daily life. Wearable devices should meet users' needs, withstand real-world conditions, operate with efficient power usage, and provide reliable data to ensure their successful incorporation into everyday routines[202–204].

4. Types of wearable sensors

4.1. Wireless body sensor networks

One of the challenges in wearable technology, specifically wearable sensors or wearable computing, is establishing a wearable sensor network. Recent advancements in wireless technology hold the potential to facilitate the provision of cost-effective and continuous healthcare services through the concept of a body sensor network (BSN) [205–207]. A specific category within wireless sensor networks, BSNs are tailored for "on-body" applications (Fig. 7. A). Typically, BSNs comprise multiple sensor nodes worn on or near the body. Each sensor node can collect, process, and transmit physiological parameters. Wireless communication is facilitated by antenna components integrated into the sensor nodes, enabling data transmission to a body-worn device. Common examples of central devices that manage user interaction include PDAs or PCs. The field of BSNs is expansive, encompassing various components. The future success of this system hinges on the optimization of each component. Key factors within BSNs encompass usability, robustness, reliability, power optimization, battery life, radio design, and the security of transmitted data. Challenges within BSNs include utilizing energy resources to power sensors and the levels of information provided. As the technology evolves, addressing these challenges and optimizing BSN components will play a pivotal role in shaping the potential and effectiveness of wearable sensor networks in healthcare and other domains [208,209].

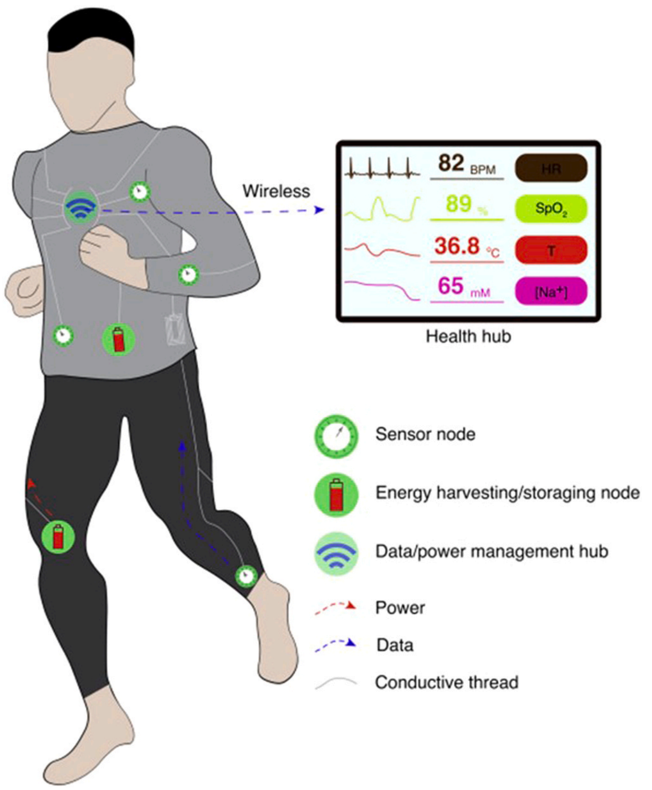

Fig. 7. Types of wearable sensors; Wireless body sensor networks [210] and Electronic textiles (reprinted from Du et al.) [211].

4.2. Design issues of wearable sensors

A Body Sensor Network (BSN) utilizes a range of sensors or nodes to gather physiological data. The devices used for tracking various physiological activities include heart rate monitors or ECG (electrocardiogram) [212,213] sensors to measure cardiac activity, EMG (electromyography) [214] sensors to monitor muscle activity, EEG (electroencephalography) [215] sensors for tracking brain electrical activity, blood pressure sensors, temperature sensors, pulse oximeters to measure blood oxygen saturation, breathing sensors for respiration tracking, tilt sensors to monitor trunk position, movement sensors (accelerometers) for tracking user activity, and "smart socks" or shoe insole sensors to monitor foot position [216,217].

The heart rate monitor is one of the most fundamental and widely recognized wearable sensors among these. Its wireless version was first developed in 1977 to aid the Finnish National Cross Country Ski team in training. More advanced iterations of this technology incorporate multiple sensors to track parameters such as temperature, altitude, pace, speed, and heart rate. A single wireless network node can support multiple physiological sensors. Gyroscopes and accelerometers are among the most sensitive motion sensors utilized in these systems, helping to provide accurate information about movement and orientation. A BSN's diverse array of sensors enables comprehensive monitoring of various physiological aspects, facilitating a holistic approach to healthcare and well-being management. Biosensors with AI-assisted designs can be found in the literature. Conventional signal reception involves using gel electrodes that are surgically placed in the body. Aside from conventional wearable devices like smartwatches and fitness trackers, wearable design devices employ machine learning techniques. These devices, known as bio-sensing epidermal devices, enable the non-invasive streaming of physiological signals used in tissue engineering applications [218].

4.2.1. Sensor node identification

Correctly identifying the specific device associated with a particular task or function within a Body Sensor Network (BSN) may be challenging, even if each sensor node possesses a distinct device ID. This challenge becomes particularly apparent when dealing with multiple sensors that might be used for different purposes, such as tracking hand and foot movements [219–221].

To address this issue, there are a couple of approaches that can be adopted:

Manual Device ID Entry: As mentioned, one option is to manually assign and enter device IDs for each sensor based on their intended function. This method requires the user to provide information about which sensor is mounted on the hand and which is on the foot. While this approach can work, it relies on accurate user input and can be prone to errors [222].

Systematic Device Recognition: An alternative approach involves implementing a systematic way to recognize and differentiate devices. This can be achieved through predefined activation methods. For

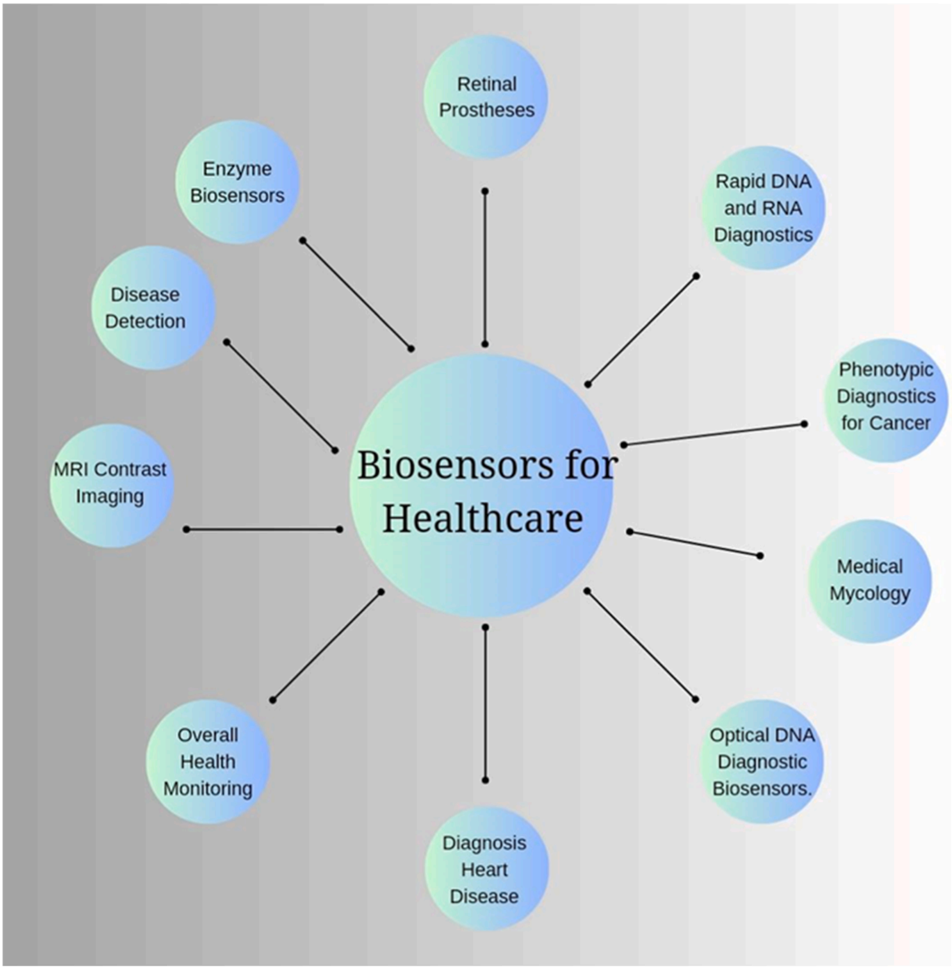

Fig. 8. Distinctive capabilities of biosensors in healthcare services.

example, the user could be instructed to perform specific movements that activate sensors in a particular order or pattern. By monitoring the activity levels of each sensor, the server can deduce which device is being activated and subsequently assign the appropriate task or function to that device [223,224].

Both of these approaches aim to enhance the accuracy of device identification and ensure that the correct sensors are associated with their intended tasks. By carefully considering the user experience and providing clear instructions, the BSN can effectively manage the identification and utilization of different sensors for various monitoring purposes.

4.2.2. *Sensor node calibration*

In a Body Sensor Network (BSN), the sensor nodes typically undergo two types of calibrations:

Inter-Sensor Calibration: This calibration compensates for variations or differences between individual sensor nodes. Sensor-to-sensor differences can arise due to manufacturing variations or other factors. The calibration method employed for this purpose depends on the specific sensor type. It helps ensure that the data collected by different sensors within the network is accurate and consistent [225].

Intra-Sensor Calibration: This type of calibration is conducted before the commencement of each monitoring session. It is specific to each sensor and calibrates it within its immediate environmental context. This calibration considers the conditions and factors affecting the sensor's performance during the monitoring period. By calibrating the sensor based on its operating environment, the accuracy and reliability of the data collected can be improved [226,227].

These two calibration processes play a crucial role in ensuring the accuracy, reliability, and consistency of the data collected by sensor nodes within the BSN. They contribute to the overall effectiveness of the network in providing reliable physiological measurements and insights for healthcare and monitoring applications.

4.2.3. *Power sources and size*

Most wearable wireless body sensor networks (WBSN) should run on batteries because they should ideally not require any maintenance. Power consumption is essential for BSNs because it affects both the battery size and the sensor's working period. Because the WBSN frequently comprises many devices, sensors must be remarkably power-efficient. Otherwise, several sensors would require frequent battery changes, lowering WBSN acceptability and raising costs. Batteries play a significant role in determining the size and weight of the sensors, and the size of the batteries ultimately decides how intrusive the system is. Extended battery life requirements directly conflict with the need for a lightweight, compact design. Reduced power requirements can be achieved through power scavenging. These sensors should be self-powered using environmental energy sources such as radiofrequency (RF) coupling, solar electricity, and fuel cells [228–230].

4.2.4. *Wireless communication range and transmission characteristics*

The radio communication in BSN consumes the most significant amount of energy. Methods for power optimization should be employed wherever possible, keeping in mind that the body should not be subjected to excessive electromagnetic radiation for prolonged periods. Power-saving techniques can be used in the following areas [231,232]:

- **Processing:** By communicating the data that has been processed rather than the raw signals, clever on-sensor signal processing offers the potential to conserve power and increase battery life. The trade-off between computing and communication would be part of an ideal design.
- **Event management:** he sensor node could be tuned to accept specific data; for example, an ECG sensor [212] may be set up to capture abnormalities while ignoring typical values. This enables a significant decrease in transferred data.
- **Using the correct technology:**
  - o The **S-MAC** protocol uses scheduling to synchronize sleeping amongst nearby nodes. Each node wakes up just at the precise moment when data should be transmitted to the server. The radios are turned off, and all nodes are put into sleep mode during inactivity, prolonging battery life by seven times.
  - o A node periodically samples, albeit briefly, as part of the WiseMAC low power listening (LPL) approach to determine whether data needs to be received. If no data are detected when the node wakes up, it goes back to sleep. If the source has data to send, a wake-up preamble is sent. The node enters sleep mode once more after receiving the data.
  - o ZigBee is a promising wireless standard for WBAN (wireless body area network) applications because of its low cost and power consumption. ZigBee can manage large sensor networks with up to 65,000 nodes.

4.2.5. *Sensor location and mounting*

The placement of the sensors is crucial because they can produce erroneous oscillations if they are not firmly fastened after a sudden movement. This may produce fictitious events or conceal actual ones. Researchers disagree on where the body sensors should be placed. A combination of hip and ankle sensors was superior, even though the most discriminative site for a motion sensor may be at the ankle. In order to track activity, researchers also inserted accelerometer sensors into the thigh [233–236]. The device's rear also has motion sensors, while Krause et al. employed accelerometers on the SenseWear armband.

4.2.6. *Seamless system configuration and simple user interface*

BSN sensors should make it simple for the user to assemble a reliable ad hoc system based on their current state of health. No matter the manufacturer, "off-the-shelf" sensors ought to be usable. Each sensor should be able to identify itself, state its range of operation, and provide easily customizable functionality for specific applications. The user interface should also be straightforward enough for users to use and comprehend [237–239].

4.2.7. *Interference and data security*

IEEE 802.11b/g wireless ethernet operates in the 2.4 GHz band, while most microwave ovens operate at 2.45 GHz. Many short-range networks, including wireless LANs and Bluetooth, operate in the ISM frequency range. Therefore, interference is a problem that must be resolved to enable a secure and functional WBSN. Additionally, if two people are close enough, their BSNs may interfere with one another. One may be able to listen exclusively to network-connected devices with device authentication. Device authentication may use individually distinct biomedical signals [240,241].

4.2.8. *Social issues*

Privacy, security, and legal challenges are among the social concerns relating to BSN systems. When processing such data, a researcher, for instance, should not be aware of the person's identity; instead, the patient's doctor should be informed of the person's identity along with the data. New algorithms should be created to deal with the information produced by these networks.

4.3. *Electronic textiles*

Wearable electronic equipment demands flexibility and stretchability to fulfill the criteria of human comfort and system durability. Sensors, substrates, and biocompatible materials are crucial in developing a wearable device. Electronic textile devices are highly appealing in the field of wearable electronics because of their exceptional ability to deform, compatibility with the human body, comfort, and ability to meet basic human needs in all weather situations. Electronic textile devices can meet the comfort needs of the human body due to their flexible and three-dimensional structure. Additionally, they can also adjust to deformations induced by human body movements [131]. Traditionally, clothing has served functions of protection and adornment. However, its non-intrusive nature also makes it an ideal platform for integrating sensor technologies. Incorporating sensing components into clothing is a rapidly expanding area of research, aiming to create cost-effective and minimally invasive solutions for long-term health monitoring at home. An early version of this concept, known as the "wearable motherboard" or "Smart Shirt," was pioneered by researchers at Georgia Tech. Sundaresan Jayaraman's innovative work laid the foundation for this concept, integrating sensing, monitoring, and information processing directly into clothing [242–246]. Initially developed for tracking vital signs of military personnel, the intelligent shirt has transitioned to commercial use in health monitoring. The bright shirt is based on a basic fabric such as cotton or polyester, onto which sensors and connectivity technology are embedded, resulting in a flexible and wearable system. Sensors can be placed strategically on the shirt, including those for body temperature, heart rate, pulse oximetry (SpO_2), respiration rate, ECG, and voice recording. The sensor readings are then transmitted via a flexible information bus integrated into the shirt to a "smart shirt controller" or Personal Status Monitor. This controller analyzes the signals before wirelessly transmitting them, often via Bluetooth, to designated recipients such as caregivers or physicians. Feedback can also be relayed to the wearer through the data bus, enabling two-way sensor communication. The intelligent shirt concept has driven advancements in the field, addressing challenges like the size of sensors and associated electrical components. This pursuit of non-intrusive monitoring has led to the emergence of electronic textiles (e-textiles), a rapidly evolving domain where fabric doubles as a sensor. The ongoing miniaturization of sensor technology has contributed to overcoming these challenges, enabling more seamless integration of monitoring capabilities into clothing.

Electronics and connections are woven into the fabric of e-textiles. Metallic, optical, or conducting polymer fibers are examples of electrically conductive fibers that provide a platform for data transmission and sensing within the fabric itself [247–250]. Steel or steel composites typically produce yarns with varying resistance in metal fibers and threads. For home health monitoring, e-textiles have several advantages over traditional electronics. E-textiles might be made using current textile technology and garment production procedures, using the economies of scale offered by these industries and enabling quick, affordable production. Additionally, they offer a chance to create systems with less wire, more discrete components, and physical flexibility. These characteristics affect a wearable sensor system's wearability, visibility, and simplicity, eventually determining whether the user will find it acceptable in their daily lives.

5. Wearable sensors in medical field

The medical industry now employs a variety of biosensors to detect drugs within sensitive biological elements such as tissues, bacteria, organelles, cell receptors, enzymes, antibodies, and nucleic acids. The development of biosensors has profoundly impacted advancements in the medical field, leading to the discovery of new, precise, and powerful analytical tools. These biosensors contribute to understanding various processes, including antibodies, catalytic enzymes, glucose levels, microbial infections, tumor growth detection, diseases, and toxins, among others. In the current context, biosensors equipped with nanomaterials play a pivotal role in detecting COVID-19. These advanced biosensors have enabled rapid and accurate virus identification, showcasing the evolving potential of biosensor technology in addressing pressing healthcare challenges [251–254].

5.1. Distinctive capabilities of biosensors in healthcare services

Biosensors have significantly benefited manufacturing industries, especially medical, healthcare, and clinical services[255]. The diverse capabilities of biosensors within the realm of healthcare and related services. These applications span a wide range, including disease detection, retinal prostheses, contrast imaging during MRI scans, cardiac diagnosis, medical mycology, health monitoring, and other essential fields. Biosensors have elevated healthcare to a new level, leveraging their exceptional capabilities to provide outstanding social services. Notably, the recent COVID-19 pandemic, caused by a highly contagious coronavirus, has highlighted the crucial role of biosensors in detecting and combating the spread of illnesses and viruses.

Similarly, other infectious diseases like avian flu, SARS, Hendra, Nipah, etc., [256,257] have recently garnered attention, underlining biosensors' potential in disease surveillance. Biosensors exhibit the potential to revolutionize the diagnosis of heart conditions, a critical aspect considering that cardiovascular disorders contribute to over 17 million deaths globally each year. In diabetes, biosensors have gained prominence among diabetic patients for monitoring blood glucose levels accurately and rapidly, even in challenging conditions. The increasing sensitivity and precision of biosensors within a small sample volume will drive market demand in the future. Portable electronic devices, including wearable biosensors, play a pivotal role in the healthcare system by enabling surveillance, treatment, diagnosis, fitness monitoring, and overall well-being. These devices empower patients to adopt preventative measures and better understand their health by merging hospital and urgent care treatment methods. The ongoing technological advancements and the expanding use of biosensors across various applications are driving market growth. Wearable biosensors enhance quality of life and alleviate the financial burden of medical expenses. The aging population and growing interest in wearable technology among younger individuals are creating new opportunities in the market. Biosensors are proving to be valuable tools for disease identification and for detecting hazardous bacteria, human contaminants, and environmental pollutants.

5.2. The significant advancement of biosensors in the medical field

In 1962, Led and Clark introduced the first oxygen biosensor, marking the inception of biosensor research [258,259]. Since then, biosensors have garnered significant attention from medical and biotechnology researchers. Over the years, these researchers have focused on diagnosing and understanding diseases. Recent advancements in both primary and clinical sciences have been made possible by detecting biomarkers at low concentrations, enabling the identification of sensitive, precise, quantitative, and multiplexed biomarkers with potential diagnostic applications. Biosensors play a crucial role in medical experimentation, enabling rapid disease detection and offering valuable insights into healthcare [255,260–262]. Electrochemical biosensors and biomarkers are employed in cancer research for faster and more accurate diagnoses. Biosensors equipped with metal-specific electrodes can detect dangerous metal concentrations in water, enhancing environmental monitoring. They can also identify harmful infections and recognize biorecognition elements such as enzymes, antibodies, and biomolecules. One of the critical advantages of biomolecular detection is its rapid processing time. The analyte is directly detected, leading to an automatic generation of a detectable signal.

Portable devices integrated with biosensors are now commonly used for point-of-care monitoring, covering many applications, including glucose measurement, addiction monitoring, and pregnancy testing. Researchers have utilized biosensors to track joint movements during various health activities, promoting better monitoring and managing health conditions. Utilizing a blood pressure monitor at home is considered one of the most effective ways to maintain good health. Advancements in biotechnology have brought about affordable and convenient medical diagnostic tools that can be used for health monitoring. Introducing biosensors has significantly improved the standard of diabetes care by enabling medical assessments to be conducted at home. This has elevated healthcare quality and driven the development of additional biosensor applications for diagnosing various health issues. Key enabling technologies influence the future of biosensors in energy harvesting hardware, which facilitates the creation of low-cost and easily manufacturable medical diagnostic and monitoring systems. Healthcare providers are particularly drawn to biosensors due to their ability to reduce the risk of contamination and lower the costs associated with sterilizing medical devices. Flexible sensors also hold promise from the patient's perspective, as they are more compatible with the natural curvature of the body, enhancing comfort and usability. Biosensors have revolutionized disease detection, healthcare monitoring, and medical diagnostics, paving the way for more personalized and effective healthcare systems.

5.3. Variety of diagnostic biosensors for cardiovascular diseases

Cardiovascular disorders are recognized as a global leading cause of death, underscoring the need for early and prompt diagnosis. A range of biomarkers, such as myoglobin, B-type natriuretic peptide (BNP), cardiac troponin I (cTnI), C-reactive protein (CRP), interleukins, and interferons, are now acknowledged for their applications in both medical and non-medical contexts [263,264]. These cardiac signature biomarkers are employed in various biosensor technologies, including magnetic, optical, acoustic, and electrochemical methods. Although many of these biomarkers possess predictive significance independently of conventional risk factors, only a subset has evolved into essential diagnostic tools within the medical field. The diverse diagnostic biosensors that find widespread applications in cardiovascular care. These diagnostic biosensors span various categories within cardiovascular and related healthcare domains. Some notable examples of biosensors employed for these applications include the triage cartridge, cardiac marker system, stratus, alpha, and more. These biosensors leverage technologies such as fluorescent microfluidics, machine analysis, disk readers, and tabletop readers, offering readout times ranging from 10 to 18 min. The advancement of artificial intelligence (AI) has introduced new avenues and resources to the field of bioscience. This has led to the development of advanced modeling and forecasting techniques tailored for clinical applications, particularly within cardiac disorders. AI-driven approaches contribute to enhanced diagnostics and prognostics, enabling healthcare professionals to make more informed decisions based on comprehensive data analysis and interpretation. As a result, integrating AI and biosensor technologies is pivotal in improving the diagnosis and management of cardiovascular conditions. The convergence of biosensors, biomarkers, and AI is revolutionizing cardiovascular care by enabling rapid and accurate diagnostics, early intervention, and personalized treatment strategies. These advancements hold the potential to significantly reduce the burden of cardiovascular diseases and improve patient outcomes on a global scale [265–268].

5.4. Novel aspects of biosensors for clinical and allied services

Developing biosensors for unique healthcare applications encompasses various approaches, including optical, spinit, piezoelectric, and more. These conceptualized biosensors have proven effective in inflammatory response research, breast and prostate cancer-related healthcare, human malignant tumors, and other medical applications—the cutting-edge features and capabilities of biosensor services in healthcare and associated therapeutic fields. Complex biosensor applications exhibit vital characteristics such as tumor targeting, volume analysis, antibody detection, rapid and accurate detections, and more. Conventional procedures often come with high costs, intricate procedures, lengthy turnaround times, and a higher rate of false-positive results. Biosensors offer advantages such as faster detection and increased sensitivity. They have demonstrated targeted detection of localized and circulating tumor cells, exhibiting specificity in distinguishing tumor cells from normal cells. As a result, biosensors hold significant promise for their application in identifying and monitoring cancer [25,267, 269–271]. Cancer biomarkers serve as significant predictors of tumor growth. These markers are employed to track and diagnose tumors, as well as to formulate treatment plans. Biosensors also play a role in analyzing biomolecular interactions, as they can assess affinities and kinetics across a wide range of molecular interactions in real-time without the need for molecular labels or tags. Non-wearable biosensors are experiencing rapid growth, becoming a popular alternative for scientific analysis due to their affordability and minimal test media requirements while delivering reliable results. These biosensors exhibit excellent sensitivity, ensuring accurate performance.

Moreover, biosensors have advanced beyond the laboratory and are integrated into mobile applications. They can take on various forms, such as patches, bright clothing, displays, blood pressure monitors, pulse rate monitors, and sweat monitors. This versatility and integration into everyday devices further expand the reach and impact of biosensors in healthcare and monitoring applications.

6. Wearable technology market and future opportunities

In 2022, the worldwide market for wearable technology was valued at US$61.30 billion. It is projected to experience a compound annual growth rate (CAGR) of 14.6% from 2023 to 2030. The business is experiencing expansion due to the rising popularity of innovative wearable technology items among customers. Companies including Fitbit, Samsung, Noise, and Fossil Group, Inc. are introducing wearable technology watches and other accessories equipped with health tracking solutions. This feature is anticipated to captivate consumers by enabling them to manage their health, thus fostering market expansion. In March 2022, Xiaomi Corp. released the most recent iteration of its smartwatch, the Xiaomi Watch S1 Series. The device offers 117 exercise modes and accurately monitors blood oxygen saturation, health, and sleep. This device possesses magnetic charging capabilities and is equipped with Amazon's Alexa voice assistant. The industry is anticipated to experience growth due to the projected increase in product demand, driven by rapid shifts in consumer demographics, including evolving lifestyle patterns and tastes. Adaptive EQ technology, introduced by Apple Inc. with the launch of AirPods in 2021, adjusts the sound in real time according to the profile and fit of the user's ear. The development of technology has led to the integration of innovative wearable technologies, also known as bright clothing, into clothing. Smart or IoT-based clothing consists of electrical components integrated into clothing that provide services that can be used in larger intelligent systems through communication-based protocols. Hats and eyewear are predicted to be the second-largest and fastest-growing product segment from 2022 to 2030. The increasing application of Virtual Reality and Augmented Reality (VR and AR) headsets in the multimedia and healthcare sectors and the increasing uptake of intelligent hats are anticipated to support the growth of this segment. Additionally, the growing popularity of intelligent borders due to data-driven insights and monitoring technologies is predicted to fuel segment development. Many companies, such as Spree Wearables and Life BEAM, are introducing bright hats to the global industry.

In 2022, the consumer electronics application segment dominated the industry, capturing over 48.95% of the total revenue, making it the most significant contributor. The rise in the use of wearable technologies, such as fitness bands and AR/VR headsets, can be attributable to the significant market share held by this segment. Garmin Ltd., Omron, Apple Inc., and Nemaura are prioritizing the development of devices that offer data integration of clinical and non-clinical information. For instance, Nemaura's SugarBEAT Wearable Technology enables regular monitoring of blood sugar levels in those with diabetes, removing the need for daily finger calibration. In 2022, North America held the global industry's highest market share of total revenue, accounting for 33.80%. The Asia Pacific and Europe regions followed it. The regional market has experienced significant expansion due to the use of advanced technologies and the smooth introduction of newly released items. There is a growing demand in the region for devices that enhance health, enable preventive treatment, and aid in managing continuing disorders. As to the National Library of Medicine, 30% of Americans utilize wearable medical devices. From 2022–2030, the Asia Pacific area will achieve the highest growth rate. Several technical obstacles must yet be overcome to achieve widespread adoption and utilization of wearables in the digital health era. Their security and privacy are two such issues. Since wearables are physically small and have enormous data storage capacities, the device may need to be recovered or compromised. To lessen privacy and security issues, more secure and encrypted wearables that may also have tracking features are desired. The personal calibration of wearable technology presents yet another technical difficulty. Each person is unique, and various factors (such as genetics, food, and family medical history) impact one's health. As a result, each person may have different early disease signs. Therefore, customized calibration of devices and machine learning-based data analysis are needed for more precise and pertinent monitoring of the patient's health state utilizing wearables. Wearable technologies should be aware of "little data" made by individuals and be prepared to harness and interpret them appropriately. Significant data approaches driven by vast populations (e.g., specific to different countries, races, etc.) are tremendously powerful but can be deceptive for individuals. A considerable data stream without outliers will statistically produce catastrophic occurrences for some patients. The misalignment of wearables, which impairs the precision and quality of their measurements, is another difficulty. If there is a mismatch between the user and the wearable, the gadget should be able to function and acquire reliable data. This calls for more intelligent designs that can withstand such misalignments, for instance, by utilizing computational methods, internal references that resemble guiding stars, or self-calibration protocols. This is particularly significant given the variability in physiology and the size or 3D conformation of various organs, which wearables rely on.

7. Conclusion

The International Data Corporation (IDC) has reported that global shipments of wearable devices experienced a 2.6% year-on-year growth in the third quarter of 2023, reaching a record-breaking 148.4 million units for that quarter. Wearable biosensors are highly sought after in academic and industrial settings because they can be monitored remotely, tracked, and moved quickly. Notably, wearable biosensors have prominently contributed to the commercialization of detecting many substances, such as blood sugar, pregnancy hormones, cancer cells, cholesterol, lactic acid, urea, and more. It possesses numerous functionalities, including drug administration and prompt intervention in severely ill individuals with medical issues. The COVID-19 pandemic has sparked a greater interest in wearable biosensors for personal healthcare. This has led to an increased focus on personalizing one's lifestyle and using point-of-care and self-medical assessment. These areas are expected to get more attention in the future. It is anticipated that in the future, there will be widespread adoption of biosensor designs and wearable technologies that utilize artificial intelligence modeling, carbon nanomaterials, and biological mimetic diversity. These advancements will enable the collection of a greater variety and volume of data, particularly concerning the original design of wearable biosensors in academic and industrial settings.

Declaration of Generative AI and AI assisted technologies in the writing process

During the preparation of this work the authors used chatGPT, quillbot, and grammarly in order to check grammar and increase readability. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

CRediT authorship contribution statement

Fatih Ciftci is Mais Haj Bakri's master thesis supervisor. Fatih Ciftci and Mais Haj Bakri conceived the ideas, designed the article, and collected relative data. Ali Can Özarslan, Azime Erarslan and Yeliz Basaran Elalmis provided valuable suggestions for the manuscript. Fatih Ciftci, Mais Haj Bakri and Ali Can Özarslan finished the final version of the manuscript, and all authors revised the paper.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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