



Hydrogel-Based Biosensors in Biomedical Applications

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Abstract

Hydrogels have significant potential for various applications due to their high water content and unique three-dimensional interconnected structure. Due to their excellent biocompatibility, tunable dynamic characteristics, and sensitive responses to environmental stimuli, including temperature, pH, and ions, hydrogels are an ideal material platform for new biosensors. While synthetic hydrogels allow precise control over structure and function through chemical or physical methods to meet the requirements of various applications, natural hydrogels offer advantages such as abundant resources and environmental sustainability. Wearable medical devices have advanced significantly. Antifouling hydrogel interfaces enable electrochemical and optical biosensing of tumor biomarkers, while functionalized conductive hydrogels support emerging strategies for cardiac tissue engineering and nerve repair. The most recent advances in sensor design, material selection, and fabrication techniques have been reviewed, alongside their potential applications across diverse domains and the remaining challenges in achieving stability, sensitivity, and clinical translation.

Keywords:

hydrogels; biosensors; 3D interconnected structure; biocompatibility of biosensors; tissue engineering

1. Introduction

A biosensor is generally defined as an analytical device that converts a biological response into a measurable and processable signal, thereby serving as a bridge between biochemical reactivity and technology [1]. Biosensors are attracting the attention of many researchers for their diverse applications in the pharmaceutical, clinical, biomedical, and healthcare sectors. These are now being used successfully to detect and monitor diseases, including bacteria, pathogens, and viruses. Also, these sensors can detect chemicals without drawing blood. It also reduces the need for hospital stays to monitor body chemistry, giving us access to information about the chemicals in our bodies from anywhere [2,3]. Biosensors can be applied to a

wide range of samples, including body fluids, food samples, cell cultures, and environmental samples [4].

A hydrogel is a three-dimensional, cross-linked polymer that is highly elastic, stable, and capable of absorbing and retaining water. It can soak up hundreds of times its weight in water. These properties further contribute to the efficiency of biosensing. The pore size and the hydrogel's swelling rate determine the diffusion constant for biomolecules and, to a greater extent, the sensor's response time. The high degree of biomolecule immobilization increases sensitivity and improves detection limits, as pore size and surface chemistry can be adjusted. Compared with traditional rigid sensor materials, the high elasticity and water-rich properties of hydrogels more closely resemble those of natural tissues, thereby improving biocompatibility

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and reducing inflammatory responses. Beyond serving as passive matrices, hydrogels function as active facilitators in highly responsive, selective, and biocompatible biosensing systems by directly linking their material properties to biosensor performance metrics. Swelling disrupts the molecular chain structure, weakens material properties, accelerates degradation, and thus reduces its application value.

Hydrogels, in contrast, can respond to a variety of stimuli, making them particularly well-suited for sensing applications [5]. Hydrogels are much more advantageous compared with conventional materials for biosensors. Poor biocompatibility, inflammation, and lack of flexibility are common problems with traditional metals, electrodes, and solid high-molecular materials. Hydrogel is more like natural tissue because it contains a lot of water and can bend. This makes it much less responsive to the environment and more sensitive. Furthermore, hydrogels are easily tunable and exhibit strong responsiveness to their environment, maintaining stability across a wide range of physiological conditions. These properties make them excellent candidates for next-generation biosensors. A signal transduction pathway that converts the hydrogel response into a measurable signal enables this [6]. A variety of synthetic polymers, including polyethylene glycol (PEG), poly(N-isopropylacrylamide) (PNIPAM), and poly(2-hydroxyethyl methacrylate) (PHEMA), as well as natural polymers such as chitosan, alginate, dextran, and hyaluronic acid, have been employed to fabricate hydrogels for biosensing applications. Because they are hygroscopic, proteins and cells can't stick to them. Their unique traits, such as biocompatibility, shape-changing ability, and controllable mechanical and chemical properties, make them useful as biosensors [7]. Photothermal therapy (PTT) typically necessitates sustaining tumor lesions at temperatures exceeding 50 °C, potentially resulting in localized inflammation and tumor metastasis. To mitigate these adverse effects, it is crucial to achieve effective anti-tumor outcomes at relatively low temperatures (42–45 °C) during photothermal therapy (PTT). Ding et al. [8] developed a polydopamine (PDA)-coated nucleic acid nanogel

for use as a therapeutic complex for siRNA-mediated low-temperature PTT. Lee et al. [9] described the biomedical applications of alginate-based hydrogels for their biocompatibility, adjustable biological behavior, and resemblance to extracellular matrices. Alginate consists of M and G units that can be cross-linked with divalent cations, such as Ca^{2+} , to form hydrogels. Covalent and light-induced (photon-to-cross-linking) approaches leverage increased stability to enable function. Alginate hydrogels, with their high water content, porosity, and mechanical flexibility, serve as effective matrices for encapsulating biologics and cells.

This review presents an overview of recent advances and key findings in hydrogel-based biosensors for biologically relevant applications, including diagnostics, drug delivery, tissue repair and regeneration, and wound healing. This review presents different types of hydrogel materials for biosensors (natural polymers, synthetic polymers, and conductive materials). It discusses the technical limitations encountered during the development, fabrication, and application of hydrogel-based biosensors. Furthermore, this article discusses various hydrogel materials used to prepare biosensors, including natural polymers, synthetic polymers, and conductive materials.

2. Hydrogel-Based Biosensors

Hydrogels are widely employed in biosensors owing to their high water content, biocompatibility, and responsiveness to environmental changes. Hydrogels can be used as biosensor matrices to immobilize transducers, biomolecules, or responsive components. Biosensors' three primary types of hydrogels are synthetic, natural, and hybrid/composite. The applications of hydrogel polymers in biosensing technologies, along with their origins, are summarized in Table 1 [9–42], Table 2 [43–79], and Table 3 [80–118]. In this study, as presented in Table 4, the advantages and disadvantages of natural, synthetic, and composite/hybrid hydrogels in biosensors are compared, and their key characteristics in biomedical applications are summarized.

Table 1: Natural hydrogels used in biosensors.

Name	Properties	Applications in Biosensing
Alginate	Biocompatibility, ease of gelation, and retaining ability [9].	• Electrochemiluminescence (ECL) based biosensor [10]. • For the early detection of liver cancer using a biosensor encapsulated in an alginate polymer film thin layer [11]. • Encapsulating Zinc Phthalocyanine Dye-Sensitized Photoelectrochemical Biosensor for Hg^{2+} detection [12]. • Alginate membranes that can be electrodeposited for enzyme-based sensors [13].

Table 1: *Cont.*

Name	Properties	Applications in Biosensing
Chitosan	Antibacterial effect, biocompatibility, biodegradability, non-toxicity, and high humidity absorption [14].	- Biosensors that use electricity and chitosan to spot lung cancer [15]. - Sensors made with chitosan and nano-composite-based biological particles to find signs of disease early and detect biomarkers [16]. - A device that uses chitosan-covered ZnS quantum dots to sense heavy metal ions [17].
Agarose	Reversible thermo-gelling behavior, high biocompatibility, structural modularity, and biodegradability [18].	- In an immobilization matrix model for a microbial biosensor [19]. - Development of a microfluidics biosensor [20]. - Electrochemical biosensor for catechol [21]. - Reagent-free colorimetric biosensing platform [22].
Gelatin	Water retention, controllable porosity, soft mechanical strength, and stimulus responsiveness [23].	- As a Matrix for immobilized biorecognition material [24]. - In electrochemical DNA biosensing [25]. - In a surface plasmon resonance-based biosensor [26]. - In preparation for the urea biosensor [27].
Pectin	Biodegradability, easy gelling ability, and simple control of pectin-based biomaterial [28].	- In an optical biosensor with immobilized lipase enzymes [29]. - In an amperometric glucose biosensor [30]. - In biosensing detection of hemoglobin [31]. - An optical pH sensor for fish freshness monitoring [32].
Hyaluronic Acid	Biodegradability, biocompatibility, nontoxicity, and non-immunogenicity [33].	- High-performance supercapacitor and antifouling biosensor [34]. - In dual-responsive electrochemical biosensors [35]. - In sensitive non-enzymatic glucose sensor [36]. - In sensitive hyaluronidase biosensor based on target-responsive hydrogel [37].
Dextran	Antifouling abilities, high water retention, and flexible structure [38].	- In fluorescence-based glucose biosensors [39]. - In prostate-specific antigen biosensors [40]. - In optical biosensor applications [41]. - SPRi sensor for small-molecule drug detection [42].

Table 2: Synthetic hydrogels used in biosensors.

Name	Properties	Applications in Biosensing
Polyethylene Glycol (PEG)	Biocompatibility, high hydrophilicity [43].	- Microfabricated protein-containing poly (ethylene glycol) hydrogel arrays for biosensing [44]. - As biosensor coatings for the detection of collagenase [45]. - In Fluorescence-Based Glucose Biosensor [46]. - In the development of electrochemical biosensors [47].

Table 2: *Cont.*

Name	Properties	Applications in Biosensing
Polyacrylamide (PAM)	Water solubility, high sensitivity, compression strength, and easy fabrication [48,49].	- An amperometric biosensor based on human cytochrome [50]. - In recyclability for sensitive and colorimetric detection of penicillin G [51]. - In an electrochemical aptasensor for detecting Aflatoxin B2 [52]. - An enzymatic electrochemical biosensor for urea [53].
Polyvinyl Alcohol (PVA)	Flexibility, biocompatibility, adhesion, self-healing, and frost resistance [54].	- In multifunctional self-healing biosensors [55]. - As wearable biosensors in sweat detection [56]. - In a novel electrochemical biosensor for sensitive detection of glucose [57]. - In the ultrasensitive detection of folic acid by fluorescence quenching [58].
Poly(2-hydroxyethyl methacrylate) (pHEMA)	Biocompatibility, softness, and transparency [59].	- In wearable contact lens biosensing [60]. - In a quartz crystal microbalance sensor [61]. - In improving the biocompatibility of biosensors [62]. - In the construction of clinically important biosensors [63].
Poly(N-isopropylacrylamide) (PNIPAM)	Stimulus responsiveness, solar water evaporation [64].	- Microgel-based optical devices for sensing and biosensing [65]. - Temperature sensor applications [66]. - Highly efficient and recyclable catalysts for biosensing [67]. - Electrochemical temperature-controlled switch for a nonenzymatic biosensor [68].
Poly(methacrylic acid) (PMAA)	Biocompatibility, pH-Responsiveness, and mechanical properties. [69,70]	- QCM biosensor for selective determination [71]. - On-chip detection of protease biomarkers [72]. - Reflectance spectroscopy-based biosensors [73]. - pH-responsive biomedical materials [74].
Poly(vinylpyrrolidone) (PVP) hydrogel.	Mechanical properties, elastic properties, and non-toxicity [75].	- Wearable electronic biosensors [76]. - Ultra-Sensitive MicroRNA Biosensor [77]. - Hexavalent chromium sensing platform [78]. - Integrated microneedle biosensor [79].

Table 3: Composite hydrogels used in biosensors.

Name	Properties	Applications
Graphene Oxide (GO)	High surface area, hydrophilicity, and biocompatibility [80].	- Fluorescent biosensor for antibiotic detection [81]. - Novel nitrite biosensor [82]. - Mechanically and thermally sensitive skin-like bioelectronics [83]. - Flexible glucose biosensor [84].

Table 3: *Cont.*

Name	Properties	Applications
Carbon Nanotube (CNT)	Pore structure, high conductivity, electrochemical stability, one-dimensional structure, low mass density, high mechanical strength, and high specific area [85].	- Enhancing the detection sensitivity of electrochemical sensors [86]. - Making target-specific probes for biosensors [87]. - In an amperometric cholesterol biosensor [88]. - Bioanode for enhanced microbial electrocatalysis [89].
Silica Nanoparticle	Physical, mechanical, thermal properties, and chemical stability [90].	- In a glucose biosensor [91]. - Microarray biosensor for metal-enhanced fluorescence detection [92]. - In environmental monitoring [93]. - DNA-based biosensors and diagnostics [94].
Gold Nanoparticle (AuNP)	Plasmonic effect, bio-functionalization, and large surface area [95,96].	- Colorimetric detection of lead (II) and uranyl ions [97]. - LSPR-based biosensors [98]. - Acetylcholinesterase-based biosensor for carbamate detection [99]. - Dual DNA biosensor [100].
Magnetic Nanoparticle (MNP)	Stimuli responsiveness, biodegradability, and biocompatibility [101,102].	- Amperometric biosensor design [103]. - Low-field nuclear magnetic sensing [104]. - Biosensor for ferrogel detection [105]. - Electrochemical biosensing [106].
Quantum Dots (QD)	Bioconjugation, photoluminescence, and optical properties [107,108].	- In multimodal biosensing [109]. - Fluorescence-based sensing platform [110]. - Electrochemiluminescence immunosensor [111]. - Enzyme-based optical biosensor [112].
Conductive Polymer	Stimuli responsiveness, biocompatibility, and controllable electronic properties [113,114].	- In doping engineering [115]. - Electrochemical biosensors [116]. - In biosensing functions of copious biological species [117]. - In noninvasive, real-time measurements [118].

Table 4: Comparative summary of natural, synthetic, and composite hydrogels in biosensors.

Hydrogel Type	Advantage	Limitations
Natural hydrogels (such as alginate, chitosan, gelatin, etc.) [9,14,18]	Good biocompatibility, biodegradable, similar to the cell and tissue environment.	Low mechanical strength, large batch variability, and limited stability.
Synthetic hydrogels (such as PEG, PAM, PVA, PNIPAM, etc.) [48,49]	Highly controllable performance, excellent mechanical strength, and easily functionalizable.	Poor biodegradability may present biocompatibility issues.
Composite/hybrid hydrogels (such as GO, CNT, AuNP, MNP, and other composite systems) [80,85,96]	Combining the advantages of natural and synthetic materials, diverse functionalities (conductivity, optical properties, etc.), and being suitable for intelligent and multimodal sensing.	Complex preparation, high cost, potential long-term stability, and safety concerns.

3. Design and Fabrication of Hydrogel-Based Biosensors

Hydrogels can respond to specific compounds, such as biomarkers or bioanalytes, present in their surrounding medium or material. Depending on the biomolecules or bioanalytes incorporated into hydrogels, these conjugated biomaterials can be readily tailored to respond to diverse biological conditions, offering significant potential for biosensor development [116]. Advanced fabrication techniques are employed to precisely control a hydrogel's structure, properties, and functionality in the development of biosensors, enabling the creation of complex architectures and finely tuned materials with enhanced sensor performance. These techniques are applied in biosensors as follows.

3.1. Photopolymerization

Photopolymerization is a stimulus-responsive technique that begins when visible or UV light interacts with light-sensitive compounds known as photoinitiators. These photoinitiators generate free radicals, which initiate polymerization, resulting in the formation of crosslinked hydrogels from monomers or macromers (Figure 1) [119]. Three main classes of photoinitiation exist based on their mechanism: photocleavage reactions, hydrogen abstraction, and cationic reactions [120], providing a plethora of options for traditional polymerization methods to be explored in the field of photopolymerization, both in space and time [121].

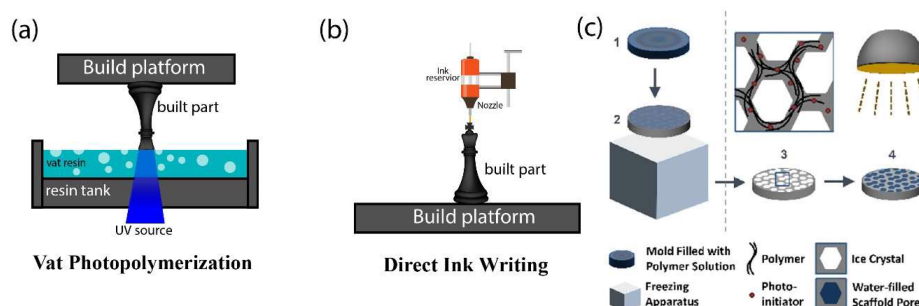


Figure 1: An illustration of the most popular hydrogel-based 3D printing methods: (a) vat photopolymerization (stereolithography (SLA/DLP) (adapted from [122] under (CC BY) license), (b) direct ink writing (DIW) (adapted from [122] under (CC BY) license), (c) photopolymerization of frozen polyethylene glycol (PEG) solutions with photoinitiators to form porous hydrogels, (adapted with permission from [123]).

3.2. Electrospinning

Electrospinning is a versatile technique that combines elements of electrospray and spinning. In this process, an electric field is applied to a fluid droplet, which serves as one of the electrodes. The electric field deforms the droplet, eventually ejecting a charged jet from the tip of the resulting cone. This jet travels toward the counter electrode, ultimately forming fine,

continuous fibers [124]. Hydrogels engineered with electrospinning techniques show excellent performance in biomedical applications and biosensors. The polymeric micro/nanofibers produced by these techniques can mimic the geometries of natural ECM by drawing micro/nanofibers from polymer precursors using electrical forces, followed by structural stabilization (Figure 2) [125,126].

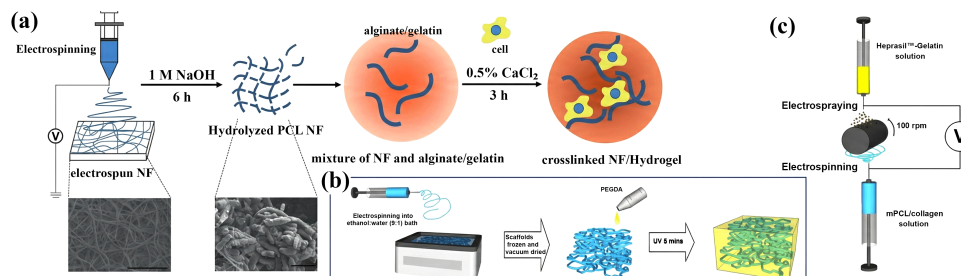


Figure 2: Schematic of the (a) presentation of preparing NF/hydrogel encapsulating cells by the electrospinning method, (adapted with permission from [127]) and (b) showing the assembly of electrospun poly(ε-caprolactone) nanofibers and poly(ethylene glycol)-diacrylate hydrogel to create a fully encapsulated and injectable composite scaffold (adapted with permission from [128]), and (c) representation comprising electrospun fibers coupled with hydrogels. (adapted with permission from [128]).

3.3. 3D Printing and Microfabrication

3D printing, also known as additive manufacturing or rapid prototyping, is a versatile technology for fabricating three-dimensional objects layer by layer through the controlled deposition of ink materials, following a pre-defined digital model created using Computer-Aided Design (CAD) [129]. Compared to conventional formative and substrate-based technologies, which typically rely on molds, tooling, and machining, 3D printing offers greater versatility by enabling the fabrication of complex and intricate structures. It is widely regarded as the next industrial revolution, with significant contributions to the chemical, pharmaceutical, and biomedical fields [130]. A vital yet limiting part of the design and application of 3D printing is selecting suitable biomaterials for use as

inks. 3D printing techniques for biomedical applications can be mainly classified based on their working principles: (i) laser-based systems by photopolymerization pathway, (ii) nozzle-based systems through the extrusion of (pre)polymers, and (iii) printer-based systems by material and binder jetting (Figure 3) [131,132]. Dutta et al. [133] discussed biodegradable 3D-printed hydrogel scaffolds of alginate, gelatin, and cellulose nanocrystals in bone tissue engineering. These scaffolds enhance cell adhesion, proliferation, and osteogenic differentiation, thereby improving bone regeneration. The key properties of these scaffolds, including mechanical strength, biocompatibility, and mineralization efficiency, have been evaluated and indicate their potential as biomaterials for tissue engineering applications.

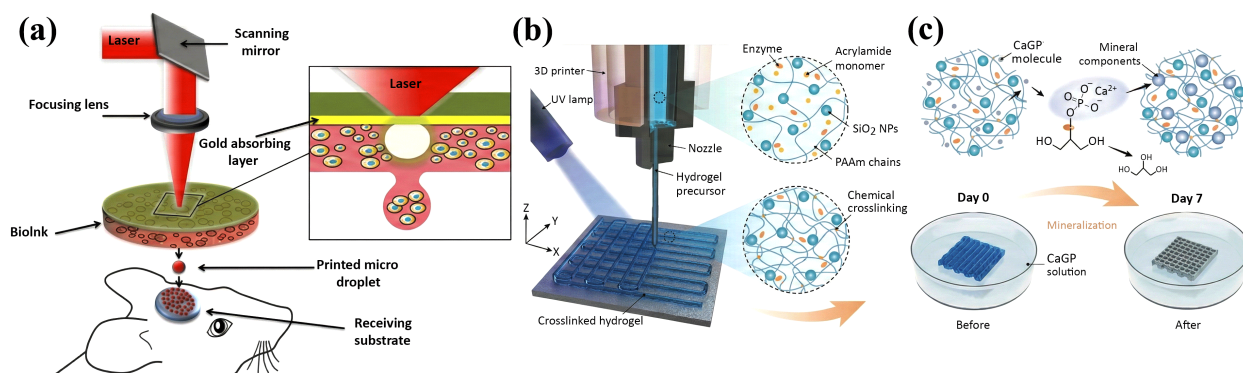


Figure 3: (a) Droplet deposition by laser-assisted 3D bioprinting process (adapted with permission from [132]). (b) Using an extrusion-based 3D printer, alkaline phosphatase (ALP)- loaded hydrogel inks were produced into 3D structures. The physical interaction between silica nanoparticles and PAAm polymer chains results in a physically cross-linked hydrogel that gels immediately after printing and can be fluidized by shear forces during ink extrusion. Induced covalent network creation with further UV curing results in the development of high-fidelity-shaped 3D hydrogel structures (adapted with permission from [134]), and (c) ALP enzyme catalyzes the dephosphorylation of calcium glycerophosphate (CaGP), which forms calcium phosphate ($\text{Ca}_3(\text{PO}_4)_2$) nanoparticles to harden the hydrogel substrates (adapted with permission from [134]).

Biosensors can be classified according to their signal transduction method, including optical, electrochemical, thermometric, piezoelectric, and magnetic techniques, among others [135]. Hydrogels' distinct physicochemical responsiveness enables them to actively participate in signal generation across various biosensor modalities. Analysts modify the hydrogel's refractive index and light-scattering properties, thereby changing the response of the optical biosensor. This allows them to be detected with high sensitivity using plasmon resonance, absorption, or reflection. In electrochemical systems, hydrogels directly affect conductivity and current responses by controlling how redox species diffuse and how easily ions can pass through. Mechanical biosensors succeed because they can alter shape and size, thereby creating stress and strain that

can be measured. Hydrogels exhibit viscoelastic properties and a high water content. This modifies how waves propagate and interact, enabling better acoustic sensing. Lastly, thermal biosensors transduce biochemical reactions into detectable temperature signals by exploiting variations in the heat capacity and phase transitions of hydrogels. These direct connections between transduction and hydrogel properties show that hydrogels can effectively serve as both structural scaffolds and biosensing enhancers.

Bio-electrochemical biosensors obtain information from living systems by measuring their electrical properties. The bio-electrochemical sections form the core of data modification. Electrochemical biosensors interface the biochemical recognition agent with an electrode where current, potential, or impedance is measured as a

result of the biochemical process [136]. Optical biosensors are essential for quantifying the amount of a substance in a bioassay, the rate at which it binds, and its molecular structure. Aimed at sorting and counting target analysts through transduction for quantitative bioassays, they have been employed for various optical phenomena, including reflection, absorption, fluorescence, and scattering-transmission and intensity [137]. The mechanical biosensor is an analytical method that may serve as a qualitative molecule finder. Mechanical biosensors convert biomolecular interactions into measurable mechanical responses, such as stress-induced deflections, shifts in resonance frequency, or cantilever bending. Recent developments include microfluidic-mechanical hybrids that enable real-time analysis of complex fluids without labeling, hydrogel-integrated mechanical biosensors that convert volume changes into measurable stress/strain signals, and nanocantilever-based devices that detect single-molecule binding events with very high sensitivity. These developments indicate that the field of biological mechanical sensing has matured into quantitative, sensitive, and, in some cases, clinically relevant detection beyond simple yes-or-no binary measurements [138]. Mechanically integrated biological sensing offers a new approach to measuring forces, displacements, and mass during cellular and subcellular processes. Mechanical biosensors are miniature cantilevers capable of detecting specific biomolecules. They can operate in either surface-stress or dynamic modes [139].

Acoustic sensors are an essential tool across numerous scientific and technological domains, as they convert sound waves into electric signals [140]. Sensors, which are a category of transducers, typically measure a physical or chemical characteristic of an environment (e.g., temperature, pressure, biological/chemical concentration) and convert that measurement into an electrical, magnetic-optic, or acoustic signal. Biosensors convert biological data into numerical values [141]. Acoustic wave devices can serve as sensors since they exhibit sensitivity to electrical, chemical, mechanical, or optical perturbations on their surfaces [142]. These sensors are used to detect minute traces of biomolecules by binding to biomarkers for pathogen and virus detection, as well as for early-stage cancer diagnosis [143]. Thermal biosensors are a type of biosensing technology that measures heat energy information released or absorbed during biochemical reactions using quantitative methods. They enable quantitative monitoring of metabolic activity and enzymatic processes by converting the minute heat changes produced during biochemical reactions into quantifiable signals.

Recent advancements, including hydrogel-based microcalorimetric platforms for sensitive detection of mi-

crobial growth and nanomaterial-enhanced thermal transducers that markedly improve sensitivity and response time, have helped transition this modality from theoretical demonstration to practical biomedical applications [144]. This biosensing device detects temperature changes associated with biological processes and has proven applications in monitoring microbial growth. Additional fabrication techniques for hydrogel-based biosensors include physical cross-linking and self-assembly via ionic or hydrogen bonding to produce biocompatible, reversible matrices; chemical cross-linking (e.g., with glutaraldehyde or genipin) to form stable covalent networks; and freeze-thaw cycling, particularly for PVA hydrogels, to enhance mechanical strength. Sol-gel processing can be used to incorporate nanomaterials for optical and electrochemical sensing. For lab-on-a-chip applications, microfluidic-assisted fabrication enables precise control over the size and geometry of hydrogel droplets. These methods can synergize with photopolymerization, electrospinning, or 3D printing to complement the toolbox of strategies available for tuning hydrogel properties and biosensor activity [145].

4. Biomedical Applications

The intensive exploration of the chemical, mechanical, and biocompatible properties of stimuli-sensitive hydrogels has led to limitless applications in biological signal sensing across various medical/biological disciplines. Although accuracy is a significant problem, monitoring physiochemical changes using biosensors has facilitated the way towards early disease detection and its management [146]. Use of hydrogels in the development of innovative biosensors has expanded their utility to a variety of biomedical areas [147], as described below:

4.1. Clinical Diagnostics

In recent years, hydrogel-based biosensing devices have emerged as valuable and sensitive tools for clinical diagnostics, owing to their high sensitivity, biocompatibility, and facile functionalization with other molecules. Commercial glucose monitoring systems are limited by glucose's inability to diffuse deeply into the thick sensing layer, the lack of control over glucose oxidase leakage, and their susceptibility to mechanical damage. In the meantime, self-healing enzyme-functionalized hydrogel-integrated biosensors based on chitosan and oxidized dextran may also be applied for glucose determination in electrochemical or optical mode in an OSN assay, such as for glucose management in diabetes. The high sensitivity, biocompatibility, and flexibility of hydrogel biosen-

sors have rendered them invaluable tools with great potential for clinical diagnostics. For example, mechanical instability, enzyme leakage, and glucose penetration into thick sensing coatings are problems for commercial glucose monitoring systems. As a promising polymer material, hyaluronic acid hydrogels have demonstrated significant potential for biosensor applications due to their tunable sensitivity, low cost, and excellent biocompatibility, particularly in areas such as continuous glucose monitoring and real-time health assessment. These problems have been addressed by incorporating self-healing matrices and by improving the analysis of diffusion pathways with hydrogel-based designs [148,149].

Early cancer diagnosis is critical for effective disease management, yet current methods remain suboptimal. New biomaterials, including hydrogels, have promising potential for biosensor development in cancer detection [150]. Indeed, the development of anti-biofouling hydrogel-based biosensors for the early non-invasive detection of oral cancer in body fluids (such as saliva) is becoming increasingly popular [151]. Comprising functional hydrogels, these biosensors are combined with electrochemical or optical measurement techniques to detect biomarkers, including tumor necrosis factor- α (TNF- α), a key biomarker for oral cancer detection (Figure 4). Hydrogel biosensors have also been demonstrated in recent research for early cancer detection. Tumor necrosis factor- α (TNF- α), an essential inflammatory biomarker for oral cancer, has been successfully detected in saliva using electrochemical hydrogel-based biosensors with a limit of detection (LOD) of ~ 1 pg/mL, which is lower than the physiological levels required for clinical screening.

Furthermore, hyaluronic acid hydrogel biosensors have been shown to detect hyaluronidase activity in serum samples with sensitivity as low as sub-ng/mL, demonstrating their utility for non-invasive cancer diagnosis. These examples show that hydrogel matrices are not only ideal microenvironments for the immobilization of biomolecules but also improve analytical accessibility by incorporating readily adjustable porosity, which, along with swelling, results in detection that is similar or even better than that of traditional biosensing platforms. However, a significant challenge in translating these advances from the laboratory to medical practice is biofouling (particularly in complex biofluids such as serum and saliva) that persists during technology deployment at the bedside. Transport of proteins to sensor surfaces, such as protein adsorption, non-specific binding, and enzymatic digestion, is often a limiting factor in sensor performance, leading to significant reductions in lifetime, sensitivity, and reproducibility. For example, the antifouling strategies reported include PEGylated hydrogels, zwitterion hydrogel

coating, and nanocomposite hydrogel systems to mitigate these issues. These methods of non-specific interaction inhibition lack biological compatibility. It will be essential to continue advancing the integration of these antifouling strategies to further bridge the gap between clinical translation and optimal performance in tissue models [152].

4.2. Drug Delivery and Monitoring

The system can regulate drug release rates, dosages, and site-specific delivery of agents to achieve optimal therapeutic effects [153,154]. TDM (Therapeutic Drug Monitoring) has been used to assess whether drug concentrations are within an optimal therapeutic range [155]. Over the past few years, hydrogels have been marketed as one of the most promising and tunable materials in these domains. Glucose-responsive hydrogel biosensors, including glucose oxidase-integrated hydrogels (GOx), can sense glucose and release insulin via hysteresis. Release of the drug leads to an observable biochemical or physical change in hydrogel-based drug delivery systems via stimuli-responsive sensing. Glucose-responsive hydrogels that conjugate glucose oxidase (GOx) can detect high glucose levels via an oxidation reaction that produces hydrogen peroxide and gluconic acid. The resulting redox shift or local pH drop triggers hydrogel swelling and/or electrochemical signals that can be linked to insulin release [156,157].

Tumors sometimes exhibit an acidic microenvironment (TME), making pH-sensitive hydrogels particularly effective under certain conditions. These hydrogels can release drugs in a controlled manner when exposed to the acidic conditions of the tumor site, thereby reducing side effects in cancer treatment [158]. pH-sensitive hydrogels take advantage of the acidic tumor microenvironment by altering their charge density, swelling behavior, and drug diffusion rate through the ionization of carboxyl or amine side groups. These changes can be observed optically or electrochemically. When bacteria secrete enzymes (such as proteases) or antigenic byproducts, hydrogel biosensors respond. Enzymatic cleavage of cross-links releases incorporated dyes or alters conductivity, which signals changes in the microenvironment caused by infection. Particular hydrogel-based biosensors respond to bacteria-induced micro-environmental changes (pH, enzymes, and antigens). In addition to targeting direct or indirect bacterial surface receptors, hydrogel biosensors can be employed for the early detection of bacterial infections in point-of-care monitoring. Additionally, by utilizing changes in fluorescence or color intensity, integrated reporter molecules, such as fluorophores or quantum dots, enable real-time visualization of drug release ki-

netics. These hydrogel systems enable simultaneous therapeutic drug monitoring (TDM) and controlled drug release by translating biochemical stimuli into measurable physical or optical signals [159].

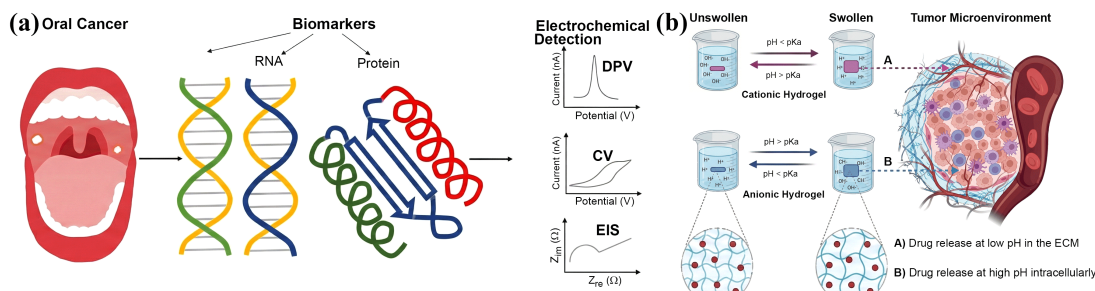


Figure 4: Schematic diagram of the (a) process of detecting oral cancer using an electrochemical biosensor (adapted from [152] under (CC BY) license) and (b) pH-sensitive hydrogel swelling. Hydrogel swelling occurs through the ionization of side-chain groups, which increases the hydrophilicity of the polymer chains and enhances electrostatic repulsion between them. ECM, extracellular matrix, hydrogen ion H⁺, hydroxyl ion OH⁻. Red circles represent drugs loaded in the hydrogels (adapted from [160] under (CC BY) license).

4.3. Tissue Engineering and Regenerative Medicine

Hydrogels are increasingly employed as artificial extracellular matrices to better replicate the physiological and pathological features of human tissues [161]. 3D bio-printed hydrogel-based tissue models are emerging as an approach due to their ability to mimic native ECM (Extracellular Matrix) and to encapsulate cells. Hydrogel-based biosensors enable real-time monitoring of cellular and microenvironmental processes and have become indispensable tools in tissue engineering and regenerative medicine. The addition of bio-sensing capabilities to hydrogel scaffolds enables dynamic feedback that can direct tissue regeneration and simulate the extracellular matrix (ECM) [162,163]. Hydrogels can more closely mimic the mechanical and biochemical characteristics of human tissues due to their high water content, softness, reticulated structure, and, importantly, their molecular diffusion properties, which resemble those of native tissues [164,165]. For this reason, hydrogel-based biosensing tools are now being used to regenerate bone, cartilage, skin, and neural tissues widely (Figure 5) [166]. Additionally, 3D-printed electrically conductive hydrogels are utilized in cardiac tissue engineering, which seeks to repair cardiovascular damage. The low immunogenicity of the hydrogels in vivo may be beneficial for cardiac tissue engineering (Figure 6). Hydrogels with integrated biosensors enable continuous monitoring of pH, oxygen concentrations, and enzymatic activity at the wound site during skin and wound healing. To hasten healing, this real-time feedback can help optimize therapeutic interventions, such as electrical stimulation or controlled drug release. Intelligent hydrogel biosensors integrated into organ-on-a-chip plat-

forms allow physiological simulation and tissue response monitoring, supporting transplantation research and drug screening applications [167–169].

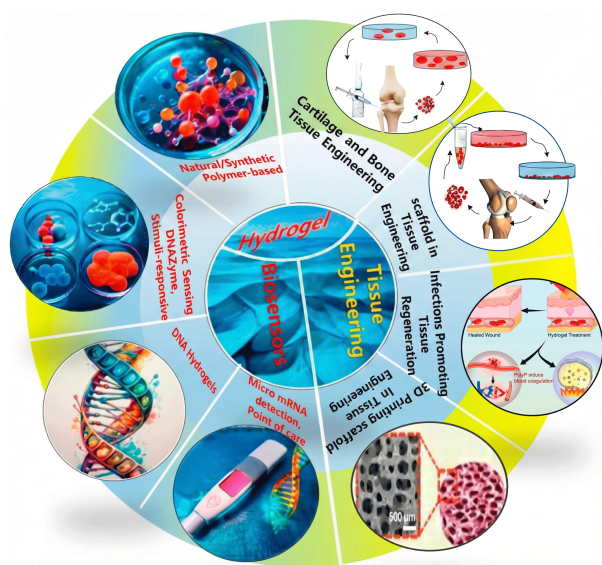


Figure 5: Schematic showing different hydrogel biosensor designs and tissue engineering applications, and their respective functions (adapted from [166] under (CC BY) license).

Hydrogel-based biosensors hold great potential for applications in neurodegenerative disorders (Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS)). Hydrogel-biosensor composites can detect alkaline phosphatase (ALP) activity and calcium ion deposition, making them valuable tools for bone tissue engineering. Inflammatory markers such as TNF- α and other cytokines are critical indicators of tissue integra-

tion and repair. Biosensor-embedded hydrogels have been used to detect them in cartilage regeneration. Cellulose and its derivatives-based biosensors show great promise for applications in sensing technology due to their renewability, biocompatibility, and chemical tunability. Similarly, conductive hydrogel-based biosensors in neural tissue engineering can monitor neurotransmitter activity and

record electrical impulses, aiding the evaluation of neural network reconstruction and functional recovery [170–172]. These biosensing tools based on hydrogels also have regenerative medicinal implications due to their uniquely tailored properties, including wound healing [173], skin regeneration (skin grafting) [174], and organ regeneration and transplantation [175].

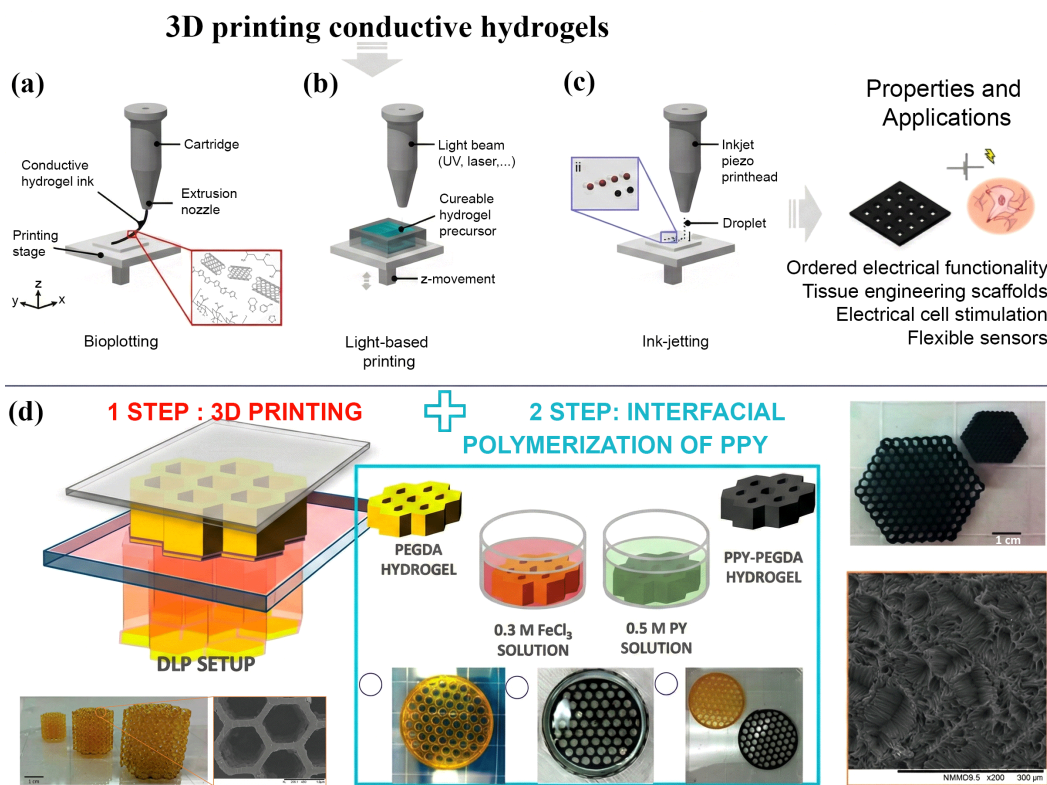


Figure 6: 3D printing technologies for processing conductive hydrogels. (a) Bioplotting (b) Light-based photo printing (c) Simultaneous deposition inkjet printing, (Adapted with permission from [167]) (d) Methyl orange (MO), the dopant of polypyrrole (PPy), and phenyl bis (2,4,6-trimethyl benzoyl) phosphine oxide, the photo initiator (PI), were used to print the PEGDA scaffold by DLP. The construct was printed and then submerged in a FeCl_3 solution to initiate the oxidative polymerization of pyrrole (Py). This created in situ polypyrrole within the hydrogel matrix, increasing its electrical conductivity (Adapted with permission from [168]).

4.4. Wearable and Implantable Devices

Applications of micro-biosensing devices in linking technology with personalized medicine are rapidly expanding, and the integration of hydrogels into these devices has introduced a novel approach in the field [176]. Despite the challenges of being an all-in-one sensor, hydrogel-fused devices that integrate long-term biological functions, multimodal responsiveness, and therapeutic capabilities have attracted growing interest as wearable and implantable devices [177]. Although wearable and implantable hydrogel-based devices have considerable potential, several significant obstacles stand in the way of their clinical translation. Hydrogels are suscep-

tible to degradation, structural fatigue, and biofouling from protein adsorption or fibrotic encapsulation, all of which can impair signal accuracy, making long-term in vivo stability a major challenge. As miniaturized systems must guarantee safe, continuous operation without heat generation or signal loss through tissue, where attenuation and scattering can reduce fidelity, dependable wireless power and data transmission are additional constraints.

Since chronic implantation frequently causes inflammation, immunological reactions, or mechanical mismatches with host tissue, maintaining proper biocompatibility is challenging after short-term tolerance. Innovations such as mechanically reinforced composites,

immune-responsive materials, antifouling hydrogel coatings, and low-power wireless communication techniques are necessary to overcome these obstacles and ensure reliable, long-lasting, and clinically feasible device performance. Various wearable devices have been designed to implement hydrogel-integrated biosensors, including hydrogel smart patches [178], electronic tattoos (e-Tattoos) [179], hydrogel foot insoles [180], and hydrogel neckbands [181]. Moreover, implantable devices, including wearables, are being developed to support the human body through real-time monitoring, wireless connectivity, and minimally invasive designs. Examples include hydrogel-based glucose monitors for continuous glucose monitoring [182], drug delivery implants [183], neural implants [184], hydrogel ocular implants [185], and wound healing implants [186].

5. Conclusions and Outlook

This paper provides a systematic summary of the various hydrogel properties and their applications in biosensors, including strategies for hydrogel design and fabrication. In the future, researchers envision that hydrogels will function intelligently and autonomously according to environmental changes. Over the last century, the understanding and engineering of the human body have advanced through interdisciplinary efforts in modern medicine, biology, and biomedical engineering. In particular, the double-crosslinked polymer hydrogel composite exhibits excellent mechanical and self-healing properties. It has enormous potential in the biomedical field, especially in tissue engineering and wound dressings. At the same time, polymer hydrogel complexes also have significant application value for the delivery of hydrophobic drugs or for co-delivery. As hydrogels continue to develop, their biosensor applications will become increasingly widespread while continually adapting to biomedical needs. Future research on hydrogel-based biosensors is expected to provide more inspiration and support for the development and innovation of related fields.

The most promising candidates for near-term commercialization in biosensing are synthetic and composite hydrogels, particularly PEG-based systems for their tunable chemistry, and hybrid nanocomposite hydrogels (e.g., incorporating graphene oxide, gold nanoparticles, or conductive polymers) for their multifunctionality. This is due to their combination of stability, scalability, and biocompatibility. Key challenges include scalable, reproducible manufacturing of clinical-grade devices, assurance of long-term in vivo stability and antifouling performance, and enabling reliable multi-analytic detection un-

der intricate physiological conditions. The development of intelligent self-healing and stimuli-responsive materials, the use of modern computational approaches such as machine learning for predictive hydrogel design, and the integration with flexible and wireless bioelectronics for real-time monitoring are therefore likely to be key drivers of future advancements. Interdisciplinary strategies to address these restrictions may advance hydrogel-based biosensors from the laboratory-prototype stage toward practical clinical hemostatic control, personalized drugs, and diagnostics. Hydrogel-based biosensors are highly attractive due to their biocompatibility, flexibility, and tunability. However, many problems with such an approach remain unsolved, including long-term stability, fabrication variation, and electronics integration. In the future, efficient tissue regeneration must be realized using smart hydrogel and composite scaffolds fabricated through advanced preparation technologies, such as three-dimensional printing, with large-scale production capacity and reproducibility ensured through multidisciplinary collaboration, to facilitate validation in clinical research. These strategies provide hydrogel biosensors with reliable and sensitive platforms for future biomedical applications, including treatments and therapeutic interventions.

List of Abbreviations

AD	Alzheimer's Disease
ALP	Alkaline Phosphatase
ALS	Amyotrophic Lateral Sclerosis
AuNP	Gold Nanoparticle
CAD	Computer-Aided Design
CaGP	Calcium Glycerophosphate
CNT	Carbon Nanotube
DLP	Digital Light Processing
DIW	Direct Ink Writing
ECL	Electrochemiluminescence
ECM	Extracellular Matrix
GelMA	Gelatin Methacrylate
GO	Graphene Oxide
GOx	Glucose Oxidase
HSA	Human Serum Albumin
LSPR	Localized Surface Plasmon Resonance
MNP	Magnetic Nanoparticle
NF	Nanofiber
PAAm	Polyacrylamide
PD	Parkinson's Disease
PEG	Polyethylene Glycol
PHEMA/pHEMA	Poly(2-hydroxyethyl methacrylate)
PNIPAM	Poly(N-isopropylacrylamide)
PMAA	Poly(methacrylic acid)

PVP	Polyvinylpyrrolidone
QD	Quantum Dot
QCM	Quartz Crystal Microbalance
SLA	Stereolithography
TDM	Therapeutic Drug Monitoring
TME	Tumor Microenvironment
TNF- α	Tumor Necrosis Factor- α

Author Contributions

Conceptualization, methodology, resources: H.S., B.D., and K.R.H.; Visualization, writing—original draft preparation: H.S. and B.D.; Writing—review and editing, supervision, project administration: K.R.H. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

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AI Declaration

The authors confirm that no AI tools were used to generate any content of this manuscript.

References

- [1] Grieshaber, D.; MacKenzie, R.; Vörös, J.; Reimhult, E. Electrochemical Biosensors—Sensor Principles and Architectures. *Sensors* **2008**, *8*, 1400–1458. [[CrossRef](#)]
- [2] Choi, J.S.; Sansoni, E.R.; Lovin, B.D.; Lindquist, N.R.; Phan, J.; Mayo, L.L.; Su, S.Y. Abscopal Effect Following Immunotherapy and Combined Stereotactic Body Radiation Therapy in Recurrent Metastatic Head and Neck Squamous Cell Carcinoma: A Report of Two Cases and Literature Review. *Ann. Otol. Rhinol. Laryngol.* **2020**, *129*, 517–522. [[CrossRef](#)] [[PubMed](#)]
- [3] Zadrán, S.; Standley, S.; Wong, K.; Otiniano, E.; Amighi, A.; Baudry, M. Fluorescence Resonance Energy Transfer (FRET)-Based Biosensors: Visualizing Cellular Dynamics and Bioenergetics. *Appl. Microbiol. Biotechnol.* **2012**, *96*, 895–902. [[CrossRef](#)] [[PubMed](#)]
- [4] Thévenot, D.R.; Toth, K.; Durst, R.A.; Wilson, G.S. Electrochemical Biosensors: Recommended Definitions and Classification. *Biosens. Bioelectron.* **2001**, *16*, 121–131. [[CrossRef](#)] [[PubMed](#)]
- [5] Pinelli, F.; Magagnin, L.; Rossi, F. Progress in Hydrogels for Sensing Applications: A Review. *Mater. Today Chem.* **2020**, *17*, 100317. [[CrossRef](#)]
- [6] Holtz, J.H.; Asher, S.A. Polymerized Colloidal Crystal Hydrogel Films as Intelligent Chemical Sensing Materials. *Nature* **1997**, *389*, 829–832. [[CrossRef](#)]
- [7] Herrmann, A.; Haag, R.; Schedler, U. Hydrogels and Their Role in Biosensing Applications. *Adv. Healthc. Mater.* **2021**, *10*, 2100062. [[CrossRef](#)]
- [8] Ding, F.; Gao, X.; Huang, X.; Ge, H.; Xie, M.; Qian, J.; Zhang, C. Polydopamine-Coated Nucleic Acid Nanogel for siRNA-Mediated Low-Temperature Photothermal Therapy. *Biomaterials* **2020**, *245*, 119976. [[CrossRef](#)]
- [9] Lee, K.Y.; Mooney, D.J. Alginate: Properties and Biomedical Applications. *Prog. Polym. Sci.* **2012**, *37*, 106–126. [[CrossRef](#)]
- [10] Ferraraccio, L.S.; Bertoncello, P. Electrochemiluminescence (ECL) Biosensor Based on Tris(2,2'-Bipyridyl)Ruthenium(II) with Glucose and Lactate Dehydrogenases Encapsulated within Alginate Hydrogels. *Bioelectrochemistry* **2023**, *150*, 108365. [[CrossRef](#)]
- [11] Attia, M.S.; Mohamed, A.A.; El-Saady, M.M.; Abou-Omar, M.N.; Afify, H.G.; Amin, T.A.; Mohy-Eldin, M.S. A New Method for Early Diagnosis of Liver Cancer Using a Biosensor Embedded in an Alginate Polymer Thin Film. *J. Mater. Chem. C* **2022**, *10*, 6464–6472. [[CrossRef](#)]
- [12] Yang, X.; Zhang, M.; Chen, Z.; Bu, Y.; Gao, X.; Sui, Y.; Yu, Y. Sodium Alginate Micelle-Encapsulating Zinc Phthalocyanine Dye-Sensitized Photoelectrochemical Biosensor with CdS as the Photoelectric Material for Hg²⁺ Detection. *ACS Appl. Mater. Interfaces* **2021**, *13*, 16828–16836. [[CrossRef](#)]
- [13] Márquez, A.; Jiménez-Jorquera, C.; Domínguez, C.; Muñoz-Berbel, X. Electrodepositable Alginate Membranes for Enzymatic Sensors: An Amperometric Glucose Biosensor for Whole Blood Analysis. *Biosens. Bioelectron.* **2017**, *97*, 136–142. [[CrossRef](#)]
- [14] Aranaz, I.; Mengibar, M.; Harris, R.; Paños, I.; Miralles, B.; Acosta, N.; Heras, Á. Functional Characterization of Chitin and Chitosan. *Curr. Chem. Biol.* **2009**, *3*, 203–230. [[View Online](#)]
- [15] Saputra, H.A.; Ashari, A.; Karim, M.M.; Sahin, M.A.Z.; Jannath, K.A. Chitosan-Based Electrochemical Biosensors for Lung Cancer Detection: A Mini-Review. *Anal. Chem. Lett.* **2023**, *13*, 337–354. [[CrossRef](#)]
- [16] Gupta, R.; Goddard, N.J. A Study of Diffraction-Based Chitosan Leaky Waveguide (LW) Biosensors. *Analyst* **2021**, *146*, 4964–4971. [[CrossRef](#)] [[PubMed](#)]

- [17] Borgohain, R.; Boruah, P.K.; Baruah, S. Heavy-Metal Ion Sensor Using Chitosan Capped ZnS Quantum Dots. *Sens. Actuators B Chem.* **2016**, *226*, 534–539. [[CrossRef](#)]
- [18] Yazdi, M.K.; Taghizadeh, A.; Taghizadeh, M.; Stadler, F.J.; Farokhi, M.; Mottaghitalab, F.; Mozafari, M. Agarose-Based Biomaterials for Advanced Drug Delivery. *J. Control. Release* **2020**, *326*, 523–543. [[CrossRef](#)] [[PubMed](#)]
- [19] Perneti, M.; Poncelet, D.; Thouand, G.; Annesini, M.C.; Merli, C. Characterization of Agarose as Immobilization Matrix Model for a Microbial Biosensor. *Hem. Ind.* **2003**, *57*, 600–604. [[View Online](#)]
- [20] Buffi, N.; Merulla, D.; Beutier, J.; Barbaud, F.; Begah, S.; Van Lintel, H.; van der Meer, J.R. Development of a Microfluidics Biosensor for Agarose-Bead Immobilized *Escherichia coli* Bioreporter Cells for Arsenite Detection in Aqueous Samples. *Lab Chip* **2011**, *11*, 2369–2377. [[CrossRef](#)]
- [21] Tembe, S.; Inamdar, S.; Haram, S.; Karve, M.; D'Souza, S.F. Electrochemical Biosensor for Catechol Using Agarose–Guar Gum Entrapped Tyrosinase. *J. Biotechnol.* **2007**, *128*, 80–85. [[CrossRef](#)]
- [22] Hur, J.; Park, H.G.; Kim, M.I. Reagentless Colorimetric Biosensing Platform Based on Nanoceria within an Agarose Gel Matrix. *Biosens. Bioelectron.* **2017**, *93*, 226–233. [[CrossRef](#)]
- [23] Mushtaq, F.; Raza, Z.A.; Batool, S.R.; Zahid, M.; Onder, O.C.; Rafique, A.; Nazeer, M.A. Preparation, Properties, and Applications of Gelatin-Based Hydrogels (GHs) in the Environmental, Technological, and Biomedical Sectors. *Int. J. Biol. Macromol.* **2022**, *218*, 601–633. [[CrossRef](#)]
- [24] Guan, Y.; Huang, Y.; Li, T. Applications of Gelatin in Biosensors: Recent Trends and Progress. *Biosensors* **2022**, *12*, 670. [[CrossRef](#)]
- [25] Topkaya, S.N. Gelatin Methacrylate (GelMA) Mediated Electrochemical DNA Biosensor for DNA Hybridization. *Biosens. Bioelectron.* **2015**, *64*, 456–461. [[CrossRef](#)]
- [26] Wardani, D.P.; Arifin, M.; Suharyadi, E.; Abraha, K. Quantitative Detection of Bovine and Porcine Gelatin Difference Using Surface Plasmon Resonance Based Biosensor. *Opt. Sens.* **2015**, *9506*, 187–194. [[CrossRef](#)]
- [27] Srivastava, P.K.; Kayastha, A.M.; Srinivasan. Characterization of Gelatin-Immobilized Pigeonpea Urease and Preparation of a New Urea Biosensor. *Biotechnol. Appl. Biochem.* **2001**, *34*, 55–62. [[CrossRef](#)] [[PubMed](#)]
- [28] Eivazzadeh-Keihan, R.; Noruzi, E.B.; Aliabadi, H.A.M.; Sheikholeslami, S.; Akbarzadeh, A.R.; Hashemi, S.M.; Esmaeili, M.S. Recent Advances on Biomedical Applications of Pectin-Containing Biomaterials. *Int. J. Biol. Macromol.* **2022**, *217*, 1–18. [[CrossRef](#)]
- [29] Tadesse, M.; Liu, Y. Recent Advances in Enzyme Immobilization: The Role of Artificial Intelligence, Novel Nanomaterials, and Dynamic Carrier Systems. *Catalysts* **2025**, *15*, 571. [[CrossRef](#)]
- [30] Sungur, S.; Günendi, G. A New Amperometric Glucose Biosensor Based on Pectin Coating. *Polym.-Plast. Technol. Eng.* **2006**, *45*, 527–531. [[CrossRef](#)]
- [31] Lakouraj, M.M.; Alipour, A.; NajafiRoudbari, M.; Ojani, R. Fabrication of a Nanocomposite Based on Pectin/Polyaniline/Graphene Oxide as Novel Electrically Conductive Biomaterial for Biosensing Detection of Hemoglobin. *Mod. Approaches Mater. Sci.* **2020**, *2*, 295–303. [[CrossRef](#)]
- [32] Hasanah, U.; Setyowati, M.; Efendi, R.; Muslem, M.; Md Sani, N.D.; Safitri, E.; Idroes, R. Preparation and Characterization of a Pectin Membrane-Based Optical pH Sensor for Fish Freshness Monitoring. *Biosensors* **2019**, *9*, 60. [[CrossRef](#)]
- [33] Sudha, P.N.; Rose, M.H. Beneficial Effects of Hyaluronic Acid. *Adv. Food Nutr. Res.* **2014**, *72*, 137–176. [[CrossRef](#)]
- [34] Liu, N.; Ma, Y.; Xu, Z.; Guo, Y.; Luo, X. High-Performance Supercapacitor and Antifouling Biosensor Based on Conducting Polyaniline-Hyaluronic Acid Hydrogels. *J. Mater. Sci.* **2023**, *58*, 1171–1182. [[CrossRef](#)]
- [35] Sheikh, K.; Hossain, K.R.; Hossain, M.A.; Sagar, M.S.I.; Raju, M.R.H.; Haque, F. 3D Printed Ionic Liquids Based Hydrogels and Applications. *J. Ion. Liq.* **2024**, *4*, 100093. [[CrossRef](#)]
- [36] Aycan, D.; Karaca, F.; Alemdar, N. Development of Hyaluronic Acid-Based Electroconductive Hydrogel as a Sensitive Non-Enzymatic Glucose Sensor. *Mater. Today Commun.* **2023**, *35*, 105745. [[CrossRef](#)]
- [37] Li, Z.; Tang, C.; Huang, D.; Qin, W.; Luo, F.; Wang, J.; Lin, Z. Sensitive Hyaluronidase Biosensor Based on Target-Responsive Hydrogel Using Electronic Balance as Readout. *Anal. Chem.* **2019**, *91*, 11821–11826. [[CrossRef](#)]
- [38] Saftics, A.; Türk, B.; Sulyok, A.; Nagy, N.; Agócs, E.; Kalas, B.; Kurunczi, S. Dextran-Based Hydrogel Layers for Biosensors. In *Nanobiomaterial Engineering: Concepts and Their Applications in Biomedicine and Diagnostics*; Springer: Singapore, 2020; pp. 139–164. [[CrossRef](#)]
- [39] Russell, R.J.; Pishko, M.V.; Gefrides, C.C.; McShane, M.J.; Cote, G.L. A Fluorescence-Based Glucose Biosensor Using Concanavalin A and Dextran Encapsulated in a Poly(Ethylene Glycol) Hydrogel. *Anal. Chem.* **1999**, *71*, 3126–3132. [[CrossRef](#)] [[PubMed](#)]
- [40] Wang, Y.; Brunsen, A.; Jonas, U.; Dostalek, J.; Knoll, W. Prostate Specific Antigen Biosensor Based on Long Range Surface Plasmon-Enhanced Fluorescence Spectroscopy and Dextran Hydrogel Binding Matrix. *Anal. Chem.* **2009**, *81*, 9625–9632. [[CrossRef](#)] [[PubMed](#)]
- [41] Mateescu, A.; Wang, Y.; Dostalek, J.; Jonas, U. Thin Hydrogel Films for Optical Biosensor Applications. *Membranes* **2012**, *2*, 40–69. [[CrossRef](#)] [[PubMed](#)]

- [42] Li, S.; Yang, M.; Zhou, W.; Johnston, T.G.; Wang, R.; Zhu, J. Dextran Hydrogel Coated Surface Plasmon Resonance Imaging (SPRi) Sensor for Sensitive and Label-Free Detection of Small Molecule Drugs. *Appl. Surf. Sci.* **2015**, *355*, 570–576. [\[CrossRef\]](#)
- [43] Cui, M.; Song, Z.; Wu, Y.; Guo, B.; Fan, X.; Luo, X. A Highly Sensitive Biosensor for Tumor Marker Alpha Fetoprotein Based on Poly(Ethylene Glycol) Doped Conducting Polymer PEDOT. *Biosens. Bioelectron.* **2016**, *79*, 736–741. [\[CrossRef\]](#)
- [44] Yadavalli, V.K.; Koh, W.G.; Lazur, G.J.; Pishko, M.V. Microfabricated Protein-Containing Poly(Ethylene Glycol) Hydrogel Arrays for Biosensing. *Sens. Actuators B Chem.* **2004**, *97*, 290–297. [\[CrossRef\]](#)
- [45] Ahmad, N.; Colak, B.; Zhang, D.W.; Gibbs, M.J.; Watkinson, M.; Becer, C.R.; Krause, S. Peptide Cross-Linked Poly(Ethylene Glycol) Hydrogel Films as Biosensor Coatings for the Detection of Collagenase. *Sensors* **2019**, *19*, 1677. [\[CrossRef\]](#)
- [46] Alharthi, S.; Alharthi, S.; Madani, M.; Alkhalidi, H.; Aldaleeli, N.; Almarri, A.; Ghobashy, M.M. Advances and Challenges in Fluorescence-Based Biosensors for Biological and Chemical Detection. *ChemBioEng Rev.* **2025**, *12*, e70006. [\[CrossRef\]](#)
- [47] Pedrosa, V.A.; Yan, J.; Simonian, A.L.; Revzin, A. Micropatterned Nanocomposite Hydrogels for Biosensing Applications. *Electroanalysis* **2011**, *23*, 1142–1149. [\[CrossRef\]](#)
- [48] Godwin Uranta, K.; Rezaei-Gomari, S.; Russell, P.; Hamad, F. Studying the Effectiveness of Polyacrylamide (PAM) Application in Hydrocarbon Reservoirs at Different Operational Conditions. *Energies* **2018**, *11*, 2201. [\[CrossRef\]](#)
- [49] Hou, W.; Sheng, N.; Zhang, X.; Luan, Z.; Qi, P.; Lin, M.; Sui, K. Design of Injectable Agar/NaCl/Polyacrylamide Ionic Hydrogels for High Performance Strain Sensors. *Carbohydr. Polym.* **2019**, *211*, 322–328. [\[CrossRef\]](#) [\[PubMed\]](#)
- [50] Sun, P.; Wu, Y. An Amperometric Biosensor Based on Human Cytochrome P450 2C9 in Polyacrylamide Hydrogel Films for Bisphenol A Determination. *Sens. Actuators B Chem.* **2013**, *178*, 113–118. [\[CrossRef\]](#)
- [51] Wang, X.; Wang, Y.L.; Yu, H.R.; Lv, X.B.; Liang, T.; Cheng, C.J. A Penicillinase-Modified Poly(N-Isopropylacrylamide-co-Acrylamide) Smart Hydrogel Biosensor with Superior Recyclability for Sensitive and Colorimetric Detection of Penicillin G. *Biosens. Bioelectron.* **2024**, *254*, 116221. [\[CrossRef\]](#)
- [52] Geleta, G.S.; Zhao, Z.; Wang, Z. A Sensitive Electrochemical Aptasensor for Detection of Aflatoxin B2 Based on a Polyacrylamide/Phytic Acid/Polydopamine Hydrogel Modified Screen Printed Carbon Electrode. *Anal. Methods* **2018**, *10*, 4689–4694. [\[CrossRef\]](#)
- [53] Das, J.; Sarkar, P. Enzymatic Electrochemical Biosensor for Urea with a Polyaniline Grafted Conducting Hydrogel Composite Modified Electrode. *RSC Adv.* **2016**, *6*, 92520–92533. [\[CrossRef\]](#)
- [54] Ji, J.; Wu, S.; Su, H.; An, S.; Ruan, J.; Zeng, D. Research Progress of PVA Conductive Hydrogel-Based Wearable Biosensors in Sweat Detection. *Chem. Eng. Sci.* **2024**, *300*, 120620. [\[CrossRef\]](#)
- [55] Miao, Z.; Song, Y.; Dong, Y.; Ge, D.; Shui, J.; He, X.; Yu, H.Y. Intrinsic Conductive Cellulose Nanofiber Induce Room-Temperature Reversible and Robust Polyvinyl Alcohol Hydrogel for Multifunctional Self-Healable Biosensors. *Nano Res.* **2023**, *16*, 3156–3167. [\[CrossRef\]](#)
- [56] Chenani, H.; Razaghi, Z.; Saeidi, M.; Aghaii, A.H.; Rastkhiz, M.A.; Orouji, M.; Simchi, A. A Stretchable, Adhesive, and Wearable Hydrogel-Based Patches Based on a Bilayer PVA Composite for On-line Monitoring of Sweat by Artificial Intelligence-Assisted Smartphones. *Talanta* **2025**, *287*, 127640. [\[CrossRef\]](#) [\[PubMed\]](#)
- [57] Sanaeifar, N.; Rabiee, M.; Abdolrahim, M.; Tahriri, M.; Vashae, D.; Tayebi, L. A Novel Electrochemical Biosensor Based on Fe₃O₄ Nanoparticles-Polyvinyl Alcohol Composite for Sensitive Detection of Glucose. *Anal. Biochem.* **2017**, *519*, 19–26. [\[CrossRef\]](#) [\[PubMed\]](#)
- [58] Chakravarty, S.; Dutta, P.; Kalita, S.; Sarma, N.S. PVA-Based Nanobiosensor for Ultrasensitive Detection of Folic Acid by Fluorescence Quenching. *Sens. Actuators B Chem.* **2016**, *232*, 243–250. [\[CrossRef\]](#)
- [59] Shyeed, M.A.; Hasan, M.K.; Khatun, M.K.; Hosain, K.R.; Hu, D.; Wang, X. Additive Manufacturing of Hydrogels in Tissue Engineering. *J. Chem. Lett.* **2024**, *5*, 17–43. [\[CrossRef\]](#)
- [60] Chen, Y.; Zhang, S.; Cui, Q.; Ni, J.; Wang, X.; Cheng, X.; Khademhosseini, A. Microengineered Poly(HEMA) Hydrogels for Wearable Contact Lens Biosensing. *Lab Chip* **2020**, *20*, 4205–4214. [\[CrossRef\]](#)
- [61] Xu, Y.; Shi, X.; Zhang, Y.; Sun, L.; Zeng, Z. Epitaxial Nucleation and Lateral Growth of High-Crystalline Black Phosphorus Films on Silicon. *Nat. Commun.* **2020**, *11*, 1330. [\[CrossRef\]](#)
- [62] Quinn, C.P.; Pathak, C.P.; Heller, A.; Hubbell, J.A. Photo-Crosslinked Copolymers of 2-Hydroxyethyl Methacrylate, Poly(Ethylene Glycol) Tetra-Acrylate and Ethylene Dimethacrylate for Improving Biocompatibility of Biosensors. *Biomaterials* **1995**, *16*, 389–396. [\[CrossRef\]](#)
- [63] Brahim, S.; Narinesingh, D.; Guiseppi-Elie, A. Polypyrrole-Hydrogel Composites for the Construction of Clinically Important Biosensors. *Biosens. Bioelectron.* **2002**, *17*, 53–59. [\[CrossRef\]](#)
- [64] Lanzalaco, S.; Mingot, J.; Torras, J.; Alemán, C.; Armelin, E. Recent Advances in Poly(N-Isopropylacrylamide) Hydrogels and Derivatives as Promising Materials for Biomedical and Engineering Emerging Applications. *Adv. Eng. Mater.* **2023**, *25*, 2201303. [\[CrossRef\]](#)

- [65] Islam, M.R.; Ahiabu, A.; Li, X.; Serpe, M.J. Poly(N-Isopropylacrylamide) Microgel-Based Optical Devices for Sensing and Biosensing. *Sensors* **2014**, *14*, 8984–8995. [CrossRef]
- [66] Ma, H.; Zou, Y.; Zhang, S.; Liu, L.; Yu, J.; Fan, Y. Nanochitin and Poly(N-Isopropylacrylamide) Interpenetrating Network Hydrogels for Temperature Sensor Applications. *Carbohydr. Polym.* **2022**, *291*, 119544. [CrossRef] [PubMed]
- [67] Li, F.; Wang, C.; Guo, W. Multifunctional Poly-N-Isopropylacrylamide/DNAzyme Microgels as Highly Efficient and Recyclable Catalysts for Biosensing. *Adv. Funct. Mater.* **2018**, *28*, 1705876. [CrossRef]
- [68] Wang, Y.Z.; Zhong, H.; Li, X.R.; Zhang, X.Q.; Cheng, Z.P.; Zhang, Z.C.; Wang, J.K. Electrochemical Temperature-Controlled Switch for Nonenzymatic Biosensor Based on Fe₃O₄-PNIPAM Microgels. *J. Electroanal. Chem.* **2019**, *851*, 113410. [CrossRef]
- [69] Holback, H.; Yeo, Y.; Park, K. Hydrogel Swelling Behavior and Its Biomedical Applications. In *Biomedical Hydrogels*; Woodhead Publishing: Cambridge, UK, 2011; pp. 3–24. [CrossRef]
- [70] Bhattacharjee, S.; Goswami, S.; Das, S.; Bhattacharjee, S.; Bhaladhare, S. pH-Responsive, Stable, and Biocompatible Functional Nanogels Based on Chitosan (CS)/Poly Methacrylic Acid (PMAA) Polymers: Synthesis and Characterization. *Mater. Today Commun.* **2023**, *36*, 106541. [CrossRef]
- [71] Prabakaran, K.; Jandas, P.J.; Luo, J.; Fu, C.; Wei, Q. Molecularly Imprinted Poly(Methacrylic Acid) Based QCM Biosensor for Selective Determination of L-Tryptophan. *Colloids Surf. A Physicochem. Eng. Asp.* **2021**, *611*, 125859. [CrossRef]
- [72] Wu, Y.; Nizam, M.N.; Ding, X.; Xu, F.J. Rational Design of Peptide-Functionalized Poly(Methacrylic Acid) Brushes for On-Chip Detection of Protease Biomarkers. *ACS Biomater. Sci. Eng.* **2017**, *4*, 2018–2025. [CrossRef]
- [73] Chen, C.W.; Chen, S.H.; Huang, C.F.; Chen, J.K. Designable Poly(Methacrylic Acid)/Silver Cluster Ring Arrays as Reflectance Spectroscopy-Based Biosensors for Label-Free Plaque Diagnosis. *Polymers* **2023**, *15*, 1919. [CrossRef]
- [74] Bell, C.L.; Peppas, N.A. Poly(Methacrylic Acid-g-Ethylene Glycol) Hydrogels as pH Responsive Biomedical Materials. *MRS Online Proc. Libr.* **1993**, *331*, 199. [CrossRef]
- [75] Pourmadadi, M.; Shamsabadipour, A.; Aslani, A.; Eshaghi, M.M.; Rahdar, A.; Pandey, S. Development of Polyvinylpyrrolidone-Based Nanomaterials for Biosensors Applications: A Review. *Inorg. Chem. Commun.* **2023**, *152*, 110714. [CrossRef]
- [76] Zhao, M.; Tang, Z.; Zhang, X.; Li, Z.; Xiao, H.; Zhang, M.; Wu, H. A Self-Healing, Stretchable, and Conductive Poly(N-Vinylpyrrolidone)/Gallic Acid Composite Hydrogel Formed via Hydrogen Bonding for Wearable Electronic Sensors. *Compos. Sci. Technol.* **2020**, *198*, 108294. [CrossRef]
- [77] Zhu, X.; Liu, L.; Cao, W.; Yuan, R.; Wang, H. Ultra-Sensitive MicroRNA Biosensor Based on Strong Aggregation-Induced Electrochemiluminescence from Bidentate Ligand-Stabilized Copper Nanoclusters in Polymer Hydrogel. *Anal. Chem.* **2023**, *95*, 5553–5560. [CrossRef]
- [78] Truskewycz, A.; Beker, S.A.; Ball, A.S.; Murdoch, B.; Cole, I. Incorporation of Quantum Carbon Dots into a PVP/ZnO Hydrogel for Use as an Effective Hexavalent Chromium Sensing Platform. *Anal. Chim. Acta* **2020**, *1099*, 126–135. [CrossRef] [PubMed]
- [79] Liu, F.; Lin, Z.; Jin, Q.; Wu, Q.; Yang, C.; Chen, H.J.; Xie, X. Protection of Nanostructures-Integrated Microneedle Biosensor Using Dissolvable Polymer Coating. *ACS Appl. Mater. Interfaces* **2019**, *11*, 4809–4819. [CrossRef]
- [80] Dreyer, D.R.; Park, S.; Bielawski, C.W.; Ruoff, R.S. The Chemistry of Graphene Oxide. *Chem. Soc. Rev.* **2010**, *39*, 228–240. [CrossRef]
- [81] Tan, B.; Zhao, H.; Du, L.; Gan, X.; Quan, X. A Versatile Fluorescent Biosensor Based on Target-Responsive Graphene Oxide Hydrogel for Antibiotic Detection. *Biosens. Bioelectron.* **2016**, *83*, 267–273. [CrossRef]
- [82] Wang, Y.; Bi, C.Y. A Novel Nitrite Biosensor Based on Direct Electron Transfer of Hemoglobin Immobilized on a Graphene Oxide/Au Nanoparticles/Multiwalled Carbon Nanotubes Nanocomposite Film. *RSC Adv.* **2014**, *4*, 31573–31580. [CrossRef]
- [83] Yang, X.; Cao, L.; Wang, J.; Chen, L. Sandwich-Like Polypyrrole/Reduced Graphene Oxide Nanosheets Integrated Gelatin Hydrogel as Mechanically and Thermally Sensitive Skinlike Bioelectronics. *ACS Sustain. Chem. Eng.* **2020**, *8*, 10726–10739. [CrossRef]
- [84] Qiu, J.D.; Huang, J.; Liang, R.P. Nanocomposite Film Based on Graphene Oxide for High Performance Flexible Glucose Biosensor. *Sens. Actuators B Chem.* **2011**, *160*, 287–294. [CrossRef]
- [85] Adewunmi, A.A.; Ismail, S.; Sultan, A.S. Carbon Nanotubes (CNTs) Nanocomposite Hydrogels Developed for Various Applications: A Critical Review. *J. Inorg. Organomet. Polym. Mater.* **2016**, *26*, 717–737. [CrossRef]
- [86] Derkus, B.; Emregul, K.C.; Emregul, E. Evaluation of Protein Immobilization Capacity on Various Carbon Nanotube Embedded Hydrogel Biomaterials. *Mater. Sci. Eng. C* **2015**, *56*, 132–140. [CrossRef]
- [87] Wang, Z.; Liu, Y.; Wang, Z.; Huang, X.; Huang, W. Hydrogel-Based Composites: Unlimited Platforms for Biosensors and Diagnostics. *View* **2021**, *2*, 20200165. [CrossRef]
- [88] Tan, X.; Li, M.; Cai, P.; Luo, L.; Zou, X. An Amperometric Cholesterol Biosensor Based on Multiwalled Carbon Nanotubes and Organically Modified Sol-Gel/Chitosan Hybrid Composite Film. *Anal. Biochem.* **2005**, *337*, 111–120. [CrossRef] [PubMed]

- [89] Liu, X.W.; Huang, Y.X.; Sun, X.F.; Sheng, G.P.; Zhao, F.; Wang, S.G.; Yu, H.Q. Conductive Carbon Nanotube Hydrogel as a Bioanode for Enhanced Microbial Electrocatalysis. *ACS Appl. Mater. Interfaces* **2014**, *6*, 8158–8164. [\[CrossRef\]](#)
- [90] Yang, J.; Zhao, J.J.; Han, C.R.; Duan, J.F. Keys to Enhancing Mechanical Properties of Silica Nanoparticle Composites Hydrogels: The Role of Network Structure and Interfacial Interactions. *Compos. Sci. Technol.* **2014**, *95*, 1–7. [\[CrossRef\]](#)
- [91] Zhang, J.; Wang, Z. Nanoparticle–Hydrogel Based Sensors: Synthesis and Applications. *Catalysts* **2022**, *12*, 1096. [\[CrossRef\]](#)
- [92] Kim, M.; Kwon, J.E.; Lee, K.; Koh, W.G. Signal-Amplifying Nanoparticle/Hydrogel Hybrid Microarray Biosensor for Metal-Enhanced Fluorescence Detection of Organophosphorus Compounds. *Biofabrication* **2018**, *10*, 035002. [\[CrossRef\]](#)
- [93] Ferro, Y.; Perullini, M.; Jobbagy, M.; Bilmes, S.A.; Durrieu, C. Development of a Biosensor for Environmental Monitoring Based on Microalgae Immobilized in Silica Hydrogels. *Sensors* **2012**, *12*, 16879–16891. [\[CrossRef\]](#)
- [94] Behyar, M.B.; Nilghaz, A.; Hasanzadeh, M.; Shadjou, N. Recent Progresses and Challenges on Mesoporous Silica Nanoparticles for DNA-Based Biosensors and Diagnostics. *TrAC Trends Anal. Chem.* **2024**, *178*, 117846. [\[CrossRef\]](#)
- [95] Monteiro, J.P.; Predabon, S.M.; da Silva, C.T.P.; Radovanovic, E.; Girotto, E.M. Plasmonic Device Based on a PAAm Hydrogel/Gold Nanoparticles Composite. *J. Appl. Polym. Sci.* **2015**, *132*, 1–6. [\[CrossRef\]](#)
- [96] Roth, A.; Murschel, F.; Latreille, P.L.; Martinez, V.A.; Liberelle, B.; Banquy, X.; De Crescenzo, G. Coiled Coil Affinity-Based Systems for the Controlled Release of Biofunctionalized Gold Nanoparticles from Alginate Hydrogels. *Biomacromolecules* **2019**, *20*, 1926–1936. [\[CrossRef\]](#)
- [97] Liu, C.; Gou, S.; Bi, Y.; Gao, Q.; Sun, J.; Hu, S.; Guo, W. Smart DNA-Gold Nanoparticle Hybrid Hydrogel Film Based Portable, Cost-Effective and Storable Biosensing System for the Colorimetric Detection of Lead (II) and Uranyl Ions. *Biosens. Bioelectron.* **2022**, *210*, 114290. [\[CrossRef\]](#)
- [98] Ziai, Y.; Rinoldi, C.; Nakielski, P.; De Sio, L.; Pierini, F. Smart Plasmonic Hydrogels Based on Gold and Silver Nanoparticles for Biosensing Application. *Curr. Opin. Biomed. Eng.* **2022**, *24*, 100413. [\[CrossRef\]](#)
- [99] Kestwal, R.M.; Bagal-Kestwal, D.; Chiang, B.H. Fenugreek Hydrogel–Agarose Composite Entrapped Gold Nanoparticles for Acetylcholinesterase Based Biosensor for Carbamates Detection. *Anal. Chim. Acta* **2015**, *886*, 143–150. [\[CrossRef\]](#) [\[PubMed\]](#)
- [100] Kowalczyk, A.; Wagner, B.; Karbarz, M.; Nowicka, A.M. A Dual DNA Biosensor Based on Two Redox Couples with a Hydrogel Sensing Platform Functionalized with Carboxyl Groups and Gold Nanoparticles. *Sens. Actuators B Chem.* **2015**, *208*, 220–227. [\[CrossRef\]](#)
- [101] Ilg, P. Stimuli-Responsive Hydrogels Cross-Linked by Magnetic Nanoparticles. *Soft Matter* **2013**, *9*, 3465–3468. [\[CrossRef\]](#)
- [102] Xu, F.; Inci, F.; Mullick, O.; Gurkan, U.A.; Sung, Y.; Kavaz, D.; Demirci, U. Release of Magnetic Nanoparticles from Cell-Encapsulating Biodegradable Nanobiomaterials. *ACS Nano* **2012**, *6*, 6640–6649. [\[CrossRef\]](#)
- [103] Carinelli, S.; Luis-Sunga, M.; González-Mora, J.L.; Salazar-Carballo, P.A. Synthesis and Modification of Magnetic Nanoparticles for Biosensing and Bioassay Applications: A Review. *Chemosensors* **2023**, *11*, 533. [\[CrossRef\]](#)
- [104] Guo, Q.Y.; Ren, S.Y.; Wang, J.Y.; Li, Y.; Yao, Z.Y.; Huang, H.; Yang, S.P. Low Field Nuclear Magnetic Sensing Technology Based on Hydrogel-Coated Superparamagnetic Particles. *Anal. Chim. Acta* **2020**, *1094*, 151–159. [\[CrossRef\]](#)
- [105] Kuryandskaya, G.V.; Fernandez, E.; Safronov, A.P.; Svalov, A.V.; Beketov, I.; Beitia, A.B.; Blyakhman, F.A. Giant Magnetoimpedance Biosensor for Ferrogel Detection: Model System to Evaluate Properties of Natural Tissue. *Appl. Phys. Lett.* **2015**, *106*, 193702. [\[CrossRef\]](#)
- [106] Hasanzadeh, M.; Shadjou, N.; de la Guardia, M. Iron and Iron-Oxide Magnetic Nanoparticles as Signal-Amplification Elements in Electrochemical Biosensing. *TrAC Trends Anal. Chem.* **2015**, *72*, 1–9. [\[CrossRef\]](#)
- [107] Park, S.A.; Jang, E.; Koh, W.G.; Kim, B. Fabrication and Characterization of Optical Biosensors Using Polymer Hydrogel Microparticles and Enzyme–Quantum Dot Conjugates. *Sens. Actuators B Chem.* **2010**, *150*, 120–125. [\[CrossRef\]](#)
- [108] Antony, J.V.; Pillai, J.J.; Kurian, P.; Nampoori, V.P.N.; Kochimoolayil, G.E. Photoluminescence and Optical Nonlinearity of CdS Quantum Dots Synthesized in a Functional Copolymer Hydrogel Template. *New J. Chem.* **2017**, *41*, 3524–3536. [\[CrossRef\]](#)
- [109] Ganguly, S.; Margel, S. Fluorescent Quantum Dots-Based Hydrogels: Synthesis, Fabrication and Multimodal Biosensing. *Talanta Open* **2023**, *8*, 100243. [\[CrossRef\]](#)
- [110] Zhang, J.; Jin, J.; Wan, J.; Jiang, S.; Wu, Y.; Wang, W.; Wang, H. Quantum Dots-Based Hydrogels for Sensing Applications. *Chem. Eng. J.* **2021**, *408*, 127351. [\[CrossRef\]](#)
- [111] Guo, Z.; Hao, T.; Duan, J.; Wang, S.; Wei, D. Electrochemiluminescence Immunosensor Based on Graphene–CdS Quantum Dots–Agarose Composite for the Ultrasensitive Detection of Alpha Fetoprotein. *Talanta* **2012**, *89*, 27–32. [\[CrossRef\]](#) [\[PubMed\]](#)
- [112] Kim, J.H.; Lim, S.Y.; Nam, D.H.; Ryu, J.; Ku, S.H.; Park, C.B. Self-Assembled, Photoluminescent Peptide Hydrogel as a Versatile Platform for Enzyme-

- Based Optical Biosensors. *Biosens. Bioelectron.* **2011**, *26*, 1860–1865. [[CrossRef](#)]
- [113] Deng, Z.; Yu, R.; Guo, B. Stimuli-Responsive Conductive Hydrogels: Design, Properties, and Applications. *Mater. Chem. Front.* **2021**, *5*, 2092–2123. [[CrossRef](#)]
- [114] Tomczykowa, M.; Plonska-Brzezinska, M.E. Conducting Polymers, Hydrogels and Their Composites: Preparation, Properties and Bioapplications. *Polymers* **2019**, *11*, 350. [[CrossRef](#)]
- [115] Ma, Z.; Shi, W.; Yan, K.; Pan, L.; Yu, G. Doping Engineering of Conductive Polymer Hydrogels and Their Application in Advanced Sensor Technologies. *Chem. Sci.* **2019**, *10*, 6232–6244. [[CrossRef](#)] [[PubMed](#)]
- [116] Li, L.; Shi, Y.; Pan, L.; Shi, Y.; Yu, G. Rational Design and Applications of Conducting Polymer Hydrogels as Electrochemical Biosensors. *J. Mater. Chem. B* **2015**, *3*, 2920–2930. [[CrossRef](#)]
- [117] Prajapati, D.G.; Kandasubramanian, B. Progress in the Development of Intrinsically Conducting Polymer Composites as Biosensors. *Macromol. Chem. Phys.* **2019**, *220*, 1800561. [[CrossRef](#)]
- [118] Gamboa, J.; Paulo-Mirasol, S.; Estrany, F.; Torras, J. Recent Progress in Biomedical Sensors Based on Conducting Polymer Hydrogels. *ACS Appl. Bio Mater.* **2023**, *6*, 1720–1741. [[CrossRef](#)]
- [119] Scranton, A.B.; Bowman, C.N.; Peiffer, R.W. *Photopolymerization: Fundamentals and Applications*; American Chemical Society: Washington, DC, USA, 1997. [[CrossRef](#)]
- [120] Nguyen, K.T.; West, J.L. Photopolymerizable Hydrogels for Tissue Engineering Applications. *Biomaterials* **2002**, *23*, 4307–4314. [[CrossRef](#)]
- [121] Christmas, B.; Kemmerer, R.; Kosnik, F. UV/EB Curing Technology: A Short History. In *High Performance Polymers: Their Origin and Development: Proceedings of the Symposium on the History of High Performance Polymers at the American Chemical Society Meeting held in New York, April 15–18, 1986*; Springer: Dordrecht, The Netherlands, 1986; pp. 331–337. [[CrossRef](#)]
- [122] Hossain, K.R.; Jiang, P.; Yao, X.; Yang, X.; Hu, D.; Wang, X. Ionic Liquids for 3D Printing: Fabrication, Properties, Applications. *J. Ion. Liq.* **2023**, *3*, 100066. [[CrossRef](#)]
- [123] Thomas, A.M.; Shea, L.D. Cryotemplation for the Rapid Fabrication of Porous, Patternable Photopolymerized Hydrogels. *J. Mater. Chem. B* **2014**, *2*, 4521–4530. [[CrossRef](#)] [[PubMed](#)]
- [124] Agarwal, S.; Wendorff, J.H.; Greiner, A. Use of Electrospinning Technique for Biomedical Applications. *Polymer* **2008**, *49*, 5603–5621. [[CrossRef](#)]
- [125] Geckil, H.; Xu, F.; Zhang, X.; Moon, S.; Demirci, U. Engineering Hydrogels as Extracellular Matrix Mimics. *Nanomedicine* **2010**, *5*, 469–484. [[CrossRef](#)]
- [126] Hossain, K.R.; Jiang, P.; Yao, X.; Wu, J.; Hu, D.; Yang, X.; Wang, X. Additive Manufacturing of Polymer-Based Lubrication. *Macromol. Mater. Eng.* **2023**, *308*, 2300147. [[CrossRef](#)]
- [127] Lee, S.; Kim, H.S.; Yoo, H.S. Electrospun Nanofibers Embedded Hydrogel Composites for Cell Cultivation in a Biomimetic Environment. *RSC Adv.* **2017**, *7*, 54246–54253. [[CrossRef](#)]
- [128] Bosworth, L.A.; Turner, L.A.; Cartmell, S.H. State of the Art Composites Comprising Electrospun Fibres Coupled with Hydrogels: A Review. *Nanomedicine* **2013**, *9*, 322–335. [[CrossRef](#)] [[PubMed](#)]
- [129] Li, J.; Wu, C.; Chu, P.K.; Gelinsky, M. 3D Printing of Hydrogels: Rational Design Strategies and Emerging Biomedical Applications. *Mater. Sci. Eng. R Rep.* **2020**, *140*, 100543. [[CrossRef](#)]
- [130] Rahman, M.H.; Liza, N.Y.; Hossain, K.R.; Kalambhe, D.R.; Shyeed, M.A.; Noor, M.D.H. Additive Manufacturing in Nano Drug Delivery Systems. *Pharm. Sci. Adv.* **2024**, *2*, 100036. [[CrossRef](#)] [[PubMed](#)]
- [131] Fatimi, A.; Okoro, O.V.; Podstawczyk, D.; Siminska-Stanny, J.; Shavandi, A. Natural Hydrogel-Based Bio-Inks for 3D Bioprinting in Tissue Engineering: A Review. *Gels* **2022**, *8*, 179. [[CrossRef](#)] [[PubMed](#)]
- [132] Keriquel, V.; Oliveira, H.; Rémy, M.; Ziane, S.; Delmond, S.; Rousseau, B.; Catros, S. In Situ Printing of Mesenchymal Stromal Cells, by Laser-Assisted Bioprinting, for In Vivo Bone Regeneration Applications. *Sci. Rep.* **2017**, *7*, 1778. [[CrossRef](#)]
- [133] Dutta, S.D.; Hexiu, J.; Patel, D.K.; Ganguly, K.; Lim, K.T. 3D-Printed Bioactive and Biodegradable Hydrogel Scaffolds of Alginate/Gelatin/Cellulose Nanocrystals for Tissue Engineering. *Int. J. Biol. Macromol.* **2021**, *167*, 644–658. [[CrossRef](#)]
- [134] Chen, G.; Liang, X.; Zhang, P.; Lin, S.; Cai, C.; Yu, Z.; Liu, J. Bioinspired 3D Printing of Functional Materials by Harnessing Enzyme-Induced Biomineralization. *Adv. Funct. Mater.* **2022**, *32*, 2113262. [[CrossRef](#)]
- [135] Damborský, P.; Švitel, J.; Katrlík, J. Optical Biosensors. *Essays Biochem.* **2016**, *60*, 91–100. [[CrossRef](#)]
- [136] Chaubey, A.; Malhotra, B. Mediated Biosensors. *Biosens. Bioelectron.* **2002**, *17*, 441–456. [[CrossRef](#)] [[PubMed](#)]
- [137] Akgönüllü, S.; Denizli, A. Recent Advances in Optical Biosensing Approaches for Biomarkers Detection. *Biosens. Bioelectron. X* **2022**, *12*, 100269. [[CrossRef](#)]
- [138] Xiao, P.; Sang, S.; Zhang, Q.; Ge, Y.; Cheng, Y.; Zhao, D. A Membrane-Type Mechanical Biosensor Based on Magnetic, Surface Stress and Electric Coupling Enhancement for HSA Detection. *Biochem. Eng. J.* **2022**, *180*, 108361. [[CrossRef](#)]
- [139] Arlett, J.L.; Myers, E.B.; Roukes, M.L. Comparative Advantages of Mechanical Biosensors. *Nat. Nanotechnol.* **2011**, *6*, 203–215. [[CrossRef](#)] [[PubMed](#)]

- [140] Gouda, M.; Ghazzawy, H.S.; Alqahtani, N.; Li, X. The Recent Development of Acoustic Sensors as Effective Chemical Detecting Tools for Biological Cells and Their Bioactivities. *Molecules* **2023**, *28*, 4855. [\[CrossRef\]](#)
- [141] Jakubik, W.P. Surface Acoustic Wave-Based Gas Sensors. *Thin Solid Film.* **2011**, *520*, 986–993. [\[CrossRef\]](#)
- [142] Fu, Y.Q.; Luo, J.K.; Nguyen, N.T.; Walton, A.J.; Flewitt, A.J.; Zu, X.T.; Milne, W.I. Advances in Piezoelectric Thin Films for Acoustic Biosensors, Acoustofluidics and Lab-on-Chip Applications. *Prog. Mater. Sci.* **2017**, *89*, 31–91. [\[CrossRef\]](#)
- [143] Länge, K.; Rapp, B.E.; Rapp, M. Surface Acoustic Wave Biosensors: A Review. *Anal. Bioanal. Chem.* **2008**, *391*, 1509–1519. [\[CrossRef\]](#)
- [144] Ramanathan, K.; Danielsson, B. Principles and Applications of Thermal Biosensors. *Biosens. Bioelectron.* **2001**, *16*, 417–423. [\[CrossRef\]](#)
- [145] Bhatnagar, A.; Masih, J.; Kumar, R. Biosensor: Application in Environmental Management. In *Harnessing Microbial Potential for Multifarious Applications*; Arora, S., Kumar, A., Ogita, S., Yau, Y.Y., Eds.; Springer: Singapore, 2024; pp. 455–488. [\[CrossRef\]](#)
- [146] Park, T.H.; Shuler, M.L. Integration of Cell Culture and Microfabrication Technology. *Biotechnol. Prog.* **2003**, *19*, 243–253. [\[CrossRef\]](#)
- [147] Völlmecke, K.; Afroz, R.; Bierbach, S.; Brenker, L.J.; Frücht, S.; Glass, A.; Kuckling, D. Hydrogel-Based Biosensors. *Gels* **2022**, *8*, 768. [\[CrossRef\]](#)
- [148] Fatimi, A.; Damiri, F.; Berrada, M.; Musuc, A.M. Patent Overview of Innovative Hyaluronic Acid-Based Hydrogel Biosensors. *Biosensors* **2024**, *14*, 567. [\[CrossRef\]](#)
- [149] Liu, H.; Chen, B.; Zhu, Q. Potential Application of Hydrogel to the Diagnosis and Treatment of Multiple Sclerosis. *J. Biol. Eng.* **2022**, *16*, 10. [\[CrossRef\]](#)
- [150] Sun, S.; Chen, J. Recent Advances in Hydrogel-Based Biosensors for Cancer Detection. *ACS Appl. Mater. Interfaces* **2024**, *16*, 46988–47002. [\[CrossRef\]](#)
- [151] Kapil, P.; Verma, D.; Pradhan, R.; Kalkal, A.; Packirisamy, G. A Bioinspired Porous and Electroactive Reduced Graphene Oxide Hydrogel Based Biosensing Platform for Efficient Detection of Tumor Necrosis Factor- α . *J. Mater. Chem. B* **2024**, *12*, 12207–12219. [\[CrossRef\]](#)
- [152] Lin, Y.T.; Darvishi, S.; Preet, A.; Huang, T.Y.; Lin, S.H.; Girault, H.H.; Lin, T.E. A Review: Electrochemical Biosensors for Oral Cancer. *Chemosensors* **2020**, *8*, 54. [\[CrossRef\]](#)
- [153] Liang, Z.; Zhang, J.; Wu, C.; Hu, X.; Lu, Y.; Wang, G.; Wang, Y. Flexible and Self-Healing Electrochemical Hydrogel Sensor with High Efficiency toward Glucose Monitoring. *Biosens. Bioelectron.* **2020**, *155*, 112105. [\[CrossRef\]](#)
- [154] Langer, R. New Methods of Drug Delivery. *Science* **1990**, *249*, 1527–1533. [\[CrossRef\]](#) [\[PubMed\]](#)
- [155] Parker, S.; Cronshaw, M.; Grootveld, M.; George, R.; Anagnostaki, E.; Mylona, V.; Walsh, L. The Influence of Delivery Power Losses and Full Operating Parametry on the Effectiveness of Diode Visible–Near Infra-Red (445–1064 nm) Laser Therapy in Dentistry—A Multi-Centre Investigation. *Lasers Med. Sci.* **2022**, *37*, 2249–2257. [\[CrossRef\]](#) [\[PubMed\]](#)
- [156] Fatimi, A. Development of the Hydrogel-Based Biosensors: An Overview of Recent Patents and Patented Technologies. *Eng. Proc.* **2023**, *48*, 41. [\[CrossRef\]](#)
- [157] Chen, Y.; Jiao, L.; Li, R.; Hu, L.; Jia, X.; Zhu, Z.; Lu, X. Immobilizing Glucose Oxidase on AuCu Hydrogels for Enhanced Electrochromic Biosensing. *Anal. Chim. Acta* **2023**, *1283*, 341977. [\[CrossRef\]](#)
- [158] Solanki, R.; Bhatia, D. Stimulus-Responsive Hydrogels for Targeted Cancer Therapy. *Gels* **2024**, *10*, 440. [\[CrossRef\]](#) [\[PubMed\]](#)
- [159] Sun, X.; Ding, C.; Qin, M.; Li, J. Hydrogel-Based Biosensors for Bacterial Infections. *Small* **2024**, *20*, 2306960. [\[CrossRef\]](#) [\[PubMed\]](#)
- [160] Andrade, F.; Roca-Melendres, M.M.; Durán-Lara, E.F.; Rafael, D.; Schwartz, S., Jr. Stimuli-Responsive Hydrogels for Cancer Treatment: The Role of pH, Light, Ionic Strength and Magnetic Field. *Cancers* **2021**, *13*, 1164. [\[CrossRef\]](#)
- [161] Mansoor, S.; Kondiah, P.P.; Choonara, Y.E. Advanced Hydrogels for the Controlled Delivery of Insulin. *Pharmaceutics* **2021**, *13*, 2113. [\[CrossRef\]](#)
- [162] Fedi, A.; Vitale, C.; Giannoni, P.; Caluori, G.; Marrella, A. Biosensors to Monitor Cell Activity in 3D Hydrogel-Based Tissue Models. *Sensors* **2022**, *22*, 1517. [\[CrossRef\]](#) [\[PubMed\]](#)
- [163] Gebeyehu, A.; Surapaneni, S.K.; Huang, J.; Mondal, A.; Wang, V.Z.; Haruna, N.F.; Singh, M. Polysaccharide Hydrogel Based 3D Printed Tumor Models for Chemotherapeutic Drug Screening. *Sci. Rep.* **2021**, *11*, 372. [\[CrossRef\]](#)
- [164] Zhang, J.; Zheng, Y.; Lee, J.; Hua, J.; Li, S.; Pan-chamukhi, A.; Wu, X. A Pulsatile Release Platform Based on Photo-Induced Imine-Crosslinking Hydrogel Promotes Scarless Wound Healing. *Nat. Commun.* **2021**, *12*, 1670. [\[CrossRef\]](#) [\[PubMed\]](#)
- [165] Zhu, D.; Li, Z.; Huang, K.; Caranasos, T.G.; Rossi, J.S.; Cheng, K. Minimally Invasive Delivery of Therapeutic Agents by Hydrogel Injection into the Pericardial Cavity for Cardiac Repair. *Nat. Commun.* **2021**, *12*, 1412. [\[CrossRef\]](#)
- [166] Parvin, N.; Kumar, V.; Joo, S.W.; Mandal, T.K. Cutting-Edge Hydrogel Technologies in Tissue Engineering and Biosensing: An Updated Review. *Materials* **2024**, *17*, 4792. [\[CrossRef\]](#)
- [167] Distler, T.; Boccaccini, A.R. 3D Printing of Electrically Conductive Hydrogels for Tissue Engineering and Biosensors—A Review. *Acta Biomater.* **2020**, *101*, 1–13. [\[CrossRef\]](#) [\[PubMed\]](#)

- [168] Fantino, E.; Roppolo, I.; Zhang, D.; Xiao, J.; Chiappone, A.; Castellino, M.; Yang, J. 3D Printing/Interfacial Polymerization Coupling for the Fabrication of Conductive Hydrogel. *Macromol. Mater. Eng.* **2018**, *303*, 1700356. [[CrossRef](#)]
- [169] Mousavi, A.; Vahdat, S.; Baheiraei, N.; Razavi, M.; Norahan, M.H.; Baharvand, H. Multifunctional Conductive Biomaterials as Promising Platforms for Cardiac Tissue Engineering. *ACS Biomater. Sci. Eng.* **2020**, *7*, 55–82. [[CrossRef](#)] [[PubMed](#)]
- [170] Kim, H.J.; Choi, W.; San Lee, J.; Choi, J.; Choi, N.; Hwang, K.S. Clinical Application of Serological Alzheimer's Disease Diagnosis Using a Highly Sensitive Biosensor with Hydrogel-Enhanced Dielectrophoretic Force. *Biosens. Bioelectron.* **2022**, *195*, 113668. [[CrossRef](#)] [[PubMed](#)]
- [171] Fatimi, A. Trends and Recent Patents on Cellulose-Based Biosensors. *Eng. Proc.* **2022**, *16*, 12. [[CrossRef](#)]
- [172] Ha, T.; Park, S.; Shin, M.; Lee, J.Y.; Choi, J.H.; Choi, J.W. Biosensing System for Drug Evaluation of Amyotrophic Lateral Sclerosis Based on Muscle Bundle and Nano-Biohybrid Hydrogel Composed of Multiple Motor Neuron Spheroids and Carbon Nanotubes. *Chem. Eng. J.* **2023**, *463*, 142284. [[CrossRef](#)]
- [173] Basu, P.; Banerjee, A.; Okoro, P.D.; Masoumi, A.; Kanjilal, B.; Akbari, M.; Noshadi, I. Integration of Functional Polymers and Biosensors to Enhance Wound Healing. *Adv. Healthc. Mater.* **2024**, *13*, 2401461. [[CrossRef](#)]
- [174] Özsoylu, D.; Janus, K.A.; Achtsnicht, S.; Wagner, T.; Keusgen, M.; Schöning, M.J. (Bio-) Sensors for Skin Grafts and Skin Flaps Monitoring. *Sens. Actuators Rep.* **2023**, *6*, 100163. [[CrossRef](#)]
- [175] Shafiee, A.; Ghadiri, E.; Kassis, J.; Pourhabibi Zarandi, N.; Atala, A. Biosensing Technologies for Medical Applications, Manufacturing, and Regenerative Medicine. *Curr. Stem Cell Rep.* **2018**, *4*, 105–115. [[CrossRef](#)]
- [176] Liu, G.; Lv, Z.; Batool, S.; Li, M.Z.; Zhao, P.; Guo, L.; Han, S.T. Biocompatible Material-Based Flexible Biosensors: From Materials Design to Wearable/Implantable Devices and Integrated Sensing Systems. *Small* **2023**, *19*, 2207879. [[CrossRef](#)]
- [177] Sun, J.; Wu, X.; Xiao, J.; Zhang, Y.; Ding, J.; Jiang, J.; Fan, H. Hydrogel-Integrated Multimodal Response as a Wearable and Implantable Bidirectional Interface for Biosensor and Therapeutic Electrostimulation. *ACS Appl. Mater. Interfaces* **2023**, *15*, 5897–5909. [[CrossRef](#)]
- [178] Liu, H.; Li, Z.; Che, S.; Feng, Y.; Guan, L.; Yang, X.; Lin, Q. A Smart Hydrogel Patch with High Transparency, Adhesiveness and Hemostasis for All-Round Treatment and Glucose Monitoring of Diabetic Foot Ulcers. *J. Mater. Chem. B* **2022**, *10*, 5804–5817. [[CrossRef](#)]
- [179] Li, H.; Tan, P.; Rao, Y.; Bhattacharya, S.; Wang, Z.; Kim, S.; Lu, N. E-Tattoos: Toward Functional but Imperceptible Interfacing with Human Skin. *Chem. Rev.* **2024**, *124*, 3220–3283. [[CrossRef](#)] [[PubMed](#)]
- [180] Peng, S.; Hassan, H.; Rosseel, S.; Matricali, G.A.; Deschamps, K.; Vandeginste, V.; Hallez, H. Recent Advances in 3D-Printed, Wearable Pressure Sensors for Plantar Pressure Monitoring: A Review. *IEEE Sens. J.* **2024**, *24*, 33903–33921. [[CrossRef](#)]
- [181] Park, T.; Mahmud, T.I.; Lee, J.; Hong, S.; Park, J.Y.; Ji, Y.; Lee, C.H. A Machine-Learning-Enabled Smart Neckband for Monitoring Dietary Intake. *PNAS Nexus* **2024**, *3*, 156. [[CrossRef](#)]
- [182] Wang, Y.; Liu, H.; Yang, X.; Shi, Z.; Li, J.; Xue, L.; Lei, Y. A Responsive Hydrogel-Based Microneedle System for Minimally Invasive Glucose Monitoring. *Smart Mater. Med.* **2023**, *4*, 69–77. [[CrossRef](#)]
- [183] Wanjale, M.V.; Sunil Jaikumar, V.; Sivakumar, K.C.; Ann Paul, R.; James, J.; Kumar, G.V. Supramolecular Hydrogel Based Post-Surgical Implant System for Hydrophobic Drug Delivery against Glioma Recurrence. *Int. J. Nanomed.* **2022**, *17*, 2203–2224. [[CrossRef](#)] [[PubMed](#)]
- [184] Nam, J.; Lim, H.K.; Kim, N.H.; Park, J.K.; Kang, E.S.; Kim, Y.T.; Kim, Y.H. Supramolecular Peptide Hydrogel-Based Soft Neural Interface Augments Brain Signals through a Three-Dimensional Electrical Network. *ACS Nano* **2020**, *14*, 664–675. [[CrossRef](#)]
- [185] Cooper, R.C.; Yang, H. Hydrogel-Based Ocular Drug Delivery Systems: Emerging Fabrication Strategies, Applications, and Bench-to-Bedside Manufacturing Considerations. *J. Control. Release* **2019**, *306*, 29–39. [[CrossRef](#)]
- [186] Khattak, S.; Ullah, I.; Xie, H.; Tao, X.D.; Xu, H.T.; Shen, J. Self-Healing Hydrogels as Injectable Implants: Advances in Translational Wound Healing. *Coord. Chem. Rev.* **2024**, *509*, 215790. [[CrossRef](#)]

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