Sensors International 5 (2024) 100277

Contents lists available at ScienceDirect

Sensors International

journal homepage: www.keaipublishing.com/en/journals/sensors-international

# Microbial biotechnology alchemy: Transforming bacterial cellulose into sensing disease- A review

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## ARTICLE INFO

*Keywords:*
Biosensors in healthcare
Rapid biomarker detection
Point-of-care testing
Wearable biosensors
Personalized medicine
Nanotechnology

## ABSTRACT

Biosensors have the potential to revolutionize healthcare by providing rapid and accurate diagnosis of diseases. Biosensors are analytical devices that convert molecular recognition of a target analyte into a measurable signal. Older diagnostic techniques, such as immunoaffinity column assays, fluorometric, and enzyme-linked immunosorbent assays, are laborious, require qualified personnel, and can be time consuming. In contrast, biosensors offer improved accuracy, sustainability, and rapidness due to their ability to detect specific biomarkers with high sensitivity and specificity. The review covers various bacterial cellulose (BC)-based biosensors, from SARS-CoV-2 detection to wearable health monitoring and interaction with human-computer interfaces. BC's integration into ionic thermoelectric hydrogels for wearable health monitoring shows its potential for real-time health tracking. Incorporating BC in biosensors for low-noise electrodes, and wearable sensors has been elaborated. The invention of a phage-immobilized BC biosensor for *S. aureus* detection is a significant contribution to the field, highlighting the biosafety and efficiency of BC in pathogen identification and demonstrating BC's versatility across multiple sensing platforms. Palladium nanoparticle-bacterial cellulose hybrid nanofibers show excellent electrocatalytic activity for dopamine detection, whereas Au-BC nanocomposite biosensors show efficacy in glucose detection, with potential therapeutic applications. The "lab-on-nanopaper" device, utilizing BC nanopaper, not only visually detects human serum albumin but also establishes itself as a new-generation optical biosensing platform with superiority over conventional substrates. This review contributes to the ongoing advancements in biosensor technology, highlighting the potential of BC as a versatile material for developing innovative biosensors. This is crucial for improving the accuracy, sensitivity, and efficiency of diagnostic tools in healthcare.

## 1. Introduction

Disease diagnosis is a key component of effective health care and serves multifaceted purposes. Early detection allows for early intervention and increases the chances of effective treatment and recovery. It helps health professionals personalize interventions for specific patients. Diagnostics contributes to public health beyond individual health by guiding preventive interventions, resource allocation, and epidemiological surveillance. It also significantly impacts medical research, helping to create novel therapies [1,2].

Microbial biotechnology has revolutionized the diagnosis of diseases. Through the development of biosensors, microbial biotechnology can aid in disease diagnosis. Engineered microorganisms such as bacteria and yeast are used because of their ability to identify disease-related biomarkers. Genetic engineering improves sensory abilities, allowing the detection of biochemicals at low concentrations. These

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https://doi.org/10.1016/j.sintl.2023.100277
Received 5 December 2023; Received in revised form 28 December 2023; Accepted 30 December 2023
Available online 5 January 2024

microorganisms act as biological components in biosensors, producing detectable signals, such as fluorescence or conductivity changes when they interact with specific disease markers. Microbial biosensor's adaptability allows them to detect various biomolecules linked with diverse diseases, providing a cost-effective and quick alternative to established diagnostic procedures. Their real-time monitoring capabilities and adaptability make microbial biosensors valuable tools for early and efficient disease detection [3–6].

Bacterial cellulose (BC) holds promise as a biosensor material in healthcare applications due to its biocompatibility, high surface area, and mechanical strength. BC is produced by certain bacteria, primarily *Gluconacetobacter*, through the fermentation of sugars [7]. Bacterial cellulose has a hydrophilic nature [8], which promotes the adsorption of biomolecules on its surface. BC also has a high surface area [9], which provides numerous anchoring points for biomolecule immobilization. Additionally, BC has a nanoscale pore structure [10], which allows for the efficient transport of biomolecules to the sensor surface. The hydrophilic nature of BC promotes the adsorption of biomolecules on its surface [11], increasing the binding affinity between the biomolecules and the sensor surface, and leading to enhanced sensitivity. Its structural functionality allows the development of customized biosensors for health monitoring, including wearable and implantable devices. The capacity of BC to respond to environmental changes and its combination with other materials helps in developing advanced biosensors with real-time monitoring capabilities. Furthermore, the biodegradability of BC is useful for environmentally sustainable applications [12–14].

This review aims to explore the potential of bacterial cellulose in healthcare biosensors. It covers various applications, including SARS-CoV-2 detection and wearable health monitoring, and highlights BC's role in ionic thermoelectric hydrogels and low-noise electrodes. The review also mentions several novel pioneering biosensors, such as the phage-immobilized BC biosensor for *S. aureus* and the BC nanopaper-based 'lab-on-nanopaper' for albumin sensing. The electrocatalytic activity of palladium nanoparticle-BC hybrids for dopamine detection and Au-BC nanocomposite biosensors for glucose detection are also noteworthy. BC's ability to shape healthcare diagnostics is emphasized.

## 2. Methodology

In writing a comprehensive literature review on the development of bacterial cellulose-based biosensors for diagnostic applications, we employed a systematic method to retrieve relevant articles from prominent databases, including PubMed, Springer, and Elsevier. The articles were searched with specific keywords such as "bacterial cellulose," "biosensors," "diagnostic tools," and "nanotechnology," with the application of Boolean operators to refine the search parameters. The article selection focused on peer-reviewed studies that focused on the development of bacterial cellulose-based biosensors and explored the incorporation of nanotechnology in diagnostic tools. Articles that did not meet these criteria or were not published in English were excluded. Following the literature retrieval, data extraction and summarization of key findings were done. The synthesized information was then compiled into a comprehensive literature review, offering valuable insights into the current knowledge of bacterial cellulose-based biosensors with an emphasis on nanotechnology integration.

## 3. Biosensors in healthcare

Biosensors play a pivotal role in healthcare by providing rapid and accurate detection of biological molecules and enabling early diagnosis, disease monitoring, and personalized treatment. These devices combine a biological component (such as enzymes, antibodies or DNA) with a transducer to convert the biological response into a detectable signal [15–18]. Biosensors are becoming more predominant in healthcare due to their ability to give speedy and reliable diagnostics, particularly in modern medicine and disease management [19]. Furthermore, biosensors are required for non-laboratory diagnostic tools such as the examination of blood, saliva, and urine, as well as real-time patient data and home-based chronic disease management [20]. Wearable biosensors are also revolutionizing healthcare by allowing real-time health monitoring, prevention, and therapy [21]. The development of innovative biosensor formats and advancements in non-invasive biological fluid sampling are essential for monitoring a broader spectrum of biomarkers. Wearable biosensors are also increasingly being used for remote patient monitoring, highlighting their broad impact on human health [22]. Overall, biosensors play a critical role in advancing healthcare and biomedical research, offering cutting-edge applications in the diagnosis and treatment of various diseases. Here are some key aspects of biosensors in healthcare (Table 1).

## 4. Bacterial cellulose in biosensors for disease diagnosis

Biosensors based on bacterial cellulose have demonstrated potential for use in healthcare and medical diagnosis. BC-based biosensors have several favorable attributes including high sensitivity, quick response, precision, and affordability. BC and its derivatives are adaptable materials that offer superior substrates for the immobilization of physiologically active compounds in biosensors. BC-based biosensors possess various desirable properties such as accuracy, sensitivity, convenience,

**Table 1**
Applications of biosensors in healthcare and biomedical research.

| Sl. No. | Application | Description | Reference |
|---|---|---|---|
| 1 | Point-of-Care Testing | Biosensors are useful for point-of-care testing as they provide rapid results without the need for sophisticated lab facilities. This is especially useful in remote or resource-limited locations. | [23] |
| 2 | Monitoring and Management | Continuous monitoring of biomarkers helps in the management of chronic diseases (e.g., diabetes, cardiovascular disease, cancer), allowing for real-time modifications to treatment strategies. | [24] |
| 3 | Personalized Medicine | Biosensors facilitate personalized medicine by providing insights into an individual's unique biological traits, allowing for customized therapeutic interventions. | [25] |
| 4 | Drug Development Research | Biosensors are useful in drug development for studying drug-biomolecule interactions for screening candidates and determining mechanisms of action. | [26] |
| 5 | Wearable and Implantable Devices | Biosensor advancements enable wearable/implantable devices for real-time biomarker monitoring, assisting in chronic condition management. | [27] |
| 6 | Infectious Disease Detection | Biosensors are critical in quickly identifying infectious diseases and allowing immediate actions to reduce pathogen transmission. Especially useful during global health crises such as the COVID-19 pandemic. | [28] |
| 7 | Environmental Monitoring | Environmental monitoring technique used to identify pollutants, toxins, and pathogens in air, water, and soil, with public health concerns due to environmental influences on human well-being. | [29] |
| 8 | Nanotechnology Integration | Advances in nanotechnology are enabling nanobiosensors that increase sensitivity and specificity. These nanobiosensors detect biomarkers at low concentrations. | [30] |

low cost, and fast response. BC has received attention in various biomedical applications [31,32]. The unique combination of properties offered by bacterial cellulose makes it a promising material for biosensor applications, and ongoing research is exploring its potential in various healthcare diagnostic and diagnostic monitoring scenarios. Some key aspects of the use of bacterial cellulose in biosensors are as follows.

### 4.1. BC biosensor for SARS-cov-2 detection

The BC-based electrochemical biosensor, with its favorable combination of affordability, environmental friendliness, portability, and efficiency, is a model solution for SARS-CoV-2 detection [33]. With limits of detection of 4.26 × 10−18 g mL−1 S P and 0.05 copies μL−1, the biosensor has outstanding sensitivity. This allows reliable results to be obtained in a short 10 min, using only 10 μL of clinical samples. Notably, the apparatus exhibited strong selectivity for SARS-CoV-2 and high repeatability (RSD = 3.78 %), proving its dependability under a range of testing conditions. This biosensor is unique because of its thoughtful environmental design, which reduces the usage of hazardous materials and chemicals [34]. By utilizing BC's biocompatibility and easily accessible ingredients, the biosensor may be produced at a reasonable cost of approximately US$3.50, requiring only 3 h of preparation time, which includes a functionalization procedure (Fig. 1). Crucially, its simplicity and independence from advanced instruments, modern laboratory facilities, additional reagents, or sample pretreatment make it an accessible and efficient choice for widespread and rapid SARS-CoV-2 testing across diverse settings [35].

### 4.2. BC in ionic thermoelectric hydrogels for wearable health monitoring

This study emphasizes the crucial role of self-powered sensors in the evolution of wearable electronics, exploring the potential of environmentally friendly ionic thermoelectric hydrogels to capture the mild heat from human skin for continuous electricity generation [36]. The study introduces a unique coordination double-network ionic thermoelectric hydrogel employing a method to oxidize carboxylated bacterial cellulose, surpassing limitations seen in existing hydrogels [37]. This hydrogel exhibited outstanding thermoelectric capabilities, producing a maximum power at a temperature differential of 20 K, utilizing a substance for ion diffusion. Featuring a high Seebeck coefficient, the design improves selective transport through interactions between ions and the hydrogel matrix. Notably, the hydrogel's mechanical strength is

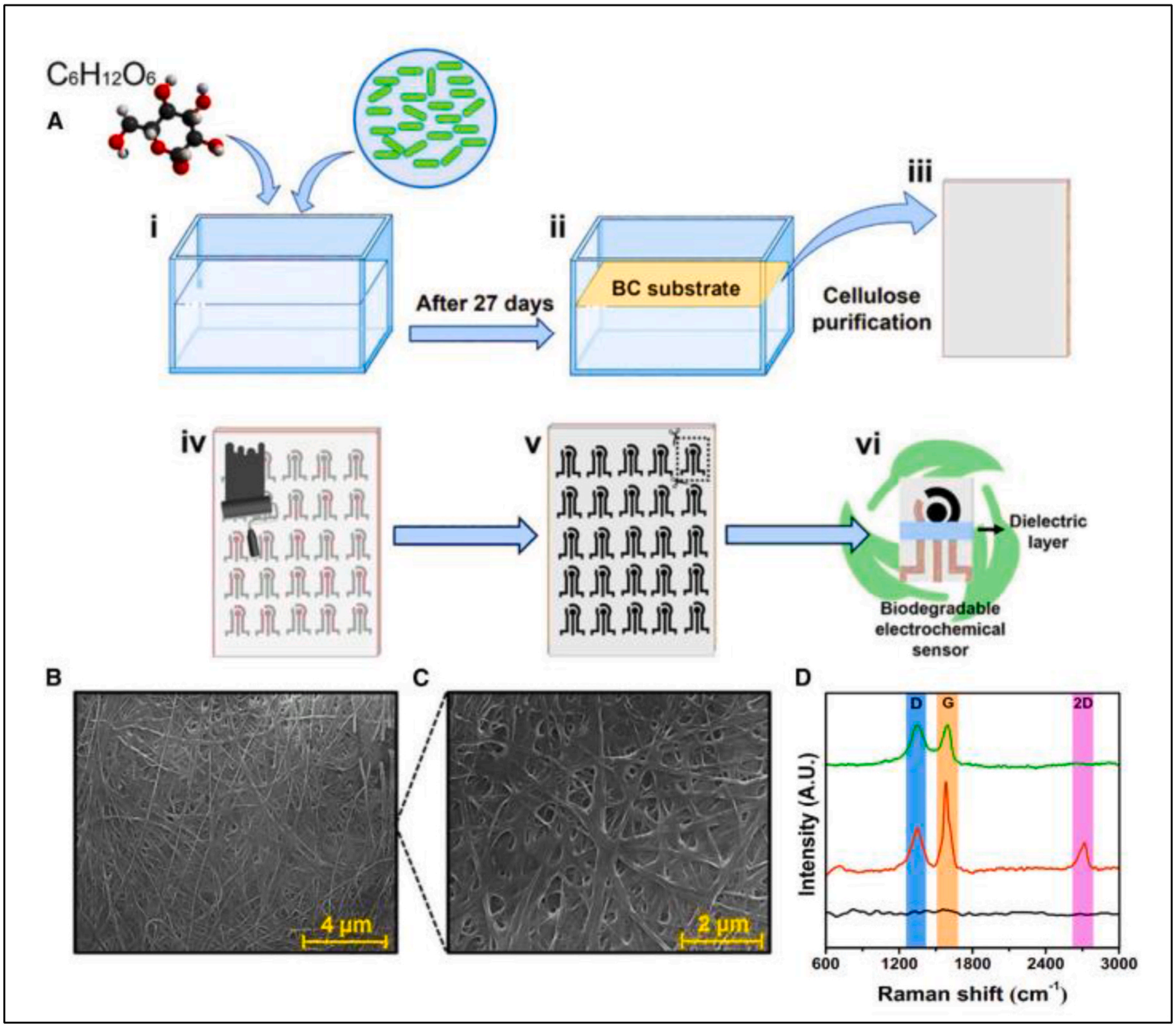

**Fig. 1.** Development and analysis of the SARS-CoV-2 electrochemical biosensor utilizing bacterial cellulose. (A) Sequential stages in the creation of the BC substrate and the electrochemical sensor. (i) Initially, *Gluconacetobacter hansenii* bacteria were cultivated in HS medium. (ii) After an incubation period BC substrate was harvested and subjected to purification. (iii) resulting in a transparent sheet. (iv) Subsequently, the biodegradable BC substrate was screen-printed with carbon and Ag/AgCl conductive ink. (v) Forming a device with three electrodes. (vi) The device was then cut using scissors, yielding a portable, biodegradable, and cost-effective BC-based biosensor. (B and C) Scanning electron microscopic images of the BC substrate at magnifications of (B) 13,000 and (C) 25,000. (D) Raman spectra of the BC substrate, BC/carbon ink electrode, and BC/carbon ink/G-PEG electrode [35]. © with permission from Elsevier.

reinforced by hydrogen bonding in the polyacrylamide network and interactions within the borate ester bond of the carboxylated bacterial cellulose, achieving a stress value at a tensile deformation [38]. This integrated approach positions ionic thermoelectric hydrogels as a promising option for self-powered sensor applications, combining robust mechanical properties with high ionic thermo voltage.

### *4.3. BC bioaerogel for human-computer interaction*

This study introduces an innovative and environmentally friendly strain sensor using bacterial cellulose. The sensor fabrication involves a unique combination of BC and biodegradable Ecoflex (EF) with a three-dimensional conductive network [39]. Through a biofabrication process [40], the BC structure is enhanced for human sensing without the need for fermentation or the incorporation of specific materials. The strain sensor exhibited exceptional long-term stability and retained sensitivity even after 1000 cycles of stretching. It has a wide strain range (up to 90 %), an incredibly low strain detection limit (0.05 %), and high sensitivity. This versatile sensor accurately records diverse bodily movements, making it suitable for applications like monitoring breathing. Its seamless integration with textiles makes it a promising component for human-computer interactions. The study underscores the importance of sustainable fabrication methods in the development of wearable devices [41], contributing to advancements in human-computer interface technologies.

### *4.4. BC/graphene hybrid biosensor for sleep monitoring*

Those who suffer from sleep apnea syndrome must have their respiratory status constantly monitored while they sleep [42,43]. The disadvantages of traditional monitoring techniques, like stiff chip sensors and polysomnography [44,45], include pain and poor wearability. This study provides a low-power, low-complexity, low-integration wireless sensing device based on biocompatible graphene and bacterial cellulose hybrids [46]. This technology is excellent for wireless communication using Morse code, in addition to monitoring physiological signals including respiration. Combining the mechanical qualities of BC with the conductivity of graphene, the 3D porous graphene/BC bio-aerogel exhibited remarkable pressure sensing capabilities with a wide operating range (20–30 kPa), high sensitivity, and cycling stability. Furthermore, the graphene oxide (GO)/BC shows remarkable humidity sensing capabilities, allowing respiratory waveform and frequency to be monitored in real-time. These wireless flexible pressure and humidity sensors provide diagnostic data when worn for prolonged durations of sleep, making them a handy and comfortable replacement for traditional monitoring techniques [47].

### *4.5. BC photonic biosensor for lysozyme detection*

Since structural colors from short-range ordered colloidal particles are non-iridescent and non-fading, there is growing interest in the development of optical biosensors based on them [48]. A study presents a biomimetic approach using biopolymers, this novel approach heavily relies on bacterial cellulose, which is well-known for its wide adjustable surface area, strong mechanical strength, and biocompatibility [49]. A molecularly imprinted photonic sensing layer was built on top of the functionalized BC. In addition to producing a black background for ideal color saturation, polydopamine (PDA) modification improves the mechanical and adhesive properties of the BC substrate. For lysozyme biomarkers, recognition sites are formed by a PDA-based molecularly imprinted polymer (MIP). A monodisperse colloidal suspension of silica particles formed the core of the MIP shell, and a photonic structure was constructed on the PDA-BC membrane. The resultant biosensor shows selectivity against cystatin C and a detection limit of about 0.8 nmol L−1 for lysozyme in spiked human serum. This biosensor offers an environmentally benign, economically viable, and biocompatible sensing platform, with great promise for healthcare applications.

### *4.6. Phage-immobilized BC biosensor for S. Aureus detection*

This study presents the development of a biosensor using bacteriophage immobilization in a bacterial cellulose matrix with surface modification [50]. BC's high porosity and fibrous structure enable dense phage immobilization and provide a substantial surface area for carboxylated multi-walled carbon nanotubes (c-MWCNTs) impregnation [51]. The addition of polyethyleneimine (PEI) to BC/c-MWCNTs created a positive charge, simplifying the orientation of phage immobilization. Confocal microscopy revealed that phage particles were trapped in the BC matrix, indicating anti-staphylococcal activity, with distinct lytic zones and reduced bacterial growth. Differential pulse voltammetry analysis in phosphate-buffered saline and milk detected *S. aureus* within 30 min at neutral pH. Stability over six weeks at 4 °C was confirmed (Fig. 2). The biosensor effectively differentiated live *S. aureus* from dead cells in a combination of live and mixed cultures, demonstrating high specificity for *S. aureus* in both scenarios. The limit of detection was 5 CFU $mL^{-1}$. The developed biosensor is an easily deployable, sensitive, selective, and accurate tool for early detection of *S. aureus*.

### *4.7. BC localized surface plasmon resonance (LSPR) sensor*

This study focuses on a green sensor that uses a thin-slab waveguide made of bacterial cellulose and localized surface plasmon resonance (LSPR) phenomena. It is simple to build these LSPR sensors using gold sputtering on BC waveguides [52]. Their performance was investigated by comparing the thickness of the BC substrate and the presence of ionic liquids (ILs) with and without ILs. The effect of ILs on LSPR may be either beneficial or detrimental, depending on the thickness of the BC layer. For the experimental setup of this extrinsic optical fiber LSPR sensor, two optical fibers connect a spectrometer and a white light source to the green LSPR sensor chip [53]. The outcomes highlight the effectiveness of this strategy for creating biosensors with unique features. These platforms for LSPR exhibit potential in the development of disposable biosensors by the covalent attachment of certain bioreceptors to the gold surface.

### *4.8. BC biosensor for low noise electrodes*

Designing low-noise devices in the millihertz frequency band is particularly challenging due to the 1/f type and intrinsic thermal noise produced by the sensor electrode [54,55]. Research has revealed that a low electrical double-layer resistance can be established with liquid solutions by coating bacterial cellulose nanofibers with conducting PEDOT:PSS ink, resulting in a nanostructured surface. The collaborative effect of the low interfacial resistance and large effective sensing area of PEDOT:PSS electrodes serves to minimize thermal noise and reduce the amplitude detection limit of the sensor. The electrode noise decreases with frequency, enabling the measurement of low-frequency bioelectrical communication signals, a feature of non-electrogenic cells that has previously been difficult to explore with metallic-based microelectrode arrays. The biosensor electrodes demonstrate their performance by recording signals generated by populations of glioma cells, achieving a high signal-to-noise ratio (Fig. 3). Analyzing low-frequency bioelectrical communication signals typical of non-electrogenic cells, which was previously difficult with metallic-based microelectrode arrays, becomes feasible owing to this low noise. The effectiveness of these biosensor electrodes is illustrated by the recording of signals from glioma cell populations, showcasing the efficacy of these electrodes [56].

### *4.9. BC for wearable sensor*

This work demonstrates a versatile method for creating wearable

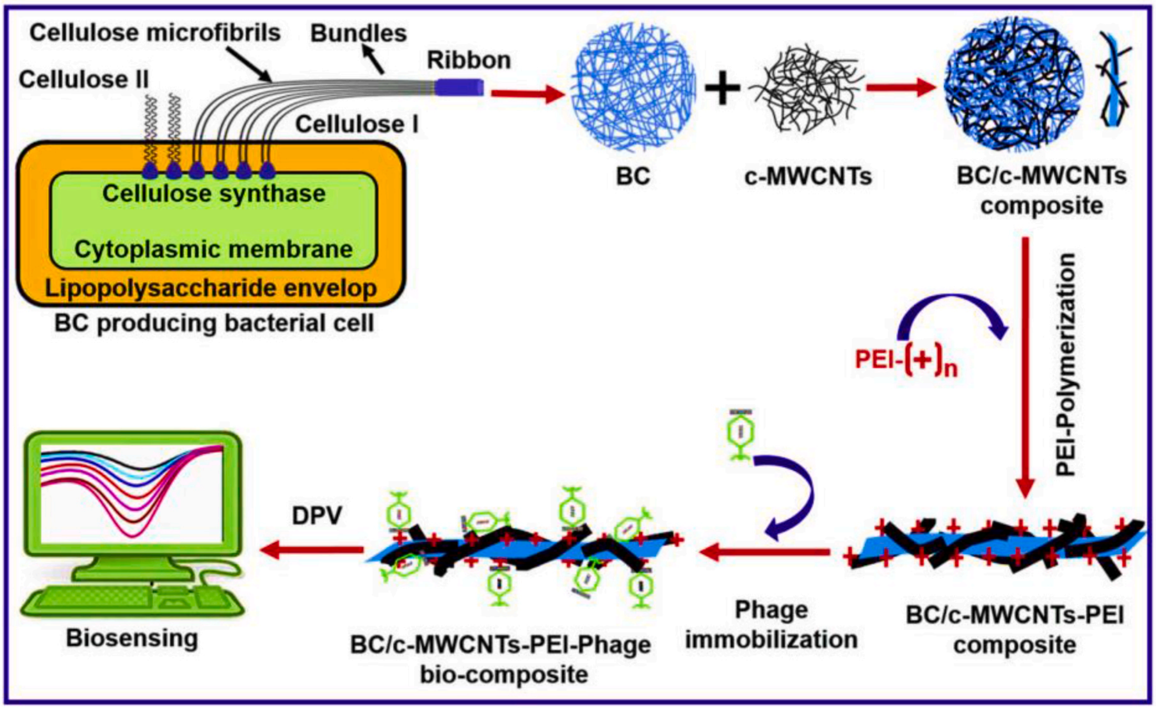

**Fig. 2.** An illustration showing the steps involved in producing bacterial cellulose includes, adding carboxylated multiwalled carbon nanotubes (c-MWCNTs) to the BC matrix, modifying the BC fibers by cationic modification with polyethyleneimine (PEI), and immobilizing the phages inside the PEI-modified BC fibers. The bio-interface that was developed is utilized in the electrochemical detection of bacteria by differential pulse voltammetry (DPV) technology [50]. © with permission from Elsevier.

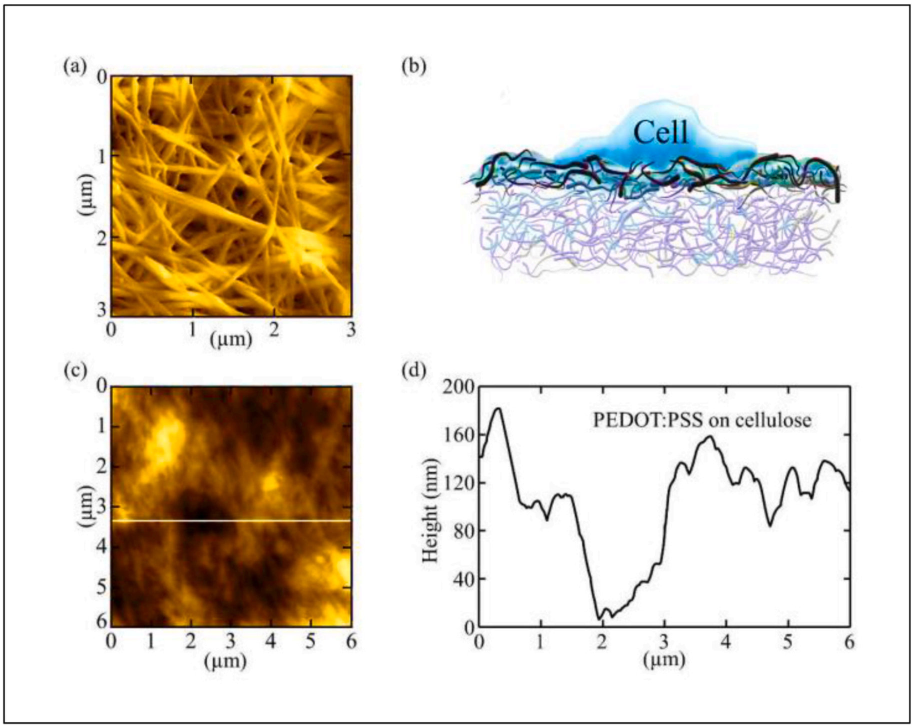

**Fig. 3.** Structural Characteristics of the Bacterial Cellulose Substrate. (a) The low impedance is attributed to the entangled mesh structure of BC, consisting of nanofibers approximately 100 nm thick and several microns long. (b) Schematic representation of the 3D-like surface of BC, providing a biomimetic environment for living cells. (c) AFM topography image of cellulose coated with a PEDOT:PSS thin film, and (d) corresponding profile view revealing cellulose roughness and enhanced active electrode area due to PEDOT:PSS ink impregnation [56]. © with permission from Elsevier.

sensing platforms: sensing units made of screen-printed carbon electrodes (SPCEs) on bacterial cellulose. The SPCEs in their as-prepared state showed effectiveness in identifying hazardous metals, particularly lead ($Pb^{2+}$) and cadmium ($Cd^{2+}$), with detection limits of 1.01 and 0.43 μM, respectively. These cutoff points work well enough to identify metal ions in human body fluids. After undergoing anodic pretreatments to achieve functionalization, SPCEs were utilized to detect 1.8 μM for uric acid and 0.58 μM for 17β-estradiol in artificial sweat (Fig. 4). The carbon surfaces underwent electrochemical treatment, which led to the production of oxygen groups, thereby improving their wettability and hydrophilicity. BC was used as a highly skin-adherent, adhesive-free base for wearable sensor devices [57]. BC's potential for this purpose is further enhanced by utilizing its semi-permeable, non-allergenic, and renewable qualities [58]. The results of this study have important implications for the development of environment-friendly, biocompatible, and effective substrates. They may also open the door for the combination of immunosensing devices with drug-delivery therapies.

### 4.10. BC for wearable electrochemical biosensor

In this research, a bacterial cellulose (BC) substrate was employed to create an effective electrochemical biosensor. Instead of immobilizing lactate oxidase (LOx) on the electrode surface, researchers directly place it on the BC substrate, showcasing its potential for detecting lactate in synthetic sweat. BC, known for its nanofibers and commonly used in wound dressings due to its biocompatibility, possesses excellent mechanical properties [59]. The proposed biosensor substrate offers key benefits, including biocompatibility, the ability to produce large quantities of screen-printed electrodes (SPE) on BC, and higher mechanical resistance compared to plant cellulose, even when wet. On the electrochemical sensing platform, LOx was adsorbed directly onto the BC surface. The platform utilized a carbon-based working electrode modified with Prussian blue nanocubes, serving as an effective electron mediator for hydrogen peroxide. The biosensor developed demonstrated an impressive amperometric response to lactate in synthetic sweat detection limit of 1.31 mmol $L^{-1}$. This described sensing platform with a BC substrate could lead to the development of wearables with improved biocompatibility and mechanical robustness [60].

### 4.11. BC-based device for albumin sensing

A study presents a novel approach to the visual detection of human serum albumin (HSA) in human blood serums [61]: the nanopaper-based analytical device (NAD), also referred to as the "lab-on-nanopaper" device. Because HSA prevents curcumin from degrading in alkaline conditions, the color changes of curcumin embedded in BC nanopaper (CEBC) occur. These color changes can be measured spectroscopically with a spectrophotometer or visually observed with the naked eye or a smartphone camera. As a novel albumin assay kit, the developed NAD/CEBC was successfully used to measure HSA in samples of human blood serum, yielding satisfactory findings. "Lab-on-nanopaper" devices, or NADs, are a new generation of optical biosensing platforms that combine the benefits of nanopaper, outperforming conventional paper, glass, or plastic substrates. This is achieved by emphasizing the notable features of BC nanopaper as a promising bioplatform in optical biosensing applications [62].

### 4.12. Nano-bacterial cellulose-based biosensor for detection of dopamine, glucose and real-time health monitoring

The integration of nanotechnology can elevate the performance of

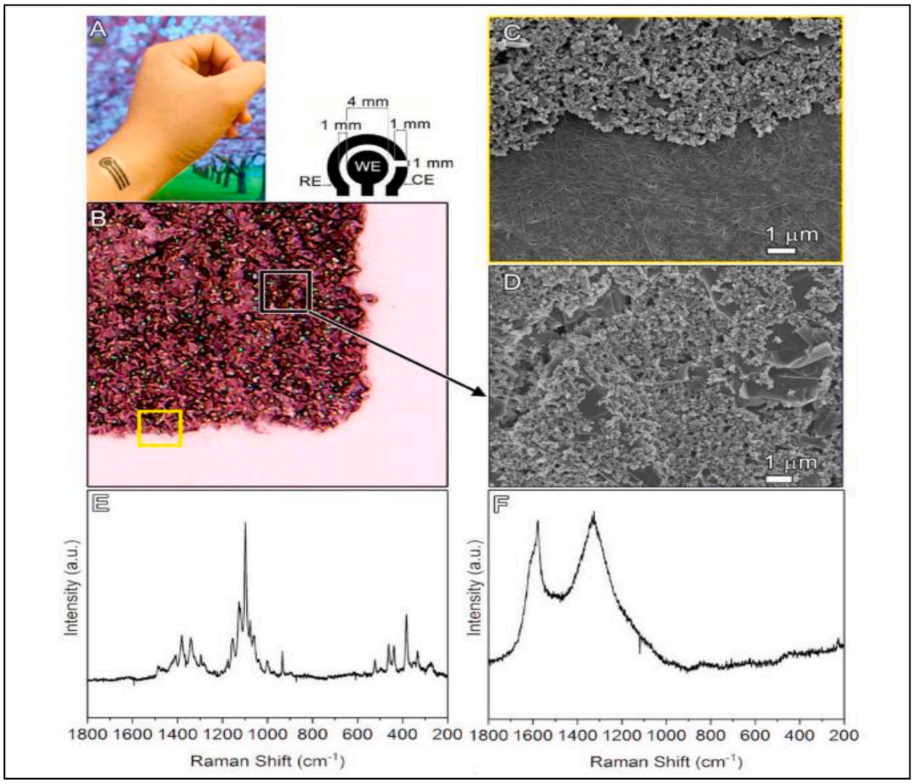

**Fig. 4.** Visual representation of screen-printed carbon electrodes affixed onto Bacterial nanocellulose (BC) adhered to the skin, accompanied by the corresponding dimensions (A). Optical micrograph illustrating the electric contact edge on a screen-printed carbon electrode (SPCE) (B). The yellow and black squares indicate the intersections of the BC/carbon paste and SPCE surfaces, respectively. Scanning electron microscopy (SEM) images depicting the convergence of BC/carbon paste (C) and operational SPCE (D) surfaces. Raman spectra capturing the molecular signatures of BC (E) and a conventional SPCE positioned on a BC sheet (F) [58]. © with permission from Elsevier.

any desired application [63]. An in-situ chemical reduction process was used to create hybrid nanofibers of palladium nanoparticle-bacterial cellulose (PdBC). The outcomes showed that Pd nanoparticles were uniformly distributed over the BC nanofiber surfaces. After being synthesized, the PdBC nanofibers were mixed with Nafion and laccase (Lac) to create a suspension. A novel biosensing platform was developed as a result of applying this suspension to alter the electrode surface. This led to the creation of an electrochemical biosensor, which was used to detect dopamine. Promising results were obtained from the investigation, which demonstrated good electrocatalytic activity towards dopamine with a broad linear range (5–167 μM), a low detection limit (1.26 μM), and high sensitivity (38.4 μA $mM^{-1}$). It presented a possible technique for clinical applications in dopamine analysis and successfully demonstrated applicability in detecting dopamine in human urine [64].

Another study investigates the use of a gold nanoparticle and bacterial cellulose nanofiber (Au-BC) nanocomposite as a platform for glucose amperometric measurement. Horseradish peroxidase (HRP) and glucose oxidase (GOx) enzymes were immobilized at the same time after the glassy carbon electrode was altered with the Au-BC nanocomposite. A sensitive and quick amperometric response to glucose was made possible by the presence of the electron mediator (HQ). Crucially, GOx and HRP successfully preserved their biocatalytic capabilities within the Au-BC nanocomposite. With a linear range of 10 μM–400 μM, the biosensor demonstrated a low detection limit of 2.3 μM for glucose when operating under optimal conditions. The successful determination of glucose levels in human blood samples was demonstrated by using this biosensor [65].

A triboelectric nanogenerator (SBB-TENG) based on bacterial cellulose, integrating barium titanate (BTO) nanoparticles for improved performance was proposed. The BC nanofibers, boasting a substantial specific surface area, interact with BTO nanoparticles, resulting in a uniformly dispersed and encapsulated configuration within the BC network. The SBB-TENG demonstrates exceptional sensitivity in mechanical response and significant electrical output, generating a short-circuit current, an open-circuit voltage, and a transmitted charge. Within a mere 60 s of finger tapping, the TENG charges a capacitor, efficiently energizing portable electronics. Distinct outputs are observed during various activities for real-time monitoring, like computer mouse

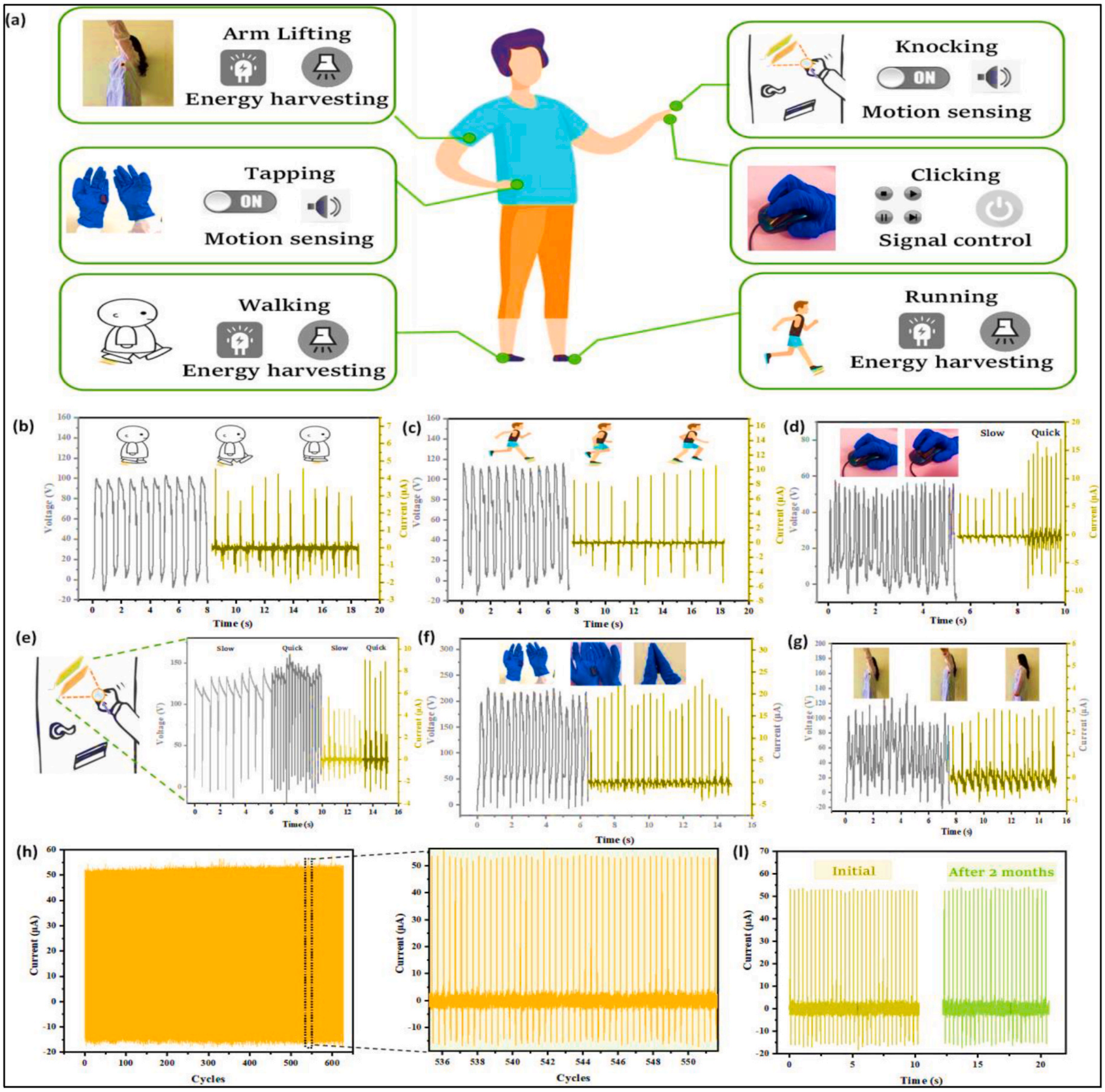

**Fig. 5.** (a) Illustration of bacterial cellulose-based biosensor for real-time health monitoring. The output voltage is plotted against time while (b) walking, (c) running, (d) clicking the computer mouse, (e) knocking on the door, (f) tapping, (g)lifting the arm. (h) Output voltage stability of the biosensor. (l) The stability of biosensor in air [66]. © with permission from Elsevier.

clicks, displaying varying currents, and distinct voltages during walking and running (Fig. 5). The SBB-TENG holds the potential to monitor human fatigue, athlete training, and physical rehabilitation [66].

## 5. Conclusions and future perspective

Bacterial cellulose has emerged as a highly promising material for biosensors in medical diagnostics due to its exceptional properties. BC offers great surface area, mechanical stability, and biocompatibility, making it an ideal material for the development of reliable and effective biosensors. Moreover, BC-based membranes can be fully decomposed by cellulase solution. To further advance the field, future efforts should focus on enhancing multi-analyte detection capabilities, integrating BC biosensors with emerging technologies like artificial intelligence, and validating their clinical efficacy for point-of-care applications. Validation of BC biosensors in clinical contexts is essential to translate these advancements into practical healthcare solutions, as they provide quick and accurate data that could significantly impact patient care. The unique properties of BC make it a promising candidate for the development of next-generation biosensors for medical diagnostics. Additionally, considering long-term stability and standardization of manufacturing processes is not discussed in this review which may provide a more balanced perspective on the practical implementation of bacterial cellulose-based biosensors in real-world healthcare scenarios.

## Funding information

This research received no external funding.

## Ethical approval

The conducted research is not related to either human or animal use.

## Data availability statement

The data set generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## CRediT authorship contribution statement

**Ali Jawad Akki:** Writing – original draft. **Pratheek Jain:** Conceptualization. **Ravindra Kulkarni:** Visualization. **Raghavendra Rao Badkillaya:** Methodology. **Raghavendra V. Kulkarni:** Project administration. **Farhan Zameer:** Project administration. **V Raghu Anjanapura:** Supervision. **Tejraj M. Aminabhavi:** Funding acquisition.

## Declaration of competing interest

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

## Abbreviations

| | |
|---|---|
| BC | Bacterial Cellulose |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome Coronavirus 2 |
| RSD | Relative Standard Deviation |
| GO | Graphene Oxide |
| SPCE | Screen-Printed Carbon Electrode |
| ILs | Ionic Liquids |
| LOx | Lactate Oxidase |
| SPE | Screen-Printed Electrode |
| HSA | Human Serum Albumin |
| NAD | Nanopaper-Based Analytical Device |
| CEBC | Curcumin Embedded in BC Nanopaper |
| Lac | Laccase |
| HRP | Horseradish Peroxidase |
| GOx | Glucose Oxidase |
| HQ | Hydroquinone |

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