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Printed Electronics-Based Biosensors

Basılı Elektronik Tabanlı Biyosensörler

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ABSTRACT

Printed electronics have attracted enormous interest owing to their significant production capability, low cost, and environmentally friendly properties. Printed electronics-based biosensors have also achieved increasing attention in different domains that range from laboratory to home for many applications. They will be necessary for implementing next-generation platforms because printing simplifies the fabrication of platforms on several thin, rigid, and flexible substrates. Moreover, the printed electronics-based biosensors show an excellent chance to facilitate fast, sensitive, and real-time screening of several molecules to exploit their features. Printing technology strongly impacts assembling more customizable and straightforward production of biosensors with great resolution and combined with microfluidic and electronics systems. This review summarizes recent progress in printed electronics-based biosensors to produce various electronic devices and circuits. Also, it supplies a review of the properties of printed electronics-based biosensors in different applications. In the end, up-to-date experiments of the latest studies of the printed electronics-based biosensors for various target molecules are reported.

Key Words
Bioelectronics, biomolecule detection, biosensors, printed electronics, printing technologies.

ÖZ

Basılı elektronikler, geniş üretim kapasitesi, düşük maliyeti ve çevre dostu özellikleri nedeniyle büyük ilgi görmüştür. Basılı elektronik tabanlı biyosensörler, laboratuvarlardan ev içi kullanımlara kadar birçok uygulamada ve farklı alanlarda da artan bir ilgiye sahiptir. Baskılamanın çeşitli ince, sert veya esnek alt tabakalar üzerindeki platformların üretimini kolaylaştırması ile de yeni nesil platformlara ulaşılması noktasında gelecek vaat etmektedirler. Dahası, basılı elektronik tabanlı biyosensörler, çeşitli moleküllerin özelliklerinden yararlanacak şekilde, hızlı, hassas ve gerçek zamanlı taranmasını kolaylaştırmak için mükemmel imkan sağlamaktadır. Baskı teknolojisi, biyosensörlerin daha özelleştirilebilir ve daha basit üretiminin büyük çözünürlükte ve mikroakışkan ve elektronik sistemlerle birleştirilmesinde güçlü bir etkiye sahiptir. Bu inceleme, çeşitli elektronik cihazlar ve devreler üretmek için basılı elektronik tabanlı biyosensörlerdeki son gelişmeleri özetlemekte ve aynı zamanda farklı uygulamalardaki basılı elektronik tabanlı biyosensörlerin özelliklerinin de incelemesini sunmaktadır. Sonuca doğru, çeşitli hedef moleküller için basılı elektronik tabanlı biyosensörlere ait en son çalışmaların güncel deneyleri raporlanmaktadır.

Anahtar Kelimeler
Biyoelektronik, biyomolekül tespiti, biyosensörler, basılı elektronik, baskı teknolojileri.

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INTRODUCTION

Printed electronics are electronic devices set produced via traditional printing techniques. They can also be described as the printing and ink chemistry combination for electronic components manufacture. The most significant utility of printing procedures is a cost-friendly and high-volume production. Compared to conventional electronics-based systems, printed electronics will put forward the probability of making ready micro- and nano-scale platforms more rapidly and simply [1]. It is a very promising subject of research showing powerful developments. Compared to the traditional lithographic techniques such as photolithography, vacuum deposition, and electroless plating processes, the printed electronics would guide the fabrication of cost-effective, flexible, and environmentally friendly electronics owing to the large range of printing possible. All these traditional lithographic techniques are multi-staged, need high-cost equipment, and the usage of undesirable chemicals results in large amounts of waste formation [2]. However, the market of printed electronics, which is predicted to be $300 billion over the next 20 years, needs production methods that are cheaper, faster, and eco-friendly compared to traditional methods [3]. Traditional printing processes include screen-printing, inkjet, and coating for obtaining conductive layers and tracks. Recently, three-dimensional (3D) printing has also been paid attention thanks to the complex designs of printed electronics [4]. Attention in printed electronics has exponentially risen in the last 20 years [5]. With a focus on medical applications, printed electronics have found use in the development of biosensors. In this regard, printed electronics-based biosensors have obtained thoroughly realized attention in several areas, which range from research to applications at home. So, the probability of acquiring a sensitive detection in a time and cost-effective way is highly requested by researchers, including doctors, chemists, and biologists [6]. Furthermore, in research, biosensors provide the probability of associating detectable signals with biomolecule concentrations [7]. The probability of integrating the printed electronics-based biosensors in standalone platforms such as wearables, usable even by patients at home, could supply an impactful help to e-Health applications [8].

The latest progress in developing biosensors that can detect the biosensors' response down to the molecular level has sorely speeded up the development of biosensors [9]. Those characteristic issues include selectivity, sensitivity, reusability, and storage stability [10]. Another helpful quantity generally accepted to check results in biosensing is the detection limit, which indicates the lowest amount of a target molecule that could be differentiated from the lack of the target molecule with a specified trusted level [11]. This value is evaluated from blank mean, blank deviation, calibration curve slope, and determined confidence factor [12]. Biosensors that combine chemistry, physics, nanotechnology, electronics, and bioengineering can trace growths in management attempts due to their distinctive properties, including specificity, ease of use, sensitivity, and real-time monitoring ability [13]. Briefly, the biosensor is a detection tool that combines a sensing molecule with a transducer (optic, electrochemical, or piezoelectric) by which the interaction between targets and recognition elements is turned into a measurable signal [14]. They provide fast, real-time, and specific detection with no time-consuming sample pre-processing procedures and are powerful options compared to traditional techniques. They have excellent implementations in food safety, environmental screening, drug development, and clinical areas [15-20]. A biosensor has three major parts: a biosensing receptor, a transducer, and a detector. In principle, the target molecule interacts with the biosensing receptor, and the biosensing element recognizes a target molecule through physical or chemical interactions. After that, the transducer turns the changes into a measurable signal evaluated via the detector. As depicted in Figure 1, the biosensors provide many properties such as fast response, user-friendly operation, high sensitivity and selectivity, storage stability, low cost, and portability. Over the last years, biosensor studies have broadened quickly, indicating a wide range of applications [21-23]. These days, scientists propose increasing the detection methods' selectivity and sensitivity via focalizing biosensor production quality, improving sophisticated surface chemistry methods, enhancing the affinity between ligands and targets, and utilizing different materials for signal amplification studies [24]. For this aim, the increase in printed electronics-based biosensors draw attention.

Printed electronics-based biosensors present a cutting-edge intersection of technology and biology, offering several new and important aspects that contribute to their significance. For instance, printed electronics enable the creation of flexible and lightweight biosensors. This feature is particularly advantageous in app-

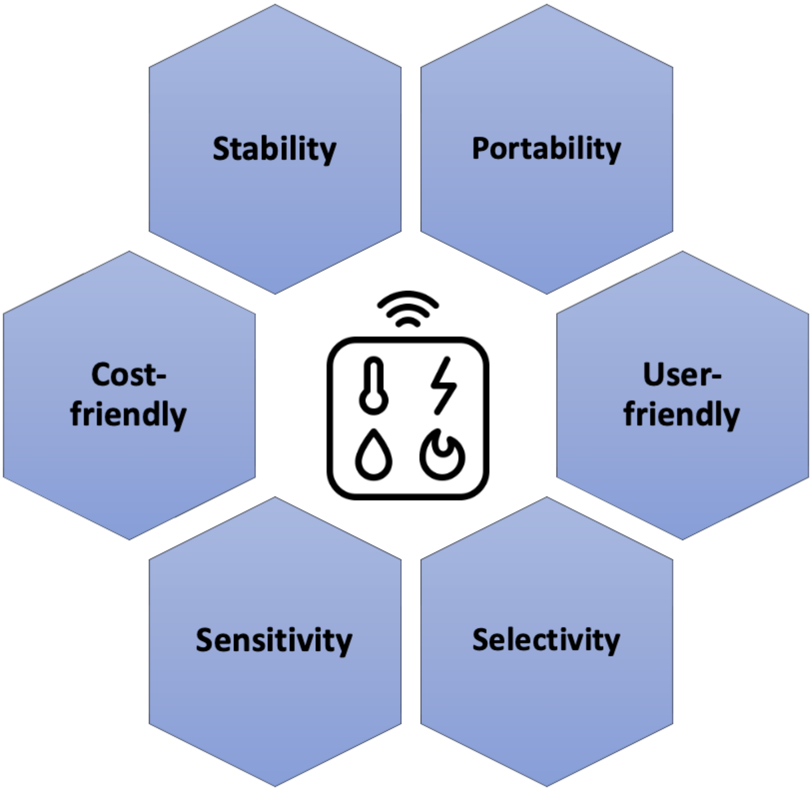

Figure 1. Main properties of biosensors.

lications where conformability to various surfaces or wearable devices is essential, opening up possibilities for continuous monitoring in dynamic environments [25]. The printing processes used in manufacturing these biosensors are often cost-effective and scalable. This makes them accessible for mass production, potentially reducing the overall cost of biosensor technology and facilitating broader adoption in both developed and developing regions [26]. The printing techniques allow for the easy customization of biosensors to detect specific target molecules. Researchers and manufacturers can rapidly prototype and iterate designs, expediting the development of biosensors tailored to particular applications or diagnostic needs [27]. In addition, the materials used in printed electronics are often more environmentally friendly compared to traditional manufacturing processes. This aligns with the growing emphasis on sustainability, making printed electronics-based biosensors an eco-friendlier choice for various applications [28]. The portability and ease of use of printed electronics-based biosensors make them particularly suitable for point-of-care applications. This can revolutionize healthcare by enabling rapid, on-site diagnostics, reducing the need for centralized laboratory facilities and expediting treatment decisions [29]. These biosensors can be engineered to detect multiple analytes simultaneously, providing a comprehensive view of complex biological or environmental samples. This multi-modal detection capability enhances their versatility and utility in a range of scientific and medical scenarios [30]. Advances in materials science and fabrication techniques contribute to improved sensitivity and specificity in detection. This heightened performance is crucial for applications requiring precise measurements, such as early disease detection or environmental monitoring at low concentrations [31]. Ongoing research focuses on enhancing the long-term stability and reliability of printed electronics-based biosensors. Addressing these factors is essential for ensuring sustained accuracy over extended periods, especially in applications that demand continuous monitoring [32]. As research and development in printed electronics-based biosensors continue, these aspects collectively contribute to their growing importance in revolutionizing fields such as healthcare, environmental monitoring, and beyond.

In this review, brief information about different types of biosensors is first given, and then recent progress in printed electronics-based biosensors to produce various platforms and also ensures a review of the chances of printed electronics-based biosensors in different applications. A critical discussion is ensured to understand the promising trends.

Biosensors and Printed Electronics-Based Biosensors

The biosensors can be designed with various operating principles with different transducers, including optic, mass, and electrochemical. The electrochemical biosensors are utilized to achieve a broad range of usages. These biosensors have a platform to construct screen-printed electrodes and semiconductors. They also detect any changes in dimension, dielectric properties, charge distribution, and shape while interaction occurs on the surface of the electrode. The electrochemical biosensors are categorized into major sub-groups such as amperometry, potentiometric, and impedimetric. In addition, the electrochemical biosensors can be utilized to detect many target molecules [33-35]. The piezoelectric biosensors have been used to evaluate acceleration, pressure, strain, temperature, and force alterations by transforming them into charge. Quartz crystal microbalance biosensors are the most widespread piezoelectric biosensors sub-group, which evaluate the viscoelasticity and mass change of biosensors surfaces via saving a frequency and a quartz crystal resonator damping alteration. Owing to the sensitivity to environments, the biosensing operation notably needs a piece of isolation hardware that reduces the obstacle reasons, including vibration. The piezoelectric biosensors can be employed in a broad range of implementations, including low-molecular-weight target molecules [36-38]. The optic biosensors focalize on detecting the optic properties alteration of the transducer plane when the target molecule and recognition element interact with each other. The optic biosensors are divided into sub-groups. Response production is based on the complex formation of the transducer plane in the direct ones. The indirect ones generally use different labels, including fluorophores and chromophores, to determine the binding activity and increase the response. Though indirect optic biosensors can generate superior signals, they endure non-specific interaction and high-cost labeling procedures. Many research studies can be obtained from the literature about optic biosensors, such as time-resolved fluorescence, optrode-based fiber, surface plasmon resonance, evanescent wave fiber, interferometric, and resonant mirror. The detection windows of these optic biosensors are very well-rounded, and they can detect several kinds of molecules [39-41].

The suitable tools for explaining printing technologies scopes from affordable platforms to the costliest platforms that provide a significant geometric resolution with no requirement for extra steps such as a lot of preparation steps and clean rooms [42]. The printing technologies used for developing biosensors can be categorized between contact (flexographic, gravure, offset, screen printing, and micro-contact dispensing) and non-contact (inkjet, laser-induced forward transfer, aerosol jet, micro-, and nano-pen) printings. The contact printing covers entire mask-depended techniques with a substrate, and inked surfaces are in physical interaction. These mask-depended techniques provide superior throughput, low-cost, and fastly produced biosensors [43]. However, due to the huge waste, low resolution, and scale of materials, non-contact printing techniques have increasingly been paid attention. These techniques are depended on ink distributed thanks to openings and describe the structures via acting the stage. So, they authorized to reduce the waste, simplify the printing procedure, improve flexibility and control, increase resolution, complex patterns, and miniaturization [44].

Along with the benefits, the relevance of the broad diversity of materials applied in the preparation of biosensors shows the main topic that must ensure the practicability and behavior of printed electronics. The latest non-contact techniques aim to optimize the ink deposition methods and reduce the dimensions. Moreover, the sintering methods are below examination for optimizing ink post methods [45,46]. These techniques face challenges, including repeatability, conductivity, and the standardization that still affects printed electronics-based biosensors when checked with the bulk partners. Also, integrating and customizing several substances and using new healing methods concerning traditional techniques turns on the way for a successful combination of sensing with directly printed electronics with accordingly developed cost and time effects [47].

3D printing is also a sophisticated technique that indicates an amazing chance for usage, supplying a strategy for the fast and straightforward prototyping of custom architectures with various materials [48]. Opposite to conventional methods, where a piece of complicated machinery is required to produce 3D objects via material-removal methods, the 3D printing technology attaches the intended material layer-by-layer via a basic one-step digitally controlled procedure. This method also prevents some drawbacks related to screen-printing, including the requirement of masking and drying steps [49]. When the first 3D-printed material was dependent on the photopolymerization of a resin using stereolithography, the present of materials has brought plenty of further 3D-printing technologies, specifically direct ink-writing, fused deposition modeling, selective laser sintering, and digital light processing [50]. The method selection depends on the complexity of the item to be produced, the material employed, the number of copies, and the cost. 3D printing also has a crucial role in evolving multifunctional devices that can respond to outer stimuli such as electrochemical, optic, and thermal. This situation has increased the attention of 3D printing to develop new biosensors. Even though the management of sophisticated functional materials in the platform has turned on novel chances for the further generation of biosensors, some traditional modification steps are still needed to insert active biomolecules toward the detection of targets [51].

Furthermore, integrating microfluidics in biosensor systems has an extended history in the application fields. A lateral-flow immunoassay is a conventional clinical example of a biochemical test that evaluates the existence of a biomarker utilizing an antibody as a recognition molecule in paper strip format [52]. Figure 2 represents the standard techniques for the preparation of printed microfluidic-based biosensors. Microfluidic systems accomplish the disadvantages of hard and time-consuming development and accelerated application translation. More significantly, just-in-time preparation of microfluidics, combined with transducers and recognition elements, obtains a rapid time for production and simplifies ease of customization for several applications, hence accelerating its translation, which generally needs fast on-site sample preparation steps [53-56].

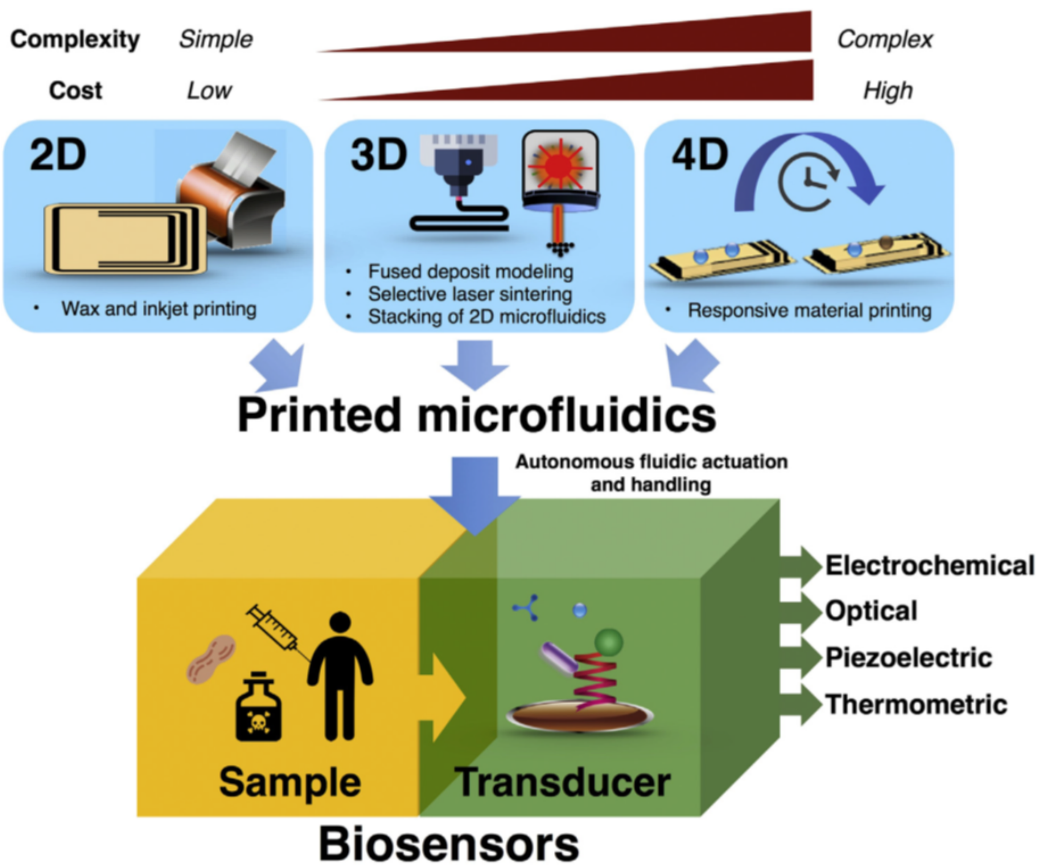

Figure 2. A schematic representation of printed microfluidics-based biosensors. Reproduced with permission from reference 56. Copyright (2019) Elsevier.

Applications of Printed Electronics-Based Biosensors

Nesaei et al. introduced 3D-printed electronics-based biosensors for glucose determination [57]. They used enzyme ink and direct-ink-writing of electrode methods for biosensor design (Figure 3) and showed that their printed electronics-based biosensor acts linearly in glucose sample solutions with a wide range (100-1000 mM). They obtained the sensitivity of printed electronics-based biosensor as 17.5 nA/mM and calculated the detection limit as 6.9 mM. They demonstrated the promising properties of printed electronics-based biosensors, including high sensitivity, high specificity, and minimal material consumption compared to conventional methods, by highlighting their electrochemical performance and surface features. Joubert et al. printed conductive silver tracks with a commercial silver nanopaste onto two types of commercial photo and chromatography papers [58]. They investigated the sintering temperature and the number of printed layers to optimize the production steps. They varied the track line width between 100 µm and 1.5 mm for both electrical and dimensional characterization analysis. They observed that the silver tracks on the photo paper have close resistivity such as bulk silver. They concluded that the conductivity on the chromatography paper was insufficient, the printing of multiple layers was essential, and the sheet resistance for a circuit frequency was removed as a helpful plan parameter for electronic networks. Cinti et al. demonstrated the probability of utilizing paper-based printed electronics as substrates to generate a new biosensor [59]. As shown in Figure 4, they used carbon nanoparticles for altering the working electrode to improve the electrochemical behaviors of the inkjet-printed biosensor and obtain a highly performant electrochemical biosensor. They characterized this biosensor both morphologically and electrochemically and used it successively towards an ascorbic acid. According to the results, they observed that the existence of carbon nanoparticles reduced the potential for ascorbic acid oxidation relating to the unmodified biosensor. They also showed the printed electronics-based biosensor's feasibility in detecting ascorbic acid in dietary supplements.

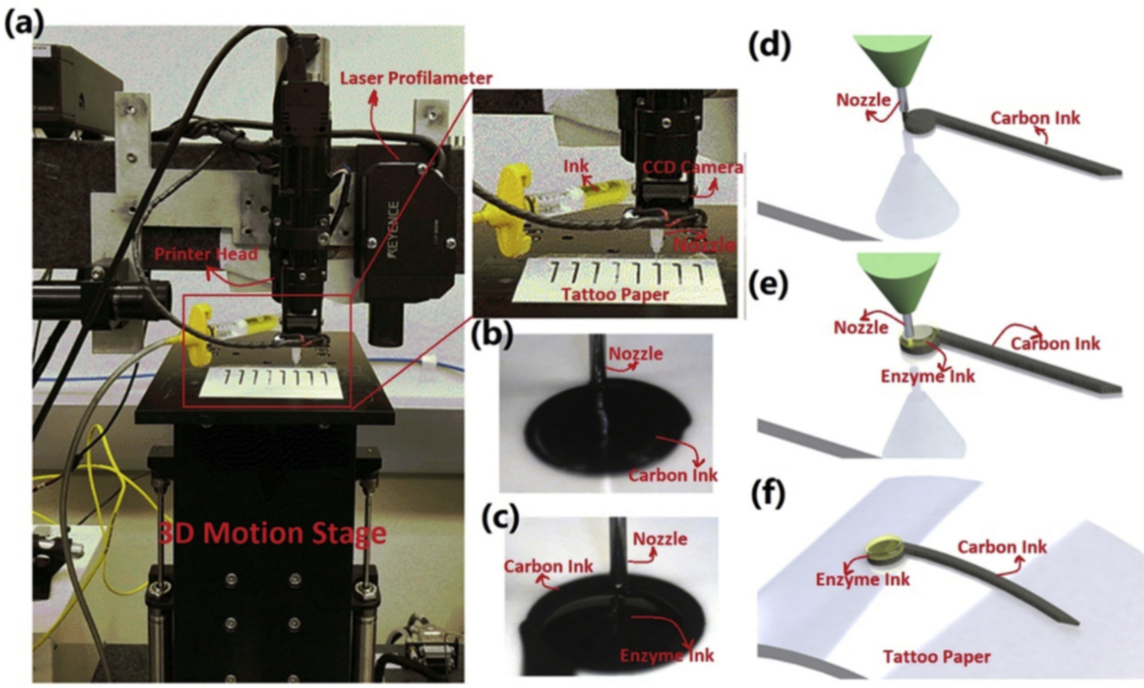

Figure 3. A schematic representation of direct-ink-writing of electrode and enzyme ink: (a) Custom-made direct-ink-write system, (b) direct-ink-write of carbon-mediated ink, (c) direct-ink-write of enzyme ink, (d) electrode printing, (e) enzyme printing, and (f) 3D printed electronics-based biosensor on a flexible substrate. Reproduced with permission from reference 57. Copyright (2018) Elsevier.

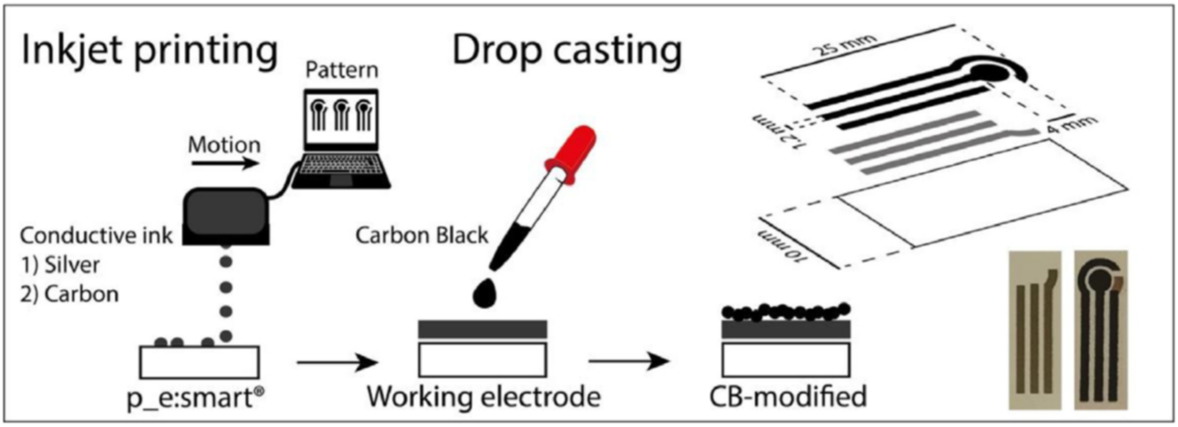

Figure 4. A schematic representation of paper-based inkjet printed electrodes production steps. Reproduced with permission from reference 59. Copyright (2018) Elsevier.

Fukuda et al. fabricated a printed organic thin-film transistor biosensor system on 125-µm-thick polyethylene naphthalate films at 120°C [60]. They employed dithieno[2,3-d;2′,3′-d′]benzo[1,2-b;4,5-b′]dithiophene as an organic semiconductor to develop the consistency of printed organic thin-film transistor devices. They combined all layers except the dielectric layers with printing technologies. They used silver nanoparticle ink formulations for the electrodes and also a printed fluoropolymer layer as a confining bank layer. They concluded that the printing techniques allowed for correct control of the patterned area of the semiconducting solution and the ink volume. Jenkins et al. discussed the usage of inkjet printing of several substrates to produce biosensors [61]. They presented some studies about printing techniques for obtaining printed electronic components and paper-based microfluidics to obtain highly integrated, robust, single-use, and diagnostic detection systems. They used inkjet printing of polydimethylsiloxane hydrophobic limits on membranes to produce microfluidic circuits that allow low-volume consumption. Moreover, they demonstrated a new printing technic depended on an agarose gel to print microfluidics on the paper directly, which may decrease cost and time. They also used printing methods to invest silver nanoparticle ink electrodes with high conductivity.

Mass et al. immobilized horseradish peroxidase onto silica nanoparticles and mixed the nanoparticles into an aqueous ink containing single-walled carbon nanotubes [62]. They characterized the electrodes printed with this formulated ink and printed the enzyme electrodes. An amperometric hydrogen peroxide biosensor was developed by inkjet printing to carry out the performance of the enzyme electrodes. They obtained the electrochemical response of the printed electrodes via cyclic voltammetry in redox species solutions. Furthermore, they observed that the printed enzyme electrodes were found to show similar sensitivity three months after the ink preparation, and catalytic activity was preserved in the proposed ink. So, they concluded that the enzyme electrodes can be printed employing a very stable formulation using nanoparticles.

CONCLUSION

In conclusion, the recent strides in biosensor systems have ushered in a transformative era, significantly enhancing the ability to characterize and quantify target molecules across diverse applications. The advantages offered by biosensors are indisputable and multifaceted. Firstly, they provide a simple, selective, and highly sensitive means of detection. The capability for long-term and automated measurements, coupled with the integration of new functional materials exhibiting unique real-time binding features, underscores the versatility of biosensors. The rapid monitoring and multi-analyte investigating capabilities further amplify their utility, while the ongoing miniaturization of recognition elements through integration with electronics and microfluidics opens up new dimensions for biosensor applications. Moreover, the establishment of networks facilitated by wireless communication techniques propels biosensors into a realm of enhanced connectivity and data accessibility. The long-term and online determination capabilities not only provide novel insights into preparation and relocation mechanisms but also contribute significantly to understanding the interplay of physical and chemical factors. Recent advances in biosensors include the incorporation of artificial intelligence algorithms for data analysis, enhancing the precision and reliability of results. Additionally, the development of biocompatible materials has expanded the scope of biosensors in medical applications, enabling real-time health monitoring and early disease detection. Despite these advances, challenges such as standardization of protocols and the need for improved reproducibility persist, hindering the seamless integration of biosensors into widespread use. Looking ahead, the future scope of biosensors appears promising. Continued research in nanotechnology holds the potential for even smaller, more efficient biosensors, while advancements in materials science may address current issues related to stability and longevity. Integration with emerging technologies, such as the Internet of Things (IoT), could further enhance the connectivity and real-time capabilities of biosensor networks. However, it is crucial for researchers, industry professionals, and regulatory bodies to collaborate closely to address current challenges and pave the way for a future where biosensors become ubiquitous tools in scientific research, medical diagnostics, and environmental monitoring.

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