chemosensors

Review

Conductive Hydrogel-Based Electrochemical Sensor: A Soft Platform for Capturing Analyte

Li Fu [1,*], Aimin Yu [2] and Guosong Lai [3]

[1] Key Laboratory of Novel Materials for Sensor of Zhejiang Province, College of Materials and Environmental Engineering, Hangzhou Dianzi University, Hangzhou 310018, China
[2] Department of Chemistry and Biotechnology, Faculty of Science, Engineering and Technology, Swinburne University of Technology, Hawthorn, VIC 3122, Australia; aiminyu@swin.edu.au
[3] Hubei Key Laboratory of Pollutant Analysis & Reuse Technology, College of Chemistry and Chemical Engineering, Hubei Normal University, Huangshi 435002, China; gslai@hbnu.edu.cn
* Correspondence: fuli@hdu.edu.cn

Abstract: Electrode modifications for electrochemical sensors attract a lot of attention every year. Among them, hydrogels are a relatively special class of electrode modifier. Since hydrogels often contain polymers, even though they are conductive polymers, they are not ideal electrode modifiers because of their poor conductivity. However, the micro-aqueous environment and the three-dimensional structure of hydrogels are an excellent platform for immobilizing bioactive molecules and maintaining their activity. This gives the hydrogel-modified electrochemical sensor the potential to perform specific recognition. At the same time, the rapid development of nanomaterials also makes the composite hydrogel have good electrical conductivity. This has led many scientists to become interested in hydrogel-based electrochemical sensors. In this review, we summarize the development process of hydrogel-based electrochemical sensors, starting from 2000. Hydrogel-based electrochemical sensors were initially used only as a carrier for biomolecules, mostly for loading enzymes and for specific recognition. With the widespread use of noble metal nanoparticles and carbon materials, hydrogels can now be used to prepare enzyme-free sensors. Although there are some sporadic studies on the use of hydrogels for practical applications, the vast majority of reports are still limited to the detection of common model molecules, such as glucose and H_2O_2. In the review, we classify hydrogels according to their different conducting strategies, and present the current status of the application of different hydrogels in electrochemical sensors. We also summarize the advantages and shortcomings of hydrogel-based electrochemical sensors. In addition, future prospects regarding hydrogel for electrochemical sensor use have been provided at the end.

Keywords: conductive hydrogels; electrochemistry; quantitative analysis; chemometrics; nanocomposites; analytical chemistry; food analysis; drug testing

Citation: Fu, L.; Yu, A.; Lai, G. Conductive Hydrogel-Based Electrochemical Sensor: A Soft Platform for Capturing Analyte. *Chemosensors* **2021**, *9*, 282. https://doi.org/10.3390/chemosensors9100282

Academic Editors: Dan Xie, Jian-Long Xu and Yilin Sun

Received: 19 August 2021
Accepted: 28 September 2021
Published: 4 October 2021

1. Introduction

Hydrogel is a soft material with a three-dimensional network structure formed by cross-linking hydrophilic macromolecules through covalent, hydrogen or ligand bonds. Due to its unique porous structure and good flexibility, hydrogel shows excellent application prospects in flexible wearable electronics, batteries, and biosensors [1–7]. These applications require hydrogels with good electrical conductivity. Therefore, conductive hydrogels have been widely studied as an important member of the smart hydrogel family [8–10]. Conductive hydrogels, as a new functional material, were first proposed by Guiseppi-Elie et al. [11] and Wallace et al. [12], as a mixture of hydrogels with conductive polymers. After more than a decade of development, conductive hydrogels can be fabricated with good electrical conductivity, stability, and mechanical properties, which makes them more valuable for practical applications.

As a special type of sensor used in modern analytical chemistry, an electrochemical sensor is one in which a specific sensing element reacts with a target analyte to produce a sensing signal. It converts this signal into a recognizable electrical signal that is proportional to the concentration of the target analyte, by means of a specific transducer, thus achieving a qualitative or quantitative analysis [13–17]. The electrochemical sensor is mainly composed of the following two parts: a solidified sensing element (recognition system) and a transducer (conversion system). Its basic structure and principle are shown in Figure 1.

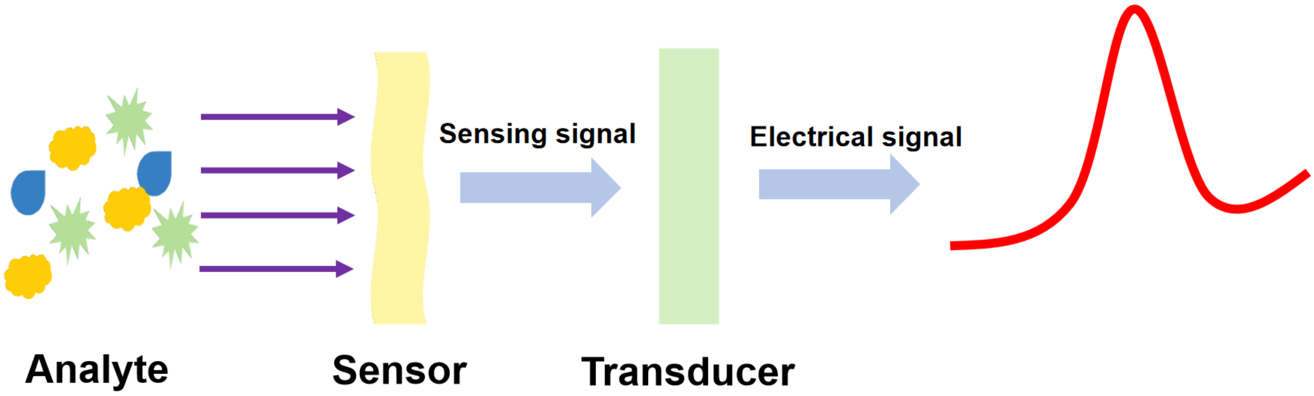

Figure 1. The structure and basic principle of electrochemical sensor.

The earliest studies of electrochemical sensors began in the 1950s, with the monitoring of oxygen. In the 1960s, based on the previous research on oxygen electrodes, new enzyme electrodes and ion-selective electrodes were developed, among which the “enzyme electrode”, firstly constructed by Clark et al. in 1962, was an important milestone [18]. They attached the dialysis membrane with fixed glucose oxidase to the oxygen electrode and then combined it with electrochemical technology. Using the chemical principle that glucose oxidase catalyzes the process of glucose oxidation by depleting dissolved oxygen, they monitored the concentration of glucose in solution by measuring the change in dissolved oxygen concentration in the solution. However, the enzyme electrodes constructed in this way could not be reused and therefore were not yet ready for practical use. It was not until 1967 that Updike and Hicks made a breakthrough on the issue of reproducibility [19]. They developed the world’s first glucose electrochemical sensor by using the new method of immobilizing glucose oxygenase on the surface of an oxygen electrode. Since then, electrochemical sensors have been widely used in the fields of pharmaceutical analysis and environmental monitoring, which is opening up a new era of electrochemical sensor research. After the 1970s, with the increasing amount of research, the existing electrochemical sensor technology is no longer sufficient for more precise scientific research. Therefore, the use of functional changes in the surface structure of the sensitive elements in electrochemical sensors, to control the surface electrochemical processes, can bring electrochemical sensor technology to a more precise level of differentiation [20–27].

As the basic theoretical research progressed, breakthroughs in the commercialization of electrochemical sensors were gradually achieved. The first commercialization of sensors was achieved in 1975, with the introduction of an enzyme electrode-based glucose detector by YSI Corporation (Yellow Springs, OH, USA). In 1984, Cass et al. [28] published the first paper on the development of an enzyme electrode method for media. This paper led directly to the successful development of the MediSene enzyme electrode sensor in 1987. Over the next few decades, new types of electrochemical sensors were gradually commercialized and became widely used in real-life applications. For example, a portable home blood glucose meter can measure the glucose concentration in blood samples at any time and is available in the market for only a few hundred China Yuan(CNY).

Generally speaking, nanomaterials are most commonly used for the modification of sensor electrodes [29–32]. Nanomaterials exhibit some properties that are unique from microscopic particles and macroscopic objects because of their particle size up to the nanoscale and the special effects of their large surfaces; for example, surface effect, volume effect, quantum size effect, and macroscopic quantum tunneling effect. These properties are incomparable to other conventional materials, and thus nanomaterials are widely used in electroanalysis [33]. By modifying the electrode with the above nanomaterials, the electrode will have a large specific surface area and more active sites on the surface, which can effectively accelerate the electron transfer rate and increase the rate of electrochemical reactions [34].

One- and two-dimensional nanomaterials were often used as modifiers [35]. However, designing three-dimensional gel structures allows for more rational control of chemical and physical properties [36]. In general, composite hydrogels are cross-linked polymer networks that are swollen with water at the nanoscale. These polymer networks often have unique mechanical, optical, thermal, magnetic and electrical response properties. In particular, the hydrogel itself can form a microenvironment that can confine the analyte. This is a strategy that allows the sensor to detect with high sensitivity [4,8]. Hydrogel is also an excellent material for the assembly of molecularly imprinted sensors because it provides a miniature aqueous environment and is able to maintain biological activity [37]. Therefore, in recent years, a number of works have also focused on the use of hydrogels for the preparation of electrochemical sensors.

This review focuses on the use of hydrogels as a sensing platform for electrochemical analysis applications. Since electrochemical sensors use electrical signals, hydrogels need to be conductive in some way. This review divides hydrogels into four sections according to their conductivity strategies. First, we briefly described the principles of each conductive strategy with some representative preparation methods. Then, we listed the applications of such hydrogels in electrochemical analysis. We compared the detection performance of the same detection substance by different electrochemical sensors. Based on the performance, we discussed their advantages and limitations. In addition, we highlighted their potential for future development in this field.

2. Polyelectrolyte Conductive Hydrogel

Polyelectrolyte conductive hydrogels are generally hydrogels formed by chemical or physical cross-linking polymerization of hydrophilic monomers containing ionic groups. The ionic groups in these hydrogels are the key to the high electrical conductivity of the hydrogels.

Wang et al. [38] prepared poly(2-propylene-amine-2-methylpropanesulfonate) (PAMPS) hydrogels with high ionic conductivity by the solid solution method (Figure 2A). They also investigated the effect of the content of the cross-linking agent sodium montmorillonite (NaMMT) on the ionic conductivity and tensile strength of the hydrogels. The results showed that the ionic conductivity and tensile strength of the hydrogels were good at the mass fraction of Na-MMT of 5–7%, where the ionic conductivity was 5.91×10^{-2} S/cm and the tensile strength was 8.9 MPa. Later, they prepared polyelectrolyte hydrogels with high ionic conductivity and mechanical properties through a semi-interpenetrating polymer network (s-IPN) composed of PAMPS, polyvinyl alcohol (PVA), and Na-MMT [39]. In this work, they investigated the effect of the content of Na-MMT and PVA on the ionic conductivity and tensile strength of this hydrogel. The results showed that when the ratio of PVA/AMPS was 0.8:1 and the MMT was 7 wt.%, the ionic conductivity and tensile strength reached 6.4×10^{-2} S/cm and 24.3 MPa, respectively. Diao et al. [40] prepared polyelectrolyte conducting hydrogels with PVA as the first network, and acrylamide copolymer with sulfobetaine methacrylate (P(AMco-SBMA)) as the second network, using a simple two-step copolymerization freeze–thaw method (Figure 2B). The effect on the ionic conductivity of this hydrogel was investigated by varying the content of amphoteric SBMA monomer. The results showed that the conductivity of the hydrogels increased from 0.33 to 2.89 S/m with the addition of 5 wt.% of SBMA, compared to no SBMA. The conductivity of the hydrogel was increased from 0.33 to 2.89 S/m with the addition of 5 wt.% SBMA, and reached a maximum of 7.49 S/m with 15 wt.% SBMA. The highest conductivity of 7.49 S/m was achieved at 15 wt.% of SBMA. However, since their works were not focused on electrochemical sensors, the need for an interfacial response of electrochemical sensors was not taken into account in the design of the hydrogel. Therefore, although these works greatly enhance the conductivity of the electrodes, it does not mean that these hydrogels can be directly used for the assembly of electrochemical sensors.

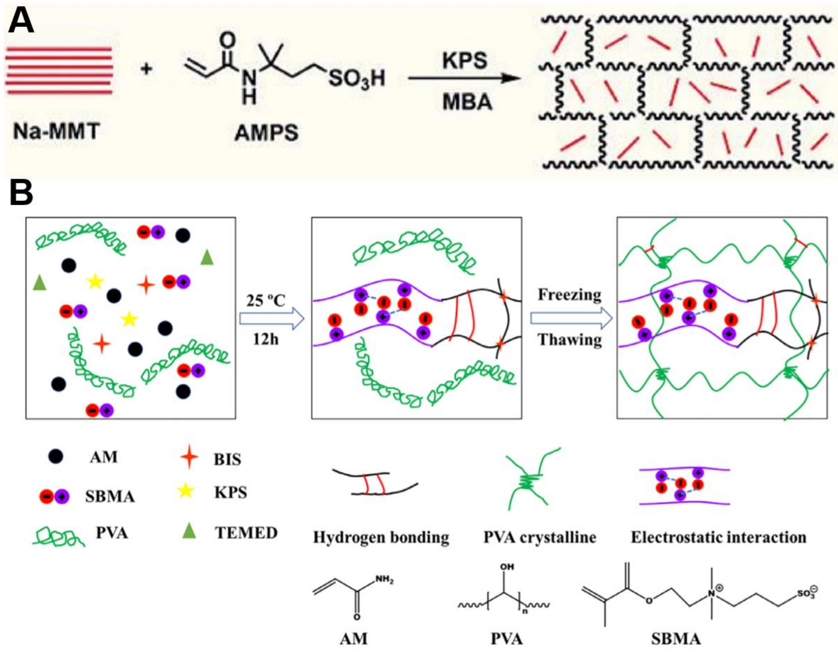

Figure 2. (**A**) Schematic presentation of the PAMPS/MMT composite hydrogel [38]. (**B**) Schematic of fabrication of PVA/P(AM-co-SBMA) hydrogel [40]. Copyright: Elsevier B.V. and John Wiley and Sons.

This class of hydrogels is often used as a carrier for enzyme or probe loading, to achieve specific recognition in electrochemical analysis; for example, aldehyde oxidoreductase, isolated from *Escherichia coli*, can be loaded in poly(vinyl)imidazole hydrogels after using poly (ethylene glycol) diglycidyl ether as a crosslinker [41]. N,N-dimethylamino moieties can be used for loading pyrroloquinoline quinone-dependent glucose dehydrogenase, flavin adenine dinucleotide-dependent glucose dehydrogenase, and FAD-dependent dehydrogenase [42]. The polyelectrolyte conductive hydrogel has also been used in the immobilization of acetylcholinesterase [43,44], horseradish peroxidase [45,46], glucose oxidase [47,48], lactate oxidase [49], alkaline phosphatase [50], horse heart cytochrome c [51,52], *Saccharomyces cerevisae* cytochrome c peroxidase [51], organoselenium [53], and deoxyribonucleic acid (DNA) [54]. There are exceptions, such as Cizek et al. [55], who directly modified screen-printed electrodes with agar hydrogels and then used them for TNT detection. Liu et al. [56] reported the use of aldehyde-agarose hydrogel films for the detection of the promyelocytic leukemia/etinoic acid receptor alpha (PML/RARa) fusion gene in acute promyelocytic leukemia (APL). The diol group in the hydrogel was converted to an aldehyde group by a reaction with $NaIO_4$. With methylene blue as an electrochemical indicator, this sensor allows the highly sensitive detection of the PML/RARa fusion gene in APL. Since specific recognition is the underlying methodology of these sensors, hydrogels do not require particularly superior electrical properties.

Ionic liquids have also been used in the synthesis of hydrogels [57]; for example, Wang et al. [58] reported a sensor based on the photochemistry of polymerized ionic liquids. After polymerization, the ionic liquid can be used as a molecular imprinting platform for protein detection. Of course, the ionic liquid itself cannot provide an obvious signal. Therefore, AuNPs and ZnCdHgSe quantum dots (QDs) have also been used for the assembly of the molecularly imprinted platform. AuNPs and ZnCdHgSe QDs were not used to enhance the conductivity of the hydrogel, but to provide a signal for detection. They investigated how well this sensor could detect human epididymis protein 4 (HE4). Under optimal conditions, a linear detection range of 25 pg/mL to 4.0 ng/mL, with a limit of detection of 15.4 pg/mL, could be achieved. Hydrogel is an excellent material for the assembly of molecularly imprinted sensors because it provides a miniature aqueous environment and is able to maintain biological activity. Except HE4, hemoglobin [59] has also been detected using this strategy. It is worth noting, however, that in our opinion ionic liquids are not a suitable candidate for promotion as electrochemical sensors, due to their cost.

The polymerization can also be conducted by means of electropolymerization. For example, chitosan can be deposited on the electrode surface by electrodeposition with negative potential, and a hydrogel can be formed [60]. If AgNPs were added during the polymerization process, they can be embedded at the same time. The prepared hydrogel can be used for the electrochemical detection of trichloroacetic acid. Electrochemical polymerization has the problem of certain reproducibility. Electrochemical polymerization is not a homogeneous reaction, so the electrode type, parameters during polymerization, and even the temperature and purity of the monomer during polymerization can affect the performance of the final sensor. Therefore, hydrogels synthesized using electrochemical polymerization require special attention for quality control.

3. Acid-Doped Conductive Hydrogel

In general, the conductive property of hydrogels can be improved by doping them with appropriate amounts of acid. As the dopant changes, the conductive property of the hydrogel also changes.

Li et al. [61] prepared poly(aniline)(PANI)/poly(propylene amide) hydrogels by in situ polymerization. The effect of two different acids (hydrochloric acid and p-toluenesulfonic acid), doped with PANI, on the hydrogel properties was investigated. The results showed that the high doping amount of hydrochloric acid and the low doping amount of p-toluenesulfonic acid helped to improve the electrical conductivity. The best electrical conductivity of the hydrogel was achieved when the ratio of hydrochloric acid to benzene was 10:3, and the ratio of p-toluenesulfonic acid to aniline was 1:2. Similarly, Prabhakar et al. [62] synthesized conductive polyacrylamide (PAM)/PANI hydrogels by interfacial polymerization, using PANI-impregnated PAM as the conductive material (Figure 3). Sulfuric acid (H_2SO_4), hydrochloric acid (HCl), and perchloric acid ($HClO_4$) were used as the different acidic dopants. This work explored the effect of dopant ions on the mechanical and conductive properties of the hydrogel. The conductivity of the different acid-doped hydrogels is as follows: $H_2SO_4 > HCl > HClO_4$. The H_2SO_4-doped PAM/PANI hydrogels showed the highest electrical conductivity and the best mechanical toughness compared with other dopants. In another work, they prepared PANI-impregnated acrylate conductive hydrogels using aqueous solution polymerization of interpenetrating polymer networks [63]. This work explored the effect of hydrochloric acid, nitric acid, and sulfuric acid dopants on the conductive properties of the hydrogels. The results showed that among the three inorganic acid dopants, sulfuric acid-doped hydrogels had the highest electrical conductivity, while nitric acid had the lowest. Since sulfuric acid is strongly acidic, the hydrochloric acid-doped hydrogel, with a good electrical conductivity of about 3.71 mS/cm, was prepared under optimized conditions. However, acids can affect not only the conductivity of hydrogels, but also the electrochemical behavior. The electrochemical behavior of molecules is often strongly related to the pH environment. Therefore, it is a challenge to try to strike a balance between detection performance and hydrogel conductivity.

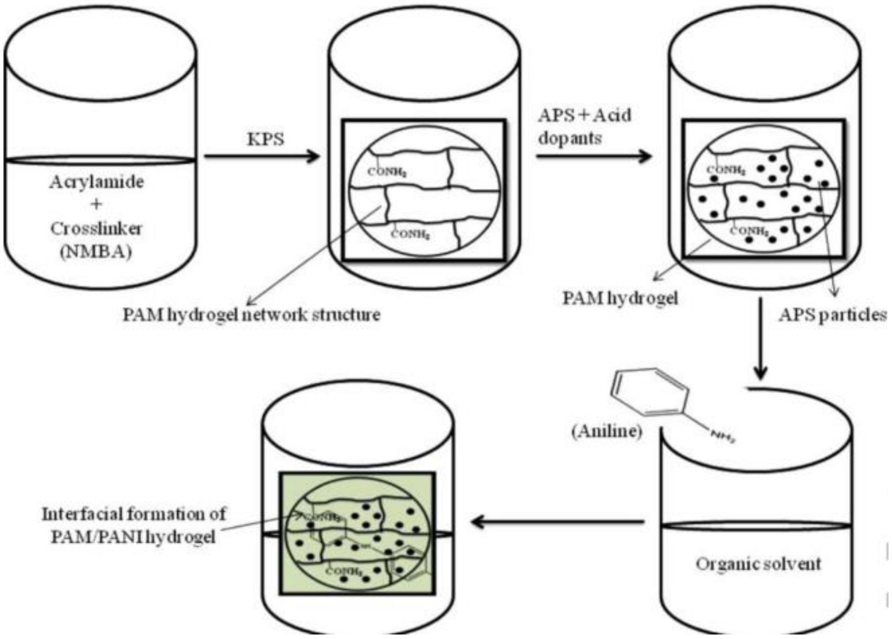

Figure 3. Schematic of PAM and polyacrylamide/PANI hydrogel [62]. Copyright: Taylor & Francis.

Phytic acid (PA) is an exception that is used to form hydrogels, and is consequently used for sensing purposes [64,65]. A highly sensitive electrochemical detector for copper ions can be prepared by multiple interactions of dopamine (DA), acrylamide (AAM), and PA, under mild environmental conditions [64]. In this case, AAM is polymerized by free radicals, DA undergoes a multicoupling reaction, and PA crosslinks polydopamine (PDA) and PAM by hydrogen bonding. This hydrogel not only exhibits the highly sensitive detection of copper ions, but also acts as an adsorbent to remove copper ions from aqueous conditions. The change in boronic acid groups in hydrogels can also affect the capacitance of hydrogels [66]. Therefore, when glucose and boronic acid groups interact, the capacitance of the hydrogel changes in a positive correlation. This change can be used for the highly sensitive detection of glucose.

4. Inorganic Material Filled Conductive Hydrogel

Some inorganic particles have good electrical conductivity, such as metal nanoparticles, metal oxide nanoparticles, and some non-metal nanoparticles. The doping of inorganic materials with hydrogels gives the inorganic materials unique flexibility and ductility. On the other hand, this combination can also lead to enhanced mechanical properties of the hydrogel, overcoming the defect of coagulation and fragility; For example, Bao et al. [67] obtained an oligomeric suspension with a small relative molecular weight by mixing and reacting the supramolecular organic polymer Empol 1016 (Kerr, Italy) with diethylenetriamine. Then, micronickel with nanoscale surface characteristics was dispersed in this oligomeric matrix, which can effectively avoid its agglomeration phenomenon. The oxide layer on the surface of nanoparticles provides a large number of hydrogen bonds, which facilitates their binding to supramolecular organic polymers. The above two factors allow inorganic micronickel to be uniformly dispersed in supramolecular oligomers. This suspension is then reacted with uric acid under a strictly controlled reaction temperature and time, to convert only the primary amine to the urea group. The inorganic doped conductive hydrogel can be produced after mold shaping. The conductivity of the hydrogel was tested by a four-probe tester up to 40 S/cm. The mechanical tensile stress test showed that the addition of micronickel also greatly enhanced its mechanical properties. In addition, the presence of a large number of supramolecular hydrogen bonding forces in the hydrogel gives an excellent self-healing performance.

Alam et al. [68] prepared novel graphene/polyacrylic acid (PA) composite conductive hydrogels. They dissolved graphene in an aqueous solution of acrylic acid monomer, using N,N-methylenebisacrylamide and potassium persulfate as the crosslinker and initiator, respectively. They investigated the changes in the mechanical and conductive properties of this hydrogel after the addition of graphene. It was shown that the compressive strength increased from 0.37 to 6.9 Mpa with the addition of 1 vol% graphene, an increase of 1764%. The Young's modulus increased from 1.64 to 19.03 Mpa. The electrical conductivity of the composite hydrogel was 1.56×10^{-5} S/m. More similarly, Chen et al. [69] prepared PAM/CNF/CNT composite conductive hydrogels by the in situ polymerization of carbon nanotubes (CNTs) and cellulose nanofibers (CNFs) mixed in a solution of acrylamide (AM) (Figure 4). Among them, CNTs were used as conductive fillers. CNFs were used as reinforcing fillers for PAM and dispersing agents for CNTs. In this work, the effects of the additives CNT and CNF on the electrical conductivity and mechanical properties of the hydrogel were investigated. In addition, the results showed that the conductivity of the PAM/CNF/CNT hydrogel was 8.5×10^{-4} S/cm after adding 1 wt.% CNF and 1 wt.% CNT to the PAM. At the same time, its tensile strength at break was three times higher than that of the pure PAM hydrogel, and the conductivity was twice as high as that of the PAM/CNT hydrogel.

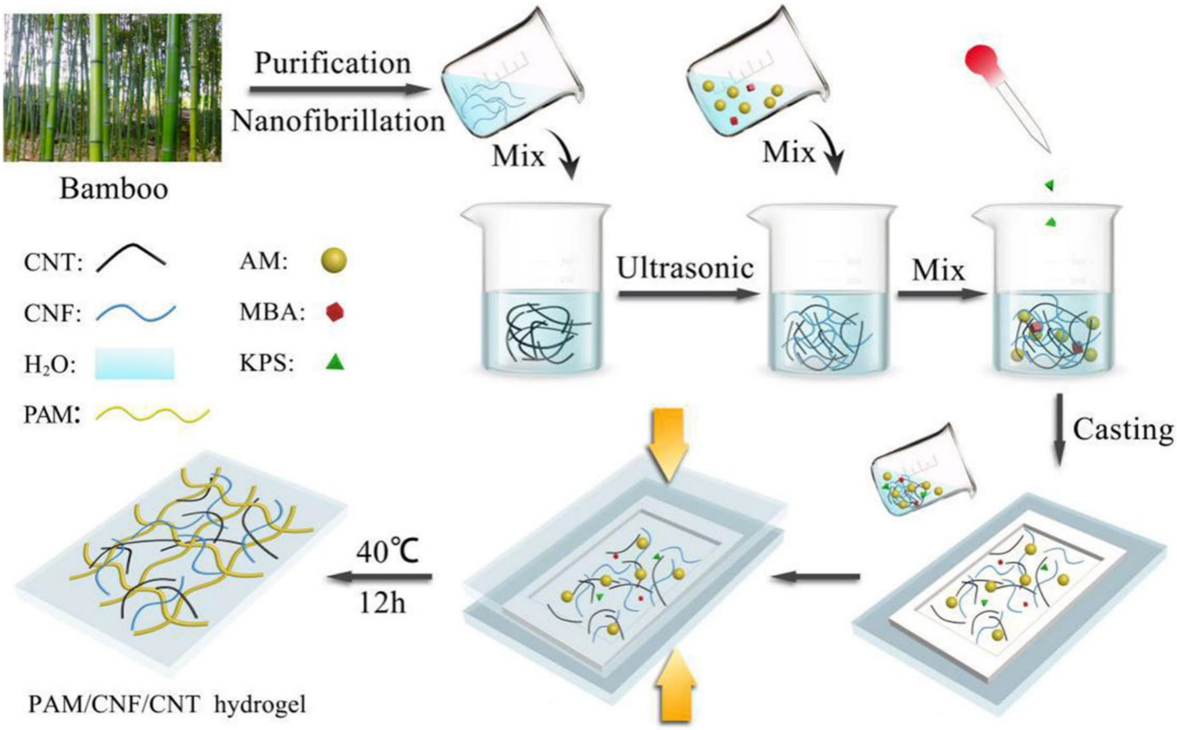

Figure 4. Schematic of the fabrication of PAM/CNF/CNT-n hydrogels [69]. Copyright: Springer Nature.

Our previous works proposed an electrochemical sensor cross-linked with metal ions [70–72]. Zinc and silver ions can be used as cross-linking ions to enable the formation of hydrogels from chitosan and sodium alginate. The key point for the formation of these hydrogels is a suitable pH environment. A weakly acidic environment is required to enable the formation of such hydrogels. This hydrogel can easily depolymerize and release metal ions when subjected to oxidizing agents. Therefore, we used this hydrogel as an electrochemical sensing platform to measure the antioxidant activity. As shown in Figure 5A, the presence of antioxidants prevents the attack of hydrogen peroxide on chitosan and mitigates the polymerization process. The electrochemical reduction signal of metal ions, compared to the presence of antioxidants, can be used to assess the antioxidant activity of the analyte. In addition to our use of this technique for the antioxidant assessment of bee products [72,73], some other works have extended this technique for more sensitive sensing [74–76]. In addition to the Ag^+ and Zn^{2+} that we used, additional K^+ was successfully used as a cross-linking agent. As shown in Figure 5B, K^+ can facilitate the cation-templated assembly of the guanosine-quartet motif [77]. These guanosine-quartet motifs, stacked together with hemin, can form enzyme-like nanohydrogels. However, this hydrogel requires additional electrodeposition of PANI on the surface if it is to be used as an electrochemical sensor, due to its poor electrical conductivity. A similar work has been reported by Zhou et al. [78] for the detection of extracellular H_2O_2.

Carbon-based material is one of the most widely used inorganic materials for electrochemical sensing. Carbon materials are often used for electrode modifications because of their good electrical conductivity. More importantly, they do not participate in electrochemical reactions in a wide electrochemical window. In the preparation of hydrogels, many studies have incorporated carbon materials to improve the electrical conductivity and for electrochemical analysis; for example, graphite was added to chitin to prepare a hydrogel, and was used for the electrochemical determination of hydroquinone, catechol, resorcinol [79], and myoglobin [80]. The rise in carbon nanomaterials has led to their widespread incorporation into hydrogels, to provide excellent electrical conductivity. CNT are among the very important materials; for example, the deposition of poly(vinylimidazole) complexed with Os(4,4′-dimethylbpy)2Cl (PVI-dmeOs), on the surface of multi-walled carbon nanotubes (MWCNT), leads to a hydrogel [81]. This hydrogel has good electrical conductivity, and can respond quickly to glucose oxidase and lactate oxidase. Derkus et al. [82] investigated the immobilization effect of CNT-based hydrogels on proteins. A higher immobilization efficiency was obtained with the addition of CNT, due to their electrical conductivity and surface enhancement, especially in the gelatin-chitosan hydrogel.

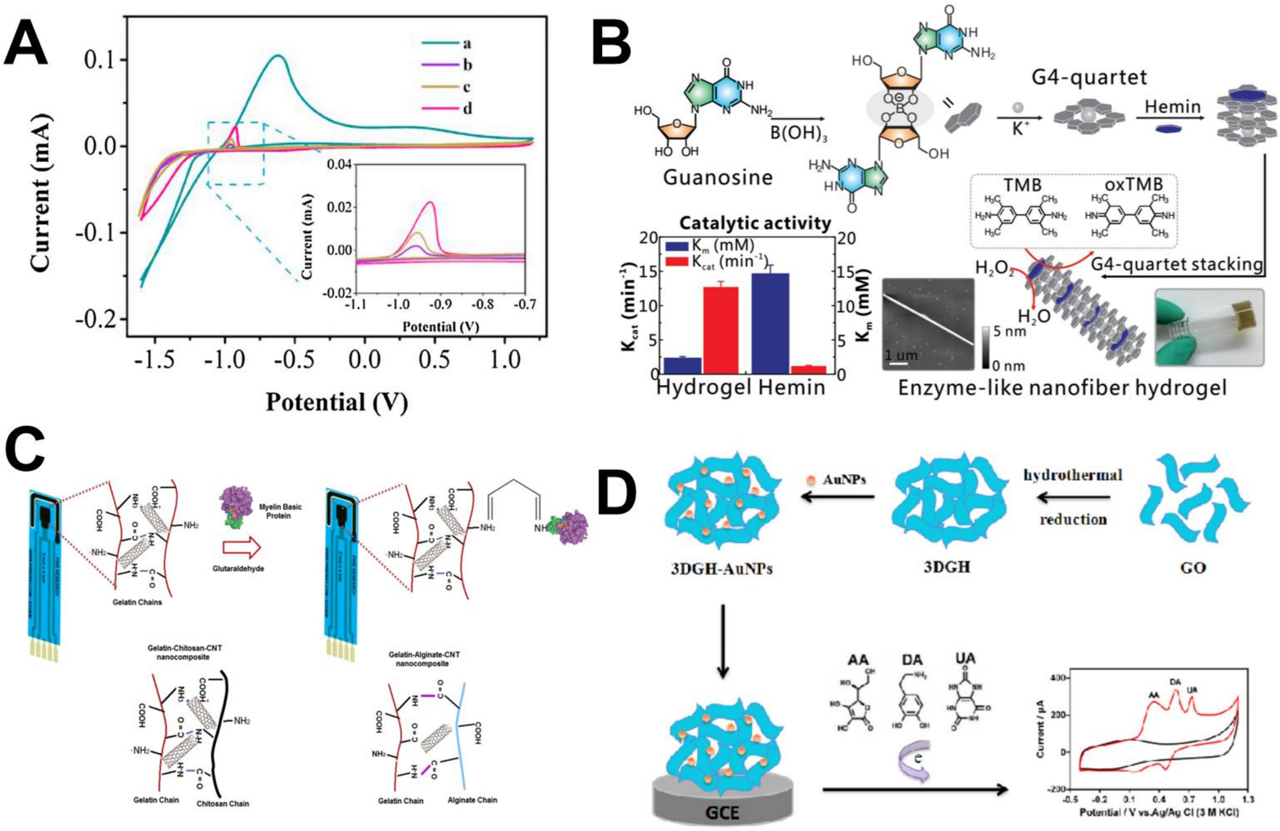

Figure 5. (**A**) CV scans of 2.5 Mm zinc ions in (a) an acetic acid-sodium hydroxide solution, (b) the chitosan hydrogel, (c) the chitosan hydrogel with 0.01 Mm H_2O_2 and (d) the chitosan hydrogel with 0.03 Mm H_2O_2 [70]. (**B**) Schematic diagram of forming enzyme-like nanofibrous hydrogel from guanosine and $B(OH)_3$ via formation of K^+-templated G4 quarte [77]. (**C**) Formation of CNT-based hydrogel [82]. (**D**) Formation of 3D graphene—AuNPs hydrogel [83]. Copyright: Elsevier B.V. and John Wiley and Sons.

After its discovery, graphene has become a new star among carbon materials. The addition of graphene to hydrogels, instead of carbon nanotubes, has become a hot research topic. The lamellar structure of graphene also makes it easier for the hydrogel to maintain a stable 3D structure; for example, Zhu et al. [83] reported a 3D graphene hydrogel. The raw material of this hydrogel only requires graphene oxide. The inorganic filler is gold nanoparticles. This hydrogel can be used for the simultaneous detection of ascorbic acid (AA), dopamine (DA), and uric acid (UA) (Figure 5C). Burrs et al. [84] systematically investigated the graphene-based hydrogel system. They prepared four graphene-based hydrogels for the immobilization of alcohol oxidase. The four hydrogels were chitosan, poly-N-isopropylacrylamide (PNIPAAM), silk fibroin, and cellulose nanocrystal (CNC) hydrogels. They used alcohol oxidase catalyzing the production of hydrogen peroxide from methanol as a model to investigate the sensing performance. It was found that these sensors were not very significantly superior in terms of detection performance, when compared to the other reports. However, all the materials of these hydrogel-based sensors are non-toxic. The sensors also do not require a mediator/adjuvant. Moreover, the shelf life and response time of these sensors were significantly improved compared to other reports. Table 1 summarizes inorganic material-filled hydrogel for electrochemical sensing. Notably, graphene is often used in the preparation of hydrogels, with its derivatives, such as graphene oxide and reduced graphene oxide. In hydrogel synthesis, the properties of graphene are difficult to control, due to the difference in the degree of reduction. Therefore, this leads to the fact that graphene-based hydrogels can have quality control challenges. This will need to be addressed in the future, with a more standard synthesis process.

Table 1. Summary of inorganic material-filled hydrogel for electrochemical sensing.

Raw Material	Inorganic Filler	Analyte	Reference
Chitosan	Zn^{2+}	Antioxidant activity	[70]
Chitosan	Ag^{+}	Antioxidant activity	[71]
1,3,5-benzenetricarboxylic acid	Fe^{2+}	Neuron-specific enolase	[85]
Guanosine, $B(OH)_3$	K^{+}	Glucose	[77]
Chitin	Graphite	Hydroquinone, catechol, resorcinol	[79]
Chitosan	Au NPs	Glucose	[86]
Chitosan	Laponite	L-lactate	[87]
Graphene oxide	Au NPs	AA, DA, UA	[83]
agarose	Au NPs	Carbamate	[88]
PA, PANI, lutetium phthalocyanine	Graphene oxide	Glucose	[89]
PVI-dmeOs	MWCNT	Glucose oxidase, lactate oxidase	[81]
PAM	Pyrolytic graphite	Myoglobin	[80]
Poly(acrylic acid-co-itaconic acid)	MWCNT	Cd^{2+}	[90]
Chitosan	Graphene	H_2O_2	[84]
Chitosan	Au NPs	H_2O_2	[91]
PNIPAAM	Graphene	H_2O_2	[84]
Silk fibroin	Graphene	H_2O_2	[84]
CNC	Graphene	H_2O_2	[84]
Graphene oxide	PdCu NPs	Glucose	[92]
Nitrogen-doped activated graphene	Au NPs	Hydroquinone, o-dihydroxybenzene	[93]
Ferrocene (Fc) modified amino acid	Phenylalanine	Prostate specific antigen	[94]
Graphene oxide	Au NPs	Indole-3-acetic acid, salicylic acid	[95]
Pyrrole	Graphene	Ammonia gas	[96]
Graphene oxide	Au NPs	Nitric oxide	[97]
β-cyclodextrin, chitosan	Au NCs	H_2O_2	[98]
Graphene	Prussian blue	H_2O_2	[99]
Graphene oxide	Co_3O_4	Glucose	[100]
Graphene oxide	$NiCo_2O_4$	H_2O_2	[101]
Graphene oxide	ZnO	H_2O_2, glucose	[102]
Graphene oxide	Au, Pt, Pd and Cu	UA	[103]
Graphene oxide	Pyrrole, Co^{2+}	Catechol, hydroquinone	[104]

5. Conductive Polymer-Based Conductive Hydrogel

Prior to the discovery of polyacetylene's high electrical conductivity, organic polymers were thought to be insulating materials. The discovery of the electrical conductivity of polyacetylene opened the research door for optoelectronics research [105]. It has demonstrated many applications in areas such as supercapacitors, chemical and biological sensors, lithium batteries, and memory materials. On one hand, conductive polymers have properties that are similar to plastics, such as a low mass density and high flexibility. At the same time, they have properties that are similar to those of metals, such as high electrical conductivity. The combination of these two properties makes them valuable in a variety of applications. In 1980, scientists reported higher-density polyacetylene [106], and then organometallics were used as catalysts to decompose cyclooctatetraene, to produce easily soluble polyacetylene [107]. More types of conductive polymers have been prepared. In particular, new types of conductive complexes have been synthesized using the original conductive polymers doped with other conductive or non-conductive components. Such polymers are synergistically enhanced with each other, in terms of conductivity, and also have the properties of another counterpart, such as catalytic, stability and oxidation resistance.

Conductive polymer-based conductive hydrogels are mixtures of polymers or the polymerization of conductive polymers doped in a three-dimensional network of hydrogels, which means that they not only have high electrical conductivity, but also have excellent properties of hydrogels. The commonly used conductive polymers are PANI and polypyrrole (PPy); Hu et al. [108] prepared polyvinyl alcohol/glycerol/polyaniline (PGA) conductive hydrogels by organically combining PANI, PVA, and glycerol. This work discussed the effects of polyvinyl alcohol, glycerol, and benzylamine/phytic acid solution concentrations on the mechanical, electrical, and freezing resistance of PGA gels. The results show that the conductive PGA hydrogels have good electrical conductivity (0.335 S/m), fracture stress (472%), and fracture stress (94 KPa). In addition, the PGA conductive gel maintained good electrical conductivity (0.32 S/m) and mechanical properties at −20 °C. Shi et al. [109] synthesized a micro- and nano-structured conductive PPy hydrogel using the organic/water biphasic interfacial polymerization method. This method modulates the mechanical and electrochemical properties of this hydrogel by controlling the ratio of phytate-to-pyrrole monomers during the synthesis process. The doping of PPy with the azo dye molecule tartrazine also allows the formation of a 3D network of hydrogels (Figure 6) [110]. The good conductivity of this hydrogel can be used directly for the electrochemical detection of AA, DA, and UA. Table 2 summarizes the conductive polymer-based hydrogel for electrochemical sensing.

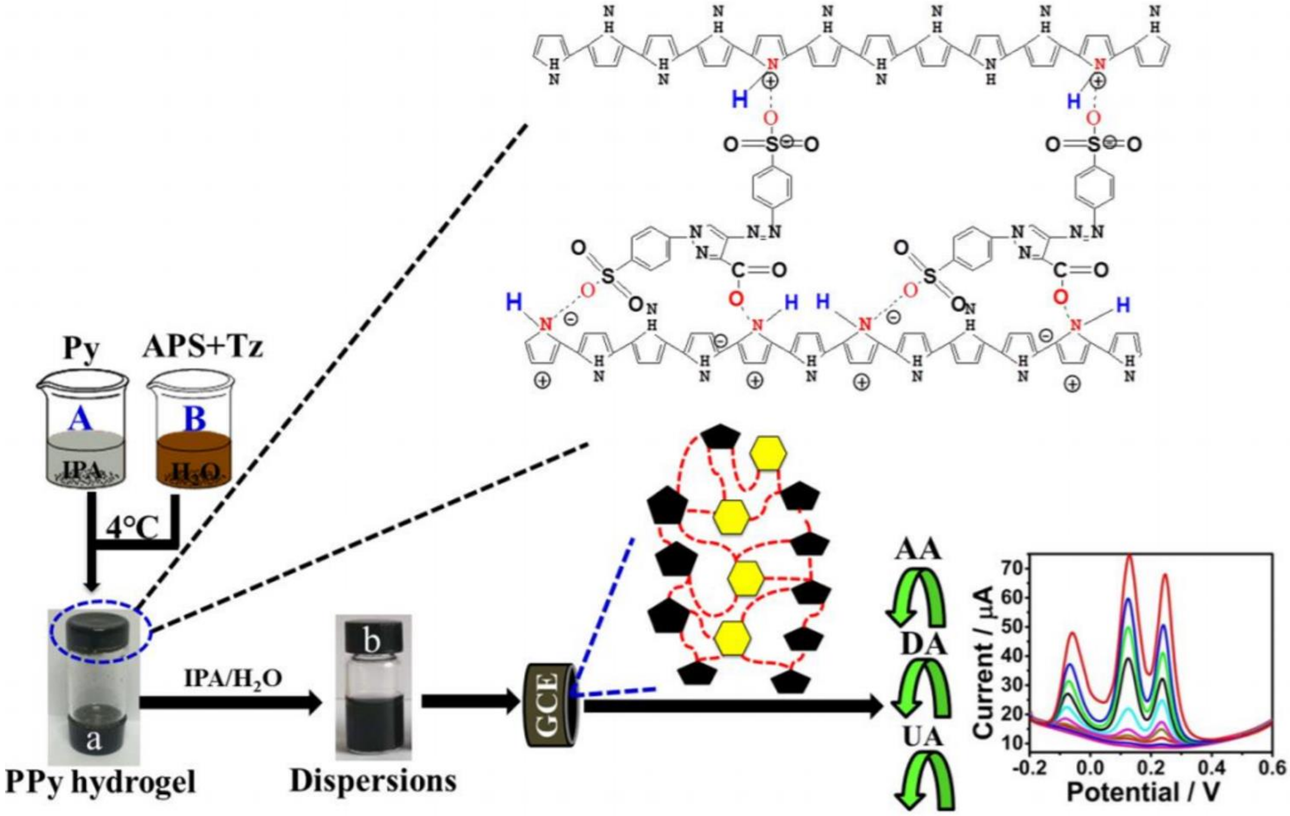

Figure 6. The fabrication process of PPy hydrogel for electrochemical determination of AA, DA, UA [110]. Copyright: Elsevier B.V.

Table 2. Summary of conductive polymer-based hydrogel for electrochemical sensing.

Conductive Polymer	Other Material	Analyte	Reference
PPy	Collagen	Glucose	[111]
PANI	PtNPs	Glucose	[112]
PPy	Tartrazine	AA, DA, UA	[110]
PANI	PAM	UA	[113]
PPy	PANI	Glucose, urea	[114]
PPy	-	Concentration of the electrolyte	[115]
PPy	p(2-hydroxyethyl methacrylate)	Glucose	[116]
PANI	Graphene	Pb^{2+}	[117]

6. Other Hydrogels

There are also some hydrogels that cannot be included in the above classifications. These types of hydrogels are used for electrochemical sensing, but do not have any components that are used to enhance their electrical properties. These hydrogels are often only used in a platform for the immobilization of biomolecules such as enzymes; for example, a peptide hydrogel composed of N-fluorenylmethoxycarbonyl-diphenylalanine was proposed for the immobilization of horseradish peroxidase enzyme [118]. This peptide hydrogel not only provides a good immobilization platform, but also maintains the enzyme activity well, and can therefore be used to detect H_2O_2 in cells. PAM and chitosan have been used for preparing hydrogel to immobilize hemoglobin. This hydrogel has also been used for detecting H_2O_2 [119].

Changes in the electrical signal upon hydrogel film cleavage can also be used for sensing analysis. Contacting a hydrogel film containing a specific cleavage site for matrix metalloproteinase-9 (MMP-9) with oxidized dextran can lead to cleavage of the hydrogel [120]. The impedance changes during this cleavage process. This change can be used for the detection of MMP-9, a peripheral biomarker of neuroinflammation in multiple sclerosis (MS). This sensor has the potential to replace MRI as diagnostic evidence for MS. A DNA hydrogel can be synthesized by target cycling and a hybridization chain reaction (HCR), with Hg^{2+}-induced activation of Mg^{2+}-specific DNAase [121]. This hydrogel can be used for the highly sensitive detection of Hg^{2+}, by alteration of the electrochemical impedance. Similar DNA hydrogels can also be formed by cross-linking ferrocene-labeled recognition probes with DNA grafted on a polyacrylamide backbone [122]. DNA hydrogels have also been used for the electrochemical detection of the platelet-derived growth factor [123] and H_2O_2 [124]. An introduction and the trends in biosensing using DNA hydrogels can be found in Li et al. article [125].

7. Conclusions and Perspectives

This review summarizes the progress of hydrogels in electrochemical sensors. Overall, hydrogels are starting to be increasingly used for the preparation of electrochemical sensors and to explore their applications in bioanalysis. Hydrogels can provide a matrix to preserve the biological activity of biomolecules, due to the special micro-water environment. At the same time, hydrogels have a very large specific surface area because of their 3D structure. Therefore, hydrogels were mainly used as a platform for the immobilization of biomolecules in early studies. These hydrogels, loaded with biomolecules, can be used for specific recognition of the analyte. However, hydrogels are mainly composed of polymers, and even though some polymers are conductive, they are still not very ideal materials for assembling electrochemical sensors. Therefore, how to improve the electrical properties of hydrogels has captured the attention of scientists in the last decade. Due to the rapid development of nanomaterials, especially carbon nanomaterials and noble metal nanomaterials, many composite hydrogels already possess excellent electrical properties. However, improving the electrochemical properties of a hydrogel does not mean that it will work well as an electrochemical sensor. Electrochemical sensors require that the analyte is involved in an electrochemical reaction at the electrode interface. Therefore, it is equally important to improve the ability of the hydrogel interface to capture the analyte. Therefore, future research needs to focus on the mechanism of interaction between different molecules and hydrogels. In addition to simple adsorption, the use of functional groups in the hydrogel composition, to grab the analytes, is also effective.

Moreover, some carbon materials, such as graphene, can be assembled into hydrogels with lamellar monomers, which ensures their usefulness in electrochemical sensors. We believe that a nanosheet of other 2D materials can also be assembled into hydrogels as monomers in the future. As different 2D materials are discovered and investigated, non-organic hydrogels will become increasingly available. This can fundamentally overcome the electrical defects of polymer-based hydrogels. At the same time, the addition of other effective components to the new hydrogels can achieve the same wide range of applications as conventional electrochemical sensors. However, due to their inherent hydrophobicity, carbon materials are often used in the synthesis of hydrogels with their oxidized derivatives. The surface oxidation of carbon materials significantly affects their electrical properties, so hydrogels are often subject to reduction after synthesis. However, the degree of reduction is a challenge for these carbon materials during their application. How to precisely control the degree of reduction in hydrogels of carbon materials is an issue to be overcome in the future.

For the time being, hydrogel electrochemical sensors do not have a performance advantage over other conventional electrochemical sensors. In many cases, their detection performance is not as good as that of the more methodologically advanced solid-state electrochemical sensors. However, hydrogel sensors have certain advantages in terms of stability, reproducibility, and shelf life. Therefore, good performance will be expected if very popular sensing methodologies, such as immunosensing and DNA sensing, are applied to hydrogel electrochemical sensors. Studies now use those molecules that are more commonly tested, such as blood glucose and H_2O_2. These molecules are already available with proven electrochemical sensors for highly sensitive detection. The special microenvironment of hydrogels can ensure a more stable performance of these sensing strategies. Therefore, how to take advantage of the hydrogel's strengths, to address some of the detection needs that require a specific microenvironment, is also the future focus of this field.

Author Contributions: Conceptualization, L.F. and G.L.; writing—original draft preparation, L.F. (with the help of A.Y.); writing—review and editing, G.L. and A.Y.; supervision, L.F. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the National Natural Science Foundation of China (22004026).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data sharing not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Kamoun, E.A.; Kenawy, E.-R.S.; Chen, X. A Review on Polymeric Hydrogel Membranes for Wound Dressing Applications: PVA-Based Hydrogel Dressings. *J. Adv. Res.* **2017**, *8*, 217–233. [CrossRef]
2. Parhi, R. Cross-Linked Hydrogel for Pharmaceutical Applications: A Review. *Adv. Pharm. Bull.* **2017**, *7*, 515–530. [CrossRef]
3. Chimene, D.; Kaunas, R.; Gaharwar, A.K. Hydrogel Bioink Reinforcement for Additive Manufacturing: A Focused Review of Emerging Strategies. *Adv. Mater.* **2020**, *32*, 1902026. [CrossRef]
4. Satarkar, N.S.; Biswal, D.; Hilt, J.Z. Hydrogel Nanocomposites: A Review of Applications as Remote Controlled Biomaterials. *Soft Matter* **2010**, *6*, 2364–2371. [CrossRef]
5. Ahmed, E.M. Hydrogel: Preparation, Characterization, and Applications: A Review. *J. Adv. Res.* **2015**, *6*, 105–121. [CrossRef]
6. Shewan, H.M.; Stokes, J.R. Review of Techniques to Manufacture Micro-Hydrogel Particles for the Food Industry and Their Applications. *J. Food Eng.* **2013**, *119*, 781–792. [CrossRef]
7. Richter, A.; Paschew, G.; Klatt, S.; Lienig, J.; Arndt, K.-F.; Adler, H.-J.P. Review on Hydrogel-Based PH Sensors and Microsensors. *Sensors* **2008**, *8*, 561–581. [CrossRef]
8. Rong, Q.; Lei, W.; Liu, M. Conductive Hydrogels as Smart Materials for Flexible Electronic Devices. *Chem. Eur. J.* **2018**, *24*, 16930–16943. [CrossRef]
9. Zhang, W.; Feng, P.; Chen, J.; Sun, Z.; Zhao, B. Electrically Conductive Hydrogels for Flexible Energy Storage Systems. *Prog. Polym. Sci.* **2019**, *88*, 220–240. [CrossRef]
10. Karimi-Maleh, H.; Orooji, Y.; Karimi, F.; Alizadeh, M.; Baghayeri, M.; Rouhi, J.; Tajik, S.; Beitollahi, H.; Agarwal, S.; Gupta, V.K. A Critical Review on the Use of Potentiometric Based Biosensors for Biomarkers Detection. *Biosens. Bioelectron.* **2021**, *184*, 113252. [CrossRef]
11. Guiseppi-Elie, A.; Wilson, A.M.; Brown, K.E. Electroconductive Hydrogels: Novel Materials for the Controlled Electrorelease of Bioactive Peptides. *Am. Chem. Soc. Polym. Prepr. Div. Polym. Chem.* **1997**, *38*, 608–609.
12. Small, C.; Too, C.; Wallace, G. Responsive Conducting Polymer-Hydrogel Composites. *Polym. Gels Netw.* **1997**, *5*, 251–265. [CrossRef]
13. Karimi-Maleh, H.; Karimi, F.; Malekmohammadi, S.; Zakariae, N.; Esmaeili, R.; Rostamnia, S.; Yola, M.L.; Atar, N.; Movaghgharnezhad, S.; Rajendran, S.; et al. An Amplified Voltammetric Sensor Based on Platinum Nanoparticle/Polyoxometalate/Two-Dimensional Hexagonal Boron Nitride Nanosheets Composite and Ionic Liquid for Determination of N-Hydroxysuccinimide in Water Samples. *J. Mol. Liq.* **2020**, *310*, 113185. [CrossRef]
14. Fu, L.; Liu, Z.; Ge, J.; Guo, M.; Zhang, H.; Chen, F.; Su, W.; Yu, A. (001) Plan Manipulation of α-Fe2O3 Nanostructures for Enhanced Electrochemical Cr(VI) Sensing. *J. Electroanal. Chem.* **2019**, *841*, 142–147. [CrossRef]
15. Wu, W.; Zhou, Q.; Zheng, Y.; Fu, L.; Zhu, J.; Karimi-Maleh, H. An Electrochemical Fingerprint Approach for Direct Soy Sauce Authentic Identification Using a Glassy Carbon Electrode. *Int. J. Electrochem. Sci.* **2020**, *15*, 10093–10103. [CrossRef]
16. Fu, L.; Zheng, Y.; Zhang, P.; Zhang, H.; Wu, M.; Zhang, H.; Wang, A.; Su, W.; Chen, F.; Yu, J.; et al. An Electrochemical Method for Plant Species Determination and Classification Based on Fingerprinting Petal Tissue. *Bioelectrochemistry* **2019**, *129*, 199–205. [CrossRef]
17. Karimi-Maleh, H.; Alizadeh, M.; Orooji, Y.; Karimi, F.; Baghayeri, M.; Rouhi, J.; Tajik, S.; Beitollahi, H.; Agarwal, S.; Gupta, V.K.; et al. Guanine-Based DNA Biosensor Amplified with Pt/SWCNTs Nanocomposite as Analytical Tool for Nanomolar Determination of Daunorubicin as an Anticancer Drug: A Docking/Experimental Investigation. *Ind. Eng. Chem. Res.* **2021**, *60*, 816–823. [CrossRef]
18. Clark, L.C., Jr.; Lyons, C. Electrode Systems for Continuous Monitoring in Cardiovascular Surgery. *Ann. N. Y. Acad. Sci.* **1962**, *102*, 29–45. [CrossRef]
19. Updike, S.J.; Hicks, G.P. The Enzyme Electrode. *Nature* **1967**, *214*, 986–988. [CrossRef]

20. Zhou, J.; Zheng, Y.; Zhang, J.; Karimi-Maleh, H.; Xu, Y.; Zhou, Q.; Fu, L.; Wu, W. Characterization of the Electrochemical Profiles of Lycoris Seeds for Species Identification and Infrageneric Relationships. *Anal. Lett.* **2020**, *53*, 2517–2528. [CrossRef]
21. Fu, L.; Wang, A.; Lai, G.; Su, W.; Malherbe, F.; Yu, J.; Lin, C.-T.; Yu, A. Defects Regulating of Graphene Ink for Electrochemical Determination of Ascorbic Acid, Dopamine and Uric Acid. *Talanta* **2018**, *180*, 248–253. [CrossRef]
22. Fu, L.; Zheng, Y.; Zhang, P.; Zhang, H.; Xu, Y.; Zhou, J.; Zhang, H.; Karimi-Maleh, H.; Lai, G.; Zhao, S.; et al. Development of an Electrochemical Biosensor for Phylogenetic Analysis of Amaryllidaceae Based on the Enhanced Electrochemical Fingerprint Recorded from Plant Tissue. *Biosens. Bioelectron.* **2020**, *159*, 112212. [CrossRef] [PubMed]
23. Wu, W.; Wu, M.; Zhou, J.; Xu, Y.; Li, Z.; Yao, Y.; Fu, L. Development of Electrochemical Sensor for Fast Liquor Authentication. *Sens. Mater.* **2020**, *32*, 2941–2948.
24. Fu, L.; Su, W.; Chen, F.; Zhao, S.; Zhang, H.; Karimi-Maleh, H.; Yu, A.; Yu, J.; Lin, C.-T. Early Sex Determination of Ginkgo Biloba Based on the Differences in the Electrocatalytic Performance of Extracted Peroxidase. *Bioelectrochemistry* **2021**, *140*, 107829. [CrossRef] [PubMed]
25. Zhang, X.; Yang, R.; Li, Z.; Zhang, M.; Wang, Q.; Xu, Y.; Fu, L.; Du, J.; Zheng, Y.; Zhu, J. Electroanalytical Study of Infrageneric Relationship of Lagerstroemia Using Glassy Carbon Electrode Recorded Voltammograms. *Rev. Mex. Ing. Quím.* **2020**, *19*, 281–291. [CrossRef]
26. Karimi-Maleh, H.; Orooji, Y.; Ayati, A.; Qanbari, S.; Tanhaei, B.; Karimi, F.; Alizadeh, M.; Rouhi, J.; Fu, L.; Sillanpää, M. Recent Advances in Removal Techniques of Cr(VI) Toxic Ion from Aqueous Solution: A Comprehensive Review. *J. Mol. Liq.* **2021**, *329*, 115062. [CrossRef]
27. Karimi-Maleh, H.; Ayati, A.; Davoodi, R.; Tanhaei, B.; Karimi, F.; Malekmohammadi, S.; Orooji, Y.; Fu, L.; Sillanpää, M. Recent Advances in Using of Chitosan-Based Adsorbents for Removal of Pharmaceutical Contaminants: A Review. *J. Clean. Prod.* **2021**, *291*, 125880. [CrossRef]
28. Cass, A.E.; Davis, G.; Francis, G.D.; Hill, H.A.O.; Aston, W.J.; Higgins, I.J.; Plotkin, E.V.; Scott, L.D.; Turner, A.P. Ferrocene-Mediated Enzyme Electrode for Amperometric Determination of Glucose. *Anal. Chem.* **1984**, *56*, 667–671. [CrossRef]
29. Fan, B.; Wang, Q.; Wu, W.; Zhou, Q.; Li, D.; Xu, Z.; Fu, L.; Zhu, J.; Karimi-Maleh, H.; Lin, C.-T. Electrochemical Fingerprint Biosensor for Natural Indigo Dye Yielding Plants Analysis. *Biosensors* **2021**, *11*, 155. [CrossRef]
30. Fu, L.; Wang, Q.; Zhang, M.; Zheng, Y.; Wu, M.; Lan, Z.; Pu, J.; Zhang, H.; Chen, F.; Su, W. Electrochemical Sex Determination of Dioecious Plants Using Polydopamine-Functionalized Graphene Sheets. *Front. Chem.* **2020**, *8*, 92. [CrossRef]
31. Fu, L.; Xie, K.; Wu, D.; Wang, A.; Zhang, H.; Ji, Z. Electrochemical Determination of Vanillin in Food Samples by Using Pyrolyzed Graphitic Carbon Nitride. *Mater. Chem. Phys.* **2020**, *242*, 122462. [CrossRef]
32. Karimi-Maleh, H.; Karimi, F.; Fu, L.; Sanati, A.L.; Alizadeh, M.; Karaman, C.; Orooji, Y. Cyanazine Herbicide Monitoring as a Hazardous Substance by a DNA Nanostructure Biosensor. *J. Hazard. Mater.* **2021**, *423*, 127058. [CrossRef]
33. Power, A.C.; Gorey, B.; Chandra, S.; Chapman, J. Carbon Nanomaterials and Their Application to Electrochemical Sensors: A Review. *Nanotechnol. Rev.* **2018**, *7*, 19–41. [CrossRef]
34. Putzbach, W.; Ronkainen, N.J. Immobilization Techniques in the Fabrication of Nanomaterial-Based Electrochemical Biosensors: A Review. *Sensors* **2013**, *13*, 4811–4840. [CrossRef]
35. Munteanu, R.-E.; Moreno, P.S.; Bramini, M.; Gaspar, S. 2D Materials in Electrochemical Sensors for in Vitro or in Vivo Use. *Anal. Bioanal. Chem.* **2021**, *413*, 701–725. [CrossRef]
36. Baig, N.; Saleh, T.A. Electrodes Modified with 3D Graphene Composites: A Review on Methods for Preparation, Properties and Sensing Applications. *Microchim. Acta* **2018**, *185*, 1–21. [CrossRef]
37. Herrmann, A.; Haag, R.; Schedler, U. Hydrogels and Their Role in Biosensing Applications. *Adv. Healthc. Mater.* **2021**, *10*, 2100062. [CrossRef] [PubMed]
38. Wang, J.; Yu, X.; Wang, C.; Xiang, K.; Deng, M.; Yin, H. PAMPS/MMT Composite Hydrogel Electrolyte for Solid-State Supercapacitors. *J. Alloys Compd.* **2017**, *709*, 596–601. [CrossRef]
39. Wang, J.; Chen, H.; Xiao, Y.; Yu, X.; Li, X. PAMPS/PVA/MMT Semi-Interpenetrating Polymer Network Hydrogel Electrolyte for Solid-State Supercapacitors. *Int. J. Electrochem. Sci.* **2019**, *14*, 1817–1829. [CrossRef]
40. Diao, W.; Wu, L.; Ma, X.; Zhuang, Z.; Li, S.; Bu, X.; Fang, Y. Highly Stretchable, Ionic Conductive and Self-recoverable Zwitterionic Polyelectrolyte-based Hydrogels by Introducing Multiple Supramolecular Sacrificial Bonds in Double Network. *J. Appl. Polym. Sci.* **2019**, *136*, 47783. [CrossRef]
41. Contin, A.; Frasca, S.; Vivekananthan, J.; Leimkühler, S.; Wollenberger, U.; Plumeré, N.; Schuhmann, W. A PH Responsive Redox Hydrogel for Electrochemical Detection of Redox Silent Biocatalytic Processes. Control of Hydrogel Solvation. *Electroanalysis* **2015**, *27*, 938–944. [CrossRef]
42. Pinyou, P.; Ruff, A.; Pöller, S.; Ma, S.; Ludwig, R.; Schuhmann, W. Design of an Os Complex-Modified Hydrogel with Optimized Redox Potential for Biosensors and Biofuel Cells. *Chem.-Eur. J.* **2016**, *22*, 5319–5326. [CrossRef]
43. Wu, Y.; Jiao, L.; Xu, W.; Gu, W.; Zhu, C.; Du, D.; Lin, Y. Polydopamine-Capped Bimetallic AuPt Hydrogels Enable Robust Biosensor for Organophosphorus Pesticide Detection. *Small* **2019**, *15*, 1900632. [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. Wang, B.; Zhang, J.; Cheng, G.; Dong, S. Amperometric Enzyme Electrode for the Determination of Hydrogen Peroxide Based on Sol–Gel/Hydrogel Composite Film. *Anal. Chim. Acta* **2000**, *407*, 111–118. [CrossRef]

46. Yan, J.; Pedrosa, V.A.; Enomoto, J.; Simonian, A.L.; Revzin, A. Electrochemical Biosensors for On-Chip Detection of Oxidative Stress from Immune Cells. *Biomicrofluidics* **2011**, *5*, 032008. [CrossRef] [PubMed]
47. Yang, W.; Xue, H.; Carr, L.R.; Wang, J.; Jiang, S. Zwitterionic Poly(Carboxybetaine) Hydrogels for Glucose Biosensors in Complex Media. *Biosens. Bioelectron.* **2011**, *26*, 2454–2459. [CrossRef] [PubMed]
48. Qu, F.; Zhang, Y.; Rasooly, A.; Yang, M. Electrochemical Biosensing Platform Using Hydrogel Prepared from Ferrocene Modified Amino Acid as Highly Efficient Immobilization Matrix. *Anal. Chem.* **2014**, *86*, 973–976. [CrossRef] [PubMed]
49. Yan, J.; Pedrosa, V.A.; Simonian, A.L.; Revzin, A. Immobilizing Enzymes onto Electrode Arrays by Hydrogel Photolithography to Fabricate Multi-Analyte Electrochemical Biosensors. *ACS Appl. Mater. Interfaces* **2010**, *2*, 748–755. [CrossRef] [PubMed]
50. Muya, F.N.; Baker, P.G.L.; Iwuoha, E.I. Polysulfone Hydrogel Nanocomposite Alkaline Phosphatase Biosensor for the Detection of Vanadium. *Electrocatalysis* **2020**, *11*, 374–382. [CrossRef]
51. De Wael, K.; Bashir, Q.; Van Vlierberghe, S.; Dubruel, P.; Heering, H.A.; Adriaens, A. Electrochemical Determination of Hydrogen Peroxide with Cytochrome c Peroxidase and Horse Heart Cytochrome c Entrapped in a Gelatin Hydrogel. *Bioelectrochemistry* **2012**, *83*, 15–18. [CrossRef]
52. Zhou, J.; Liao, C.; Zhang, L.; Wang, Q.; Tian, Y. Molecular Hydrogel-Stabilized Enzyme with Facilitated Electron Transfer for Determination of H_2O_2 Released from Live Cells. *Anal. Chem.* **2014**, *86*, 4395–4401. [CrossRef]
53. Cha, W.; Meyerhoff, M.E. S-Nitrosothiol Detection via Amperometric Nitric Oxide Sensor with Surface Modified Hydrogel Layer Containing Immobilized Organoselenium Catalyst. *Langmuir* **2006**, *22*, 10830–10836. [CrossRef] [PubMed]
54. Kowalczyk, A.; Fau, M.; Karbarz, M.; Donten, M.; Stojek, Z.; Nowicka, A.M. Hydrogel with Chains Functionalized with Carboxyl Groups as Universal 3D Platform in DNA Biosensors. *Biosens. Bioelectron.* **2014**, *54*, 222–228. [CrossRef] [PubMed]
55. Cizek, K.; Prior, C.; Thammakhet, C.; Galik, M.; Linker, K.; Tsui, R.; Cagan, A.; Wake, J.; Belle, J.L.; Wang, J. Integrated Explosive Preconcentrator and Electrochemical Detection System for 2,4,6-Trinitrotoluene (TNT) Vapor. *Anal. Chim. Acta* **2010**, *661*, 117–121. [CrossRef] [PubMed]
56. Liu, A.; Chen, X.; Wang, K.; Wei, N.; Sun, Z.; Lin, X.; Chen, Y.; Du, M. Electrochemical DNA Biosensor Based on Aldehyde-Agarose Hydrogel Modified Glassy Carbon Electrode for Detection of PML/RARa Fusion Gene. *Sens. Actuators B Chem.* **2011**, *160*, 1458–1463. [CrossRef]
57. Feng, X.; Zhang, W.; Xu, L. Surface Grafted Cross-Linked Poly(Ionic Liquid) Hydrogel for Electrocatalytic Oxidation of Cysteine. *Eur. Polym. J.* **2020**, *136*, 109928. [CrossRef]
58. Wang, C.; Ye, X.; Wang, Z.; Wu, T.; Wang, Y.; Li, C. Molecularly Imprinted Photo-Electrochemical Sensor for Human Epididymis Protein 4 Based on Polymerized Ionic Liquid Hydrogel and Gold Nanoparticle/ZnCdHgSe Quantum Dots Composite Film. *Anal. Chem.* **2017**, *89*, 12391–12398. [CrossRef]
59. Reddy, S.M.; Sette, G.; Phan, Q. Electrochemical Probing of Selective Haemoglobin Binding in Hydrogel-Based Molecularly Imprinted Polymers. *Electrochim. Acta* **2011**, *56*, 9203–9208. [CrossRef]
60. Liu, B.; Deng, Y.; Hu, X.; Gao, Z.; Sun, C. Electrochemical Sensing of Trichloroacetic Acid Based on Silver Nanoparticles Doped Chitosan Hydrogel Film Prepared with Controllable Electrodeposition. *Electrochim. Acta* **2012**, *76*, 410–415. [CrossRef]
61. Li, S.; Tao, Y.; Maryum, P.; Wang, Q.; Zhu, J.; Min, F.; Cheng, H.; Zhao, S.; Wang, C. Bifunctional Polyaniline Electroconductive Hydrogels with Applications in Supercapacitor and Wearable Strain Sensors. *J. Biomater. Sci. Polym. Ed.* **2020**, *31*, 938–953. [CrossRef]
62. Prabhakar, R.; Kumar, D. Influence of Dopant Ions on the Properties of Conducting Polyacrylamide/Polyaniline Hydrogels. *Polym.-Plast. Technol. Eng.* **2016**, *55*, 46–53. [CrossRef]
63. Prabhakar, R.; Kumar, D. Effect of Preparation Conditions on the Conductivity of Polyaniline Impregnated Polyacrylate Conducting Hydrogel. *J. Nanosci. Nanotechnol.* **2017**, *17*, 5008–5014. [CrossRef]
64. Zhao, Z.; Chen, H.; Zhang, H.; Ma, L.; Wang, Z. Polyacrylamide-Phytic Acid-Polydopamine Conducting Porous Hydrogel for Rapid Detection and Removal of Copper (II) Ions. *Biosens. Bioelectron.* **2017**, *91*, 306–312. [CrossRef]
65. Rong, Q.; Han, H.; Feng, F.; Ma, Z. Network Nanostructured Polypyrrole Hydrogel/Au Composites as Enhanced Electrochemical Biosensing Platform. *Sci. Rep.* **2015**, *5*, 11440. [CrossRef]
66. Shang, J.; Yan, J.; Zhang, Z.; Huang, X.; Maturavongsadit, P.; Song, B.; Jia, Y.; Ma, T.; Li, D.; Xu, K.; et al. A Hydrogel-Based Glucose Affinity Microsensor. *Sens. Actuators B Chem.* **2016**, *237*, 992–998. [CrossRef]
67. Tee, B.C.; Wang, C.; Allen, R.; Bao, Z. An Electrically and Mechanically Self-Healing Composite with Pressure-and Flexion-Sensitive Properties for Electronic Skin Applications. *Nat. Nanotechnol.* **2012**, *7*, 825–832. [CrossRef] [PubMed]
68. Alam, A.; Meng, Q.; Shi, G.; Arabi, S.; Ma, J.; Zhao, N.; Kuan, H.-C. Electrically Conductive, Mechanically Robust, PH-Sensitive Graphene/Polymer Composite Hydrogels. *Compos. Sci. Technol.* **2016**, *127*, 119–126. [CrossRef]
69. Chen, C.; Wang, Y.; Meng, T.; Wu, Q.; Fang, L.; Zhao, D.; Zhang, Y.; Li, D. Electrically Conductive Polyacrylamide/Carbon Nanotube Hydrogel: Reinforcing Effect from Cellulose Nanofibers. *Cellulose* **2019**, *26*, 8843–8851. [CrossRef]
70. Fu, L.; Wang, A.; Lyu, F.; Lai, G.; Yu, J.; Lin, C.-T.; Liu, Z.; Yu, A.; Su, W. A Solid-State Electrochemical Sensing Platform Based on a Supramolecular Hydrogel. *Sens. Actuators B Chem.* **2018**, *262*, 326–333. [CrossRef]
71. Fu, L.; Wang, A.; Lyv, F.; Lai, G.; Zhang, H.; Yu, J.; Lin, C.-T.; Yu, A.; Su, W. Electrochemical Antioxidant Screening Based on a Chitosan Hydrogel. *Bioelectrochemistry* **2018**, *121*, 7–10. [CrossRef]
72. Zheng, Y.; Wu, M.; Han, F.; Wu, D.; Fu, L. Evaluation of Total Antioxidant Activity of Different Floral Sources of Honeys Using Crosslinked Hydrogels. *Int. J. Electrochem. Sci.* **2019**, *14*, 1479–1487. [CrossRef]

73. Zheng, Y.; Wu, M.; Xu, Y.; Peng, X.; Zhang, M.; Wang, Q.; Du, J.; Zhang, H.; Fu, L. Electrochemical Determination of Antioxidant Activity of Different Bee Products. *Int. J. Electrochem. Sci.* **2019**, *14*, 3663–3672. [CrossRef]
74. Yan, S.; Yue, Y.; Zeng, L.; Su, L.; Hao, M.; Zhang, W.; Wang, X. Preparation of Graphene Oxide-Embedded Hydrogel as a Novel Sensor Platform for Antioxidant Activity Evaluation of Scutellaria Baicalensis. *Front. Chem.* **2021**, *9*, 220. [CrossRef] [PubMed]
75. Zhou, X.; Zhang, Y.; Jiang, B. Extraction and Electrochemical Analysis of Polyphenols in Plant Samples. *Int. J. Electrochem. Sci.* **2019**, *14*, 7410–7422. [CrossRef]
76. Zheng, P.; Wang, B.; Huang, Y.; Huang, H. Flavonoids Activity Determination of Ginkgo Sample Using Electrochemical Method. *Rev. Mex. Ing. Quím.* **2021**, *20*, 77–86. [CrossRef]
77. Zhong, R.; Tang, Q.; Wang, S.; Zhang, H.; Zhang, F.; Xiao, M.; Man, T.; Qu, X.; Li, L.; Zhang, W.; et al. Self-Assembly of Enzyme-Like Nanofibrous G-Molecular Hydrogel for Printed Flexible Electrochemical Sensors. *Adv. Mater.* **2018**, *30*, 1706887. [CrossRef] [PubMed]
78. Zhou, S.; Wang, X.; Jiang, L.; Sun, H.; Huo, D.; Hou, C. A Three-Dimensional Hydrogel-Modified Indium Tin Oxide Electrode with Enhanced Performance for in Situ Electrochemical Detection of Extracellular H_2O_2. *Analyst* **2021**, *146*, 5403–5412. [CrossRef]
79. Palanisamy, S.; Thangavelu, K.; Chen, S.-M.; Velusamy, V.; Chen, T.-W.; Kannan, R.S. Preparation and Characterization of a Novel Hybrid Hydrogel Composite of Chitin Stabilized Graphite: Application for Selective and Simultaneous Electrochemical Detection of Dihydroxybenzene Isomers in Water. *J. Electroanal. Chem.* **2017**, *785*, 40–47. [CrossRef]
80. Shen, L.; Huang, R.; Hu, N. Myoglobin in Polyacrylamide Hydrogel Films: Direct Electrochemistry and Electrochemical Catalysis. *Talanta* **2002**, *56*, 1131–1139. [CrossRef]
81. Cui, H.-F.; Ye, J.-S.; Zhang, W.-D.; Sheu, F.-S. Modification of Carbon Nanotubes with Redox Hydrogel: Improvement of Amperometric Sensing Sensitivity for Redox Enzymes. *Biosens. Bioelectron.* **2009**, *24*, 1723–1729. [CrossRef]
82. 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] [PubMed]
83. Zhu, Q.; Bao, J.; Huo, D.; Yang, M.; Hou, C.; Guo, J.; Chen, M.; Fa, H.; Luo, X.; Ma, Y. 3D Graphene Hydrogel—Gold Nanoparticles Nanocomposite Modified Glassy Carbon Electrode for the Simultaneous Determination of Ascorbic Acid, Dopamine and Uric Acid. *Sens. Actuators B Chem.* **2017**, *238*, 1316–1323. [CrossRef]
84. Burrs, S.L.; Vanegas, D.C.; Bhargava, M.; Mechulan, N.; Hendershot, P.; Yamaguchi, H.; Gomes, C.; McLamore, E.S. A Comparative Study of Graphene-Hydrogel Hybrid Bionanocomposites for Biosensing. *Analyst* **2015**, *140*, 1466–1476. [CrossRef] [PubMed]
85. Wang, H.; Han, H.; Ma, Z. Conductive Hydrogel Composed of 1,3,5-Benzenetricarboxylic Acid and Fe3+ Used as Enhanced Electrochemical Immunosensing Substrate for Tumor Biomarker. *Bioelectrochemistry* **2017**, *114*, 48–53. [CrossRef] [PubMed]
86. Feng, D.; Wang, F.; Chen, Z. Electrochemical Glucose Sensor Based on One-Step Construction of Gold Nanoparticle-Chitosan Composite Film. *Sens. Actuators B Chem.* **2009**, *138*, 539–544. [CrossRef]
87. Zanini, V.P.; López de Mishima, B.; Solís, V. An Amperometric Biosensor Based on Lactate Oxidase Immobilized in Laponite—Chitosan Hydrogel on a Glassy Carbon Electrode. Application to the Analysis of l-Lactate in Food Samples. *Sens. Actuators B Chem.* **2011**, *155*, 75–80. [CrossRef]
88. 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]
89. Al-Sagur, H.; Komathi, S.; Khan, M.A.; Gurek, A.G.; Hassan, A. A Novel Glucose Sensor Using Lutetium Phthalocyanine as Redox Mediator in Reduced Graphene Oxide Conducting Polymer Multifunctional Hydrogel. *Biosens. Bioelectron.* **2017**, *92*, 638–645. [CrossRef]
90. Chazaro-Ruiz, L.F.; Olvera-Sosa, M.; Vidal, G.; Rangel-Mendez, J.R.; Palestino, G.; Perez, F.; Zhang, W. Synthesis of Bamboo-like Multiwall Carbon Nanotube–Poly (Acrylic Acid-Co-Itaconic Acid)/NaOH Composite Hydrogel and Its Potential Application for Electrochemical Detection of Cadmium (II). *Biosensors* **2020**, *10*, 147. [CrossRef]
91. Luo, X.-L.; Xu, J.-J.; Zhang, Q.; Yang, G.-J.; Chen, H.-Y. Electrochemically Deposited Chitosan Hydrogel for Horseradish Peroxidase Immobilization through Gold Nanoparticles Self-Assembly. *Biosens. Bioelectron.* **2005**, *21*, 190–196. [CrossRef] [PubMed]
92. Yuan, M.; Liu, A.; Zhao, M.; Dong, W.; Zhao, T.; Wang, J.; Tang, W. Bimetallic PdCu Nanoparticle Decorated Three-Dimensional Graphene Hydrogel for Non-Enzymatic Amperometric Glucose Sensor. *Sens. Actuators B Chem.* **2014**, *190*, 707–714. [CrossRef]
93. Juanjuan, Z.; Ruiyi, L.; Zaijun, L.; Junkang, L.; Zhiguo, G.; Guangli, W. Synthesis of Nitrogen-Doped Activated Graphene Aerogel/Gold Nanoparticles and Its Application for Electrochemical Detection of Hydroquinone and o-Dihydroxybenzene. *Nanoscale* **2014**, *6*, 5458–5466. [CrossRef] [PubMed]
94. Huang, Y.; Ding, Y.; Li, T.; Yang, M. Redox Hydrogel Based Immunosensing Platform for the Label-Free Detection of a Cancer Biomarker. *Anal. Methods* **2015**, *7*, 411–415. [CrossRef]
95. Cao, X.; Zhu, X.; He, S.; Xu, X.; Ye, Y.; Gunasekaran, S. Gold Nanoparticle-Doped Three-Dimensional Reduced Graphene Hydrogel Modified Electrodes for Amperometric Determination of Indole-3-Acetic Acid and Salicylic Acid. *Nanoscale* **2019**, *11*, 10247–10256. [CrossRef] [PubMed]
96. Bai, H.; Sheng, K.; Zhang, P.; Li, C.; Shi, G. Graphene Oxide/Conducting Polymer Composite Hydrogels. *J. Mater. Chem.* **2011**, *21*, 18653–18658. [CrossRef]

97. Li, J.; Xie, J.; Gao, L.; Li, C.M. Au Nanoparticles-3D Graphene Hydrogel Nanocomposite To Boost Synergistically in Situ Detection Sensitivity toward Cell-Released Nitric Oxide. *ACS Appl. Mater. Interfaces* **2015**, *7*, 2726–2734. [CrossRef]
98. Manickam, P.; Vashist, A.; Madhu, S.; Sadasivam, M.; Sakthivel, A.; Kaushik, A.; Nair, M. Gold Nanocubes Embedded Biocompatible Hybrid Hydrogels for Electrochemical Detection of H_2O_2. *Bioelectrochemistry* **2020**, *131*, 107373. [CrossRef]
99. Chen, L.; Wang, X.; Zhang, X.; Zhang, H. 3D Porous and Redox-Active Prussian Blue-in-Graphene Aerogels for Highly Efficient Electrochemical Detection of H_2O_2. *J. Mater. Chem.* **2012**, *22*, 22090–22096. [CrossRef]
100. Hoa, L.T.; Chung, J.S.; Hur, S.H. A Highly Sensitive Enzyme-Free Glucose Sensor Based on Co_3O_4 Nanoflowers and 3D Graphene Oxide Hydrogel Fabricated via Hydrothermal Synthesis. *Sens. Actuators B Chem.* **2016**, *223*, 76–82. [CrossRef]
101. Lu, Z.; Wu, L.; Zhang, J.; Dai, W.; Mo, G.; Ye, J. Bifunctional and Highly Sensitive Electrochemical Non-Enzymatic Glucose and Hydrogen Peroxide Biosensor Based on NiCo2O4 Nanoflowers Decorated 3D Nitrogen Doped Holey Graphene Hydrogel. *Mater. Sci. Eng. C* **2019**, *102*, 708–717. [CrossRef]
102. Hao, N.; Zhang, X.; Zhou, Z.; Qian, J.; Liu, Q.; Chen, S.; Zhang, Y.; Wang, K. Three-Dimensional Nitrogen-Doped Graphene Porous Hydrogel Fabricated Biosensing Platform with Enhanced Photoelectrochemical Performance. *Sens. Actuators B Chem.* **2017**, *250*, 476–483. [CrossRef]
103. Du, C.; Yao, Z.; Chen, Y.; Bai, H.; Li, L. Synthesis of Metal Nanoparticle@ Graphene Hydrogel Composites by Substrate-Enhanced Electroless Deposition and Their Application in Electrochemical Sensors. *RSC Adv.* **2014**, *4*, 9133–9138. [CrossRef]
104. Qi, Y.; Cao, Y.; Meng, X.; Cao, J.; Li, X.; Hao, Q.; Lei, W.; Li, Q.; Li, J.; Si, W. Facile Synthesis of 3D Sulfur/Nitrogen Co-Doped Graphene Derived from Graphene Oxide Hydrogel and the Simultaneous Determination of Hydroquinone and Catechol. *Sens. Actuators B Chem.* **2019**, *279*, 170–176. [CrossRef]
105. Shirakawa, H.; Louis, E.J.; MacDiarmid, A.G.; Chiang, C.K.; Heeger, A.J. Synthesis of Electrically Conducting Organic Polymers: Halogen Derivatives of Polyacetylene,(CH) x. *J. Chem. Soc. Chem. Commun.* **1977**, *16*, 578–580. [CrossRef]
106. Edwards, J.H.; Feast, W. A New Synthesis of Poly (Acetylene). *Polymer* **1980**, *21*, 595–596. [CrossRef]
107. Grubbs, R.H.; Tumas, W. Polymer Synthesis and Organotransition Metal Chemistry. *Science* **1989**, *243*, 907–915. [CrossRef] [PubMed]
108. Hu, C.; Zhang, Y.; Wang, X.; Xing, L.; Shi, L.; Ran, R. Stable, Strain-Sensitive Conductive Hydrogel with Antifreezing Capability, Remoldability, and Reusability. *ACS Appl. Mater. Interfaces* **2018**, *10*, 44000–44010. [CrossRef] [PubMed]
109. Shi, Y.; Pan, L.; Liu, B.; Wang, Y.; Cui, Y.; Bao, Z.; Yu, G. Nanostructured Conductive Polypyrrole Hydrogels as High-Performance, Flexible Supercapacitor Electrodes. *J. Mater. Chem. A* **2014**, *2*, 6086–6091. [CrossRef]
110. Wang, M.; Cui, M.; Liu, W.; Liu, X. Highly Dispersed Conductive Polypyrrole Hydrogels as Sensitive Sensor for Simultaneous Determination of Ascorbic Acid, Dopamine and Uric Acid. *J. Electroanal. Chem.* **2019**, *832*, 174–181. [CrossRef]
111. Ravichandran, R.; Martinez, J.G.; Jager, E.W.H.; Phopase, J.; Turner, A.P.F. Type I Collagen-Derived Injectable Conductive Hydrogel Scaffolds as Glucose Sensors. *ACS Appl. Mater. Interfaces* **2018**, *10*, 16244–16249. [CrossRef]
112. Zhai, D.; Liu, B.; Shi, Y.; Pan, L.; Wang, Y.; Li, W.; Zhang, R.; Yu, G. Highly Sensitive Glucose Sensor Based on Pt Nanoparticle/Polyaniline Hydrogel Heterostructures. *ACS Nano* **2013**, *7*, 3540–3546. [CrossRef]
113. 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]
114. Brahim, S.; Wilson, A.M.; Narinesingh, D.; Iwuoha, E.; Guiseppi-Elie, A. Chemical and Biological Sensors Based on Electrochemical Detection Using Conducting Electroactive Polymers. *Microchim. Acta* **2003**, *143*, 123–137. [CrossRef]
115. Ismail, Y.A.; Martínez, J.G.; Al Harrasi, A.S.; Kim, S.J.; Otero, T.F. Sensing Characteristics of a Conducting Polymer/Hydrogel Hybrid Microfiber Artificial Muscle. *Sens. Actuators B Chem.* **2011**, *160*, 1180–1190. [CrossRef]
116. Brahim, S.; Narinesingh, D.; Guiseppi-Elie, A. Polypyrrole-Hydrogel Composites for the Construction of Clinically Important Biosensors. *Biosens. Bioelectron.* **2002**, *17*, 53–59. [CrossRef]
117. Muralikrishna, S.; Nagaraju, D.H.; Balakrishna, R.G.; Surareungchai, W.; Ramakrishnappa, T.; Shivanandareddy, A.B. Hydrogels of Polyaniline with Graphene Oxide for Highly Sensitive Electrochemical Determination of Lead Ions. *Anal. Chim. Acta* **2017**, *990*, 67–77. [CrossRef] [PubMed]
118. Lian, M.; Chen, X.; Lu, Y.; Yang, W. Self-Assembled Peptide Hydrogel as a Smart Biointerface for Enzyme-Based Electrochemical Biosensing and Cell Monitoring. *ACS Appl. Mater. Interfaces* **2016**, *8*, 25036–25042. [CrossRef] [PubMed]
119. Zeng, X.; Wei, W.; Li, X.; Zeng, J.; Wu, L. Direct Electrochemistry and Electrocatalysis of Hemoglobin Entrapped in Semi-Interpenetrating Polymer Network Hydrogel Based on Polyacrylamide and Chitosan. *Bioelectrochemistry* **2007**, *71*, 135–141. [CrossRef]
120. Biela, A.; Watkinson, M.; Meier, U.C.; Baker, D.; Giovannoni, G.; Becer, C.R.; Krause, S. Disposable MMP-9 Sensor Based on the Degradation of Peptide Cross-Linked Hydrogel Films Using Electrochemical Impedance Spectroscopy. *Biosens. Bioelectron.* **2015**, *68*, 660–667. [CrossRef]
121. Cai, W.; Xie, S.; Zhang, J.; Tang, D.; Tang, Y. An Electrochemical Impedance Biosensor for Hg^{2+} Detection Based on DNA Hydrogel by Coupling with DNAzyme-Assisted Target Recycling and Hybridization Chain Reaction. *Biosens. Bioelectron.* **2017**, *98*, 466–472. [CrossRef] [PubMed]
122. Liu, S.; Su, W.; Li, Y.; Zhang, L.; Ding, X. Manufacturing of an Electrochemical Biosensing Platform Based on Hybrid DNA Hydrogel: Taking Lung Cancer-Specific MiR-21 as an Example. *Biosens. Bioelectron.* **2018**, *103*, 1–5. [CrossRef]

123. Chang, Y.; Li, M.; Wu, Z.; Zhuo, Y.; Chai, Y.; Xiao, Q.; Yuan, R. Homogeneous Entropy Catalytic-Driven DNA Hydrogel as Strong Signal Blocker for Highly Sensitive Electrochemical Detection of Platelet-Derived Growth Factor. *Anal. Chem.* **2018**, *90*, 8241–8247. [CrossRef] [PubMed]
124. Mao, X.; Chen, G.; Wang, Z.; Zhang, Y.; Zhu, X.; Li, G. Surface-Immobilized and Self-Shaped DNA Hydrogels and Their Application in Biosensing. *Chem. Sci.* **2018**, *9*, 811–818. [CrossRef] [PubMed]
125. Li, F.; Lyu, D.; Liu, S.; Guo, W. DNA Hydrogels and Microgels for Biosensing and Biomedical Applications. *Adv. Mater.* **2020**, *32*, 1806538. [CrossRef]