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Review

Electrochemical and Other Methods for Detection and Determination of Dissolved Nitrite: A Review

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Nitrite has been widely used in industrial and agricultural production and is ubiquitous in food, water, biology and the environment. However, nitrite is also a toxic inorganic contaminant that is hazardous to the health of humans and other organisms. A variety of strategies have been proposed for detecting and monitoring nitrite in recent years. This article was compiled as a general review of the strategies proposed for nitrite detection, and relevant detection parameters (such as materials, detection limit, detection range, working pH and stability) were tabulated. This article is organized by the type of signal obtained from strategies, including electric and optical signals. Electrochemical methods receive an electric signal from dissolved nitrite, with voltammetric, potentiometric and impedimetric methods included. Methods that receive an optical signal include fluorescence, absorption and Raman spectrometry. Biosensors are proposed as a new detection method. The advantages/disadvantages and limitations of the techniques are discussed. Finally, methods employed to perform nitrite detection are summarized, and their future development is discussed.

Keywords: Dissolved Nitrite Detection, Review, Electrochemistry, Spectrometry, Biosensor

1. INTRODUCTION

Nitrite has been widely used in meat curing [1], food preservatives [2, 3], dyes, bleaches, fertilizers as well as for medicinal purposes [4]. Nitrite can also be converted to the potent vasodilator nitric oxide [5], which is relevant in numerous physiological processes [6].

However, nitrite is also a toxic inorganic contaminant that is hazardous to the health of humans and other organisms. Methemoglobinemia or “blue baby syndrome” [7], carcinogenic nitrosamines [8],

gastric cancer (GC) [9], spontaneous intrauterine growth restriction [10], abortions [11] and birth defects of the central nervous system [12] have been associated with high nitrite concentrations.

Nitrites can also cause damage to aquaculture through its toxicity to aquatic animals, including fish and crustaceans. As nitrite can oxidize hemoglobin to methemoglobin, which is not capable of carrying oxygen, the latter can reach toxic concentrations in a high-density aquaculture system in contaminated waters. However, other studies have suggested that methemoglobinemia may not be the primary mechanism of nitrite toxicity. [13] In aquatic animals, nitrite can be taken up across gill epithelia and can be accumulated to a high concentration in bodily fluids; thus, there is a greater risk for aquatic animals than for terrestrial animals. In addition, high nitrite concentrations have caused considerable economic losses to aquaculture production. The nitrite uptake and toxicity mechanisms have been introduced in several reviews [13-16] and are not further discussed here. Many species of fish have been investigated to determine the relationship between nitrite concentration and fish diseases. The toxicity of nitrite to fish varies with fish species. A table has been compiled with the median lethal concentrations (LC_{50}) of different fish species according to the work of William M. Lewis and coworkers [17].

Due to the damage caused by nitrite to human health and aquaculture production, relative standards have been established to limit the concentration of nitrite in potable water, food and aquaculture water. The World Health Organization (WHO) recommends a maximum nitrite concentration in drinking water of 3 mg/l as nitrite ion (or 0.9 mg/l as nitrite-nitrogen). [18] The maximum allowed nitrite concentration in meat products is 200 ppm. Similar standards have been formulated by many countries to limit nitrite concentration. With these limitations, several methods have been proposed to remove nitrite from water, including chemical/electrochemical methods [19] and bio-methods [20-22].

Because of the toxicity and impact of nitrite on industry, agriculture, environment and biological systems, our need and desire to monitor this ion are unquestionable. Many methods have been developed for trace level detection and to overcome potential interferences that would be encountered within various solutions. Electrochemical methodologies [23], including voltammetric [24, 25], potentiometric [26, 27] and impedimetric electrodes [28, 29], convert nitrite ions to current signal, potential difference and impedance, respectively. These methods are easily performed, consuming no or few reagents and requiring no complex or time-consuming pretreatment; in addition, the detection equipment is inexpensive and easily designed. Spectroscopic methodologies, including fluorescence spectrometry [30, 31], absorption spectrometry [32, 33] and Raman spectroscopy [34, 35], convert the presence of nitrite ion to optical signals. Spectroscopic methodologies can usually reach a very low detection limit with good precision. Combined with enrichment and separation methods, such as capillary electrophoresis, chromatography and liquid extraction, the detection limit can be further reduced. To perform continuous and automatic detection, flow injection analysis and related methods [30, 32, 36-38] have already been developed and introduced and include sequential flow injection analysis, microfluidic and on-chip analysis. Biosensors [39, 40] can generally be classified as electrochemical electrodes that obtain an electrical signal from an analyte through chemical reactions. However, biosensors are different from traditional electrodes, as biologically active materials are used as modifiers to achieve selectivity, specificity and catalytic activity. Due to

their higher sensitivity and specificity, the application of biosensors to nitrite detection has attracted much attention.

A number of excellent reviews have been compiled over the past decade. [23, 41-47] However, detection requirements and technology have developed in recent years. The aim of this article is to review various nitrite detection methods proposed in recent years and to summarize their technologies, advantages and disadvantages. This review is organized based on the type of signal obtained from the methods, including electric and optical signals. Biosensors are proposed as a new detection method. By tabulating the various analytical parameters (including materials, detection limit, detection range, working pH and stability) of each method, their performance and research trends can be observed. Finally, the advantages/disadvantages and limitations of each technique are discussed.

2. ELECTROCHEMICAL METHODOLOGIES

Electrochemical detection techniques have been investigated for in situ quantitative analysis and real-time monitoring of environmental parameters. [23, 43, 46] Technologies used to detect nitrite can be divided into a number of categories, of which voltammetric, potentiometric and impedimetric methods are routinely introduced. Articles using these categories are compiled, and their performances are tabulated.

2.1. Voltammetric electrodes

A voltammetric or amperometric electrode provides a current signal to represent the rate of reactions on the probe surface while a potential is applied to the working electrode. The potential applied to the working electrode is determined to avoid oxygen interference and obtain a strong electrode response to nitrite oxidation, including sensitivity and response time. [48] A typical measuring system consists of three electrodes, including working, reference and counter electrodes. A current-to-voltage converter and voltage amplifier are needed to convert the working probe current to voltage and amplify it to a suitable range for the analog-to-digital converter (ADC) to sample. The result can then be transmitted, saved, calculated, or displayed on a local instrument or remote monitor.

Voltammetric methodologies have been employed to detect and monitor nitrite since the early 1900s, when glassy carbon electrodes [49-52] were used that continuously detect without additional agent consumption. A great number of substrates have since been investigated for voltammetric detection and to improve electrode performance, such as copper, nickel, boron-doped diamond, platinum, carbon, cadmium, alloys, gold, lead and indium tin oxide. [41, 42] However, a disadvantage was discovered; the bare electrode has a poor electron-transfer rate, and the effect of electrode passivation caused by species formed during the electrochemical process tend to poison the electrode.

A number of strategies have been proposed to solve these problems, of which surface modification seems to be the most promising to greatly improve selectivity and sensitivity. Several

organic/inorganic catalysts and enzymes may be used as modifiers that can remarkably improve the sensibility and selectivity of electrodes by enhancing the reduction or oxidation of nitrite.

Ag nanoplates [53] grafted on the surface of a glassy carbon electrode may be used as a sensitive sensor for the assessment of nitrite. In addition, carbon black (CB) [54], reduced graphene oxide and dendritic copper nanoclusters [55], poly(3,4-ethylenedioxythiophene)–Au nanoparticles (PEDOT–AuNPs) composites [56], polyaniline (PANI)-Cu nanocomposites [57] and graphene oxide/palladium (ERGO-Pd) nanocomposites [58] have been investigated as modifiers on glassy carbon electrodes. Polymeric films of pyronin Y (PyY) [59] and platinum black [60] have also been reported as modifiers on pencil graphite electrodes (PGE) and platinum, respectively.

The carbon nanotube-based electrode is another promising substrate that has been investigated as a nitrite sensor with a number of modifiers. Zhang et al. constructed a composite film of vanodotungstophosphate, α_2-$K_7P_2VW_{17}O_{62}\bullet 18H_2O$ ($P_2W_{17}V$), and carbon nanotubes (CNTs) that was used as a sensitive amperometric nitrite sensor. [61] Palladium nanostructures were deposited onto pre-patterned single-walled carbon nanotube (SWCNT) thin films to perform nitrite detection with a detection limit of 0.25 μM (S/N=3). [25]

In addition to a variety of modifications, photochemical catalysis is also a potential method to facilitate the performance of electrodes and obtain a rapid response. Photocatalysis technology has been investigated by X. F. Chen et al. and Li XiuTing et al. [62, 63], but no nitrite electrodes that use photocatalysis technology have been investigated before.

Increasing the sensitivity of the electrode response can also be achieved by constructing and exposing a large and highly active surface area. This goal can be achieved by the nanoparticle electroplating technique. Appropriate ions are dissolved in an electrolyte with a potential sweeping the immersed electrode in the cathodic direction. The metal ions are then electrolytically plated onto the electrode, providing a fresh surface for nitrite to undergo the oxidation-reduction reaction. A significant advantage of this approach is that the analysis is relatively independent of the base electrode material, as the nitrite reaction occurs at the freshly deposited metal layer.

Ag nanoplate-modified electrodes (AgNP/GC), which have high current response to the electrooxidation of NO^{2-}, benefit from the enhanced surface area and high specific activity of AgNP/GC due to the exposure of many defect sites. [53] Solid paste electrodes prepared using a nanostructured carbon black [54], reduced graphene oxide and dendritic copper nanoclusters [55], AuNPs inserted into a PEDOT layer [56], single-walled carbon nanotubes (SWCNTs) [64] and carbon nanotube thin film electrodes immobilized on urchin-like palladium nanostructures [25] also benefit from large surface areas for higher current response, sensitivity and LOD.

Polarography [65-68] has also been introduced for detection of nitrite, as the behavior of a dropping mercury electrode (DME) is relatively independent of its past history. Polarography has high accuracy and reproducibility, as a liquid working electrode is used that can continuously refresh and remain unpolluted from contamination without interference among polarographic waves. Ummihan T. Yilmaz and Guler Somer [66] have reproducibly detected trace nitrite using differential pulse polarography (DPP) with a dropping mercury electrode (DME).

Materials such as indium tin oxide (ITO) and gold or diamond electrode that are fragile and expensive make fabrication difficult and not suitable for batch manufacture and application. Xuan-

Hung Pham and co-workers immobilized Pd NPs, which are highly electrocatalytic, nontoxic and chemically inert to oxygen, on SWCNT film electrodes that were fabricated on a poly(ethylene terephthalate) substrate to obtain a flexible, transparent Pd/SWCNT electrode with high sensitivity, low detection limit, high selectivity, wide linear range and low cost. [25]

Table 1. Parameters and performances of voltammetric electrodes.

Material	Working pH	Detection limit	Linear range	RSD	Stability	Reference
Urchin-like palladium nanostructures on carbon nanotube thin film	4.0	0.25 μM	2-238 μM 283-1230 μM	2.14 %	Working 14 days, 95% remained	[25]
Pyronin on pencil graphite electrode	4.0	5.0×10^{-7} M	1.0×10^{-6}-1.0×10^{-4} M	N/A	Used 100 times in one day, 84% remained	[59]
Carbon fiber	8.0	0.02 mgN	0-25 mgN	N/A	Working 17 h, 96% remained	[48]
Carbon black on solid paste electrode	4.6	5 nM	0.01-4 μM	2.5%	N/A	[54]
Reduced graphene oxide and dendritic copper nanoclusters on glassy carbon electrode	2.0	0.4 μM	1.25×10^{-3}-13 mM	3.3%	Stored at 4℃ for 4 weeks, 87% remained	[55]
Ionic liquid n-octylpyridinum hexafluorophosphate (OPFP) on single-walled carbon nanotube	7.0	0.1 μM	1.0μM-12.0 mM	3.5%	Working 60 min, 94% remained. Stored in air 100 days, 92% remained	[69]
Dawson-type vanodotungstophosphate on carbon nanotubes	7.0	0.036 μM	5×10^{-8}-2.13×10^{-3} M	3.38 %	Stored in air at room temperature for 50 days, 98.05% remained	[61]
Crystalline silver nanoplates on glassy carbon electrode	6.0	1.2×10^{-6} M	1×10^{-5}-1×10^{-3} M	N/A	N/A	[53]
Chemically reduced graphene oxide on glassy carbon electrode	5.0	1 μM	8.9-167 μM	0.726 %	Stored 9 days, 82.35% remained	[70]
Polyaniline nanofiber on glassy carbon electrode	N/A	0.05 μM	0.2μM-35 mM	5.2%	N/A	[71]
Polythionine/carbon nanotube on glassy carbon electrode	0.0	1×10^{-6} M	N/A	2.75 %	Stored 3 weeks, 81% remained	[72]

Microelectrodes [73-75] have also been fabricated and investigated to extend the detection area in cases where the electrode stick is too large for use, such as biological tissue detection [48]. Sonotrodes have also been investigated and introduced to electrochemistry detection systems to clean electrodes and eliminate the harmful effects that are caused by deposition of oxides, gas bubbles and ions of chemical compounds on its surface. The use of sonotrodes have given nitrite electrodes the ability to detect solutions with highly passivating matrices. Additionally, the in situ detection system can continuously work longer with a self-cleaning ability. [76-78]

Detailed sensor parameters are compared in

Table 1. Many materials have been investigated, and nanometric materials have been employed to obtain larger surface areas. Voltammetric electrodes can work in solutions whose pH ranges from 4.0 to 8.0, thus including neutral solutions. The lowest detection limit of the tabulated electrodes is 5 nM, which has been significantly improved, and a relative standard deviation of 2.5% has been obtained.

2.2. Potentiometric electrodes

The potentiometric electrode detects ions with the assistance of organic membranes that contain an appropriate ionophore or ion-exchanger with specific binding affinity for the target ion and carry a particular charged species from the sample to the electrode area. A potential difference is formed between the reference and indicator electrodes with the appearance of a charged species, without current flowing between electrodes, and no species are consumed or produced. The potential difference varies with the logarithm of the concentration under the condition that the concentration of the ion of interest is sufficiently low that the activity coefficients can be considered constant; otherwise, the response curve should be calibrated.

Potentiometry with ion-selective electrodes has improved significantly in recent years, notably by achieving very low detection limits. The key advantages of potentiometry are signal selectivity to the analyte of interest, the ability to probe a large range of species that are not redox-active in aqueous environments, low detection limit [23] and applicability to colored and turbid samples [79]. The required instrumentation is also simple to fabricate, easy to use, inexpensive and portable. Many researchers have sought to devise ion-selective electrodes, often covered with membranes incorporated with suitable ionophores, for potentiometric detection of nitrite. Of course, neither option is particularly favorable. Several issues exist in potentiometric methods, such as low electrode response, interference from other species, unfeasible miniaturization due to unstable potential when the electrode approaches micrometer dimensions, common fluctuation of reference potential and potential drifts with time. [23]

Two electrodes are employed by the potentiometric method. A saturated calomel electrode (SCE) or Ag/AgCl electrode is typically employed to provide a reference for the working electrode. The working electrode, which provides selectivity and sensitivity towards the species of interest, is more complex than the reference electrode.

A number of complexes have been reported as nitrite-selective ionophores, including Co(III)-cyanocobyrinate [80-82], Co(III)-phthalocyanine [83], Co(III)-tetraphenylporphyrin derivatives [84], Co(III)-aquocyanocobyrinate [85], cobalt(III) tetraazaporphyrins [86], cobalt salens [87], In(III)-tetraphenylporphyrin chloride derivatives [88], benzylbis(triphenylphosphine) palladium(II) [89], UO_2-salophen [90], corrins [80] and phthalocyanines [80].

Most biosensors suffer from poor stability due to the fragility of the protein structure, as the activity of immobilized enzymes may be rapidly annihilated by inhibition processes or denaturation due to protein unfolding, high temperatures or harsh chemical conditions. In that context, immobilized

biomimetic compounds were prepared to replace biological macromolecules that mimic the activity of the enzymes on an electrode surface that should be more stable. [91] Cosnier and coworkers demonstrated a cobalt(II) deuteroporphyrin derivative that was electropolymerized with the ability to perform potentiometric detection of nitrite by recording the shift of the reduction potential of [Dp Co(II) NO^{2-}]$^{-}$.

A number of nitrite ion-selective electrodes have been reported, but strong interference effects existed from anionic species such as perchlorate, thiocyanate and iodide in a polymeric membrane doped with Co-salen as an ionophore [92] and acetate salts of three Co(III)-tetraphenylporphyrin derivatives [93].

Table 2. Parameters and performances of potentiometric and impedimetric electrodes.

Method	Material	Working pH	Detection limit	Linear range	RSD	Stability	Reference
Potentiometry	Cobalt(III),10,15-tris(4-tert-butylphenyl) corrole in a plasticized poly(vinyl chloride) membrane	4.5	5 μM	N/A	N/A	Soaked for 14 days, <82.92% remained	[26]
Potentiometry	Rhodium(III) porphyrins and salophens in a polymeric membrane electrode	4.5	5 μM	N/A	N/A	66 days, 88.71% remained	[27]
Potentiometry	Metallo-salens of cobalt(II) in a polymer-membrane electrode	5.0	N/A	1.58×10^{-5}-0.138 M	N/A	N/A	[87]
Potentiometry	Co(III)-tetraazaporphyrin in a PVC matrix	2.3-6.4	1.0 μM	1.1×10^{-5}-1.0×10^{-1} M (NL)	N/A	Stored under 0.1 M solution of corresponding anion, 5 months	[86]
Potentiometry	Co(II)-salophen complex in a PVC matrix	4.5-11.9	8.0×10^{-7} M	1.0×10^{-6}-1.0×10^{-1} M (Nernstian)	N/A	Can be used at least 2 months without divergence	[94]
Potentiometry	Poly(pyrrole-cobalt(II)deuteroporphyrin)	N/A	N/A	2×10^{-6}-2.5×10^{-4} M	N/A	N/A	[91]
Impedimetry	Naphthylethylenediamine on a gold electrode	N/A	20 nM	0.1-4 μM	N/A	N/A	[28]
Impedimetry	PTFE membrane, zinc-filled reduction column and bulk acoustic wave impedance sensor	N/A	1.8 μM	2.5 μM-1.00 mM	1.75 %	N/A	[95]

The cobalt(III)-based complexes reported cannot adequately discriminate against the most lipophilic anions such as thiocyanate and salicylate.[96] However, a PVC-based membrane nitrite sensor based on the Co(II)-salophen complex (CSC) has also been reported that exhibits good selectivity over fluoride, bromide, iodide, sulfite, nitrate, thiocyanate, triiodide and perchlorate [94] In addition, polymeric membrane electrodes based on rhodium(III) porphyrins and salophens as

Ionophores have been proposed with better nitrite selectivity over thiocyanate, perchlorate, and salicylate. The best nitrite selectivity and longest functional lifetimes were obtained with membranes doped with carboxylated PVC and Rh-tBTPP, respectively. The response time can be partially shortened by employing polymer matrix additives such as polyurethanes or carboxylated PVC. [27]

Lipophilic vitamin B_{12} derivative complexes with cobalt(III) as the metal center have been exploited that have high selectivity for nitrite over chloride as a ionophore. However, these complexes exhibited a nearly equivalent potentiometric response to thiocyanate. A corrole ligand with a different metal ion center shows different selectivity towards different ions, and a Co(III) center can serve as a nitrite-selective ionophore. Sensors with proper amounts of lipophilic cationic sites have greatly enhanced nitrite response and selectivity. Based on the above findings, plasticized polymeric membrane electrodes incorporated with cobalt(III) corrole were investigated for potentiometric detection of nitrite. [26]

PVC membrane electrodes cooperated with nitrite-selective carriers have been fabricated as a nitrite-responsive detector with good selectivity. [83, 84, 97, 98] However, the PVC membrane has poor adhesion on certain solid substrates, such as silicon chips; thus, other polymeric matrices have been explored, including functionalized PVC, polyurethane (PU), silicone rubber and poly(acrylate or methacrylate), accompanied by poor electrochemical performance and limited plasticizer compatibility. Malinowska and coworkers investigated an anion-selective electrode based on metal(III) porphyrin ionophores in polyurethane membranes, with potentiometric responses to nitrite obtained. Significant potentiometric anion response and selectivity of the metal(III) porphyrin membranes were also observed in the presence of endogenous cationic sites in PU; in contrast, the anionic sites in PVC have no exogenous lipophilic sites added. [99]

Some of the potentiometric electrodes are compiled in

Table 2. Ccompared with voltammetric electrodes, the detection limit of potentiometric electrodes is somewhat higher, thus limiting their application in fields in which trace amounts of nitrite must be detected. But potentiometric electrodes are more easily and conveniently used, as no stimulation circuits are needed for detection.

2.3. Impedimetric electrodes

Electrochemical sensors whose impedance is proportional to an increase in nitrite concentration have also been investigated. To obtain the impedance of this electrode type, stimulation is also needed. When a voltage stimulation is applied to the electrode, the current from the electrode must be detected, and current stimulation requires voltage detection.

Wang and coworkers immobilized naphthylethylenediamine (NEA) onto a gold electrode to form positively charged self-assembled monolayers (SAMs). The positive charges on the electrode facilitated access of the negatively charged $[Fe(CN)_6]^{3-/4-}$ probes to the electrode surface. The nitrite-mediated Griess reaction between NEA and sulfanilic acid (SA) on the electrode surface lead to the formation of negatively charged SAMs, which produced a barrier to electron transfer between the

redox probe and the electrode. This Griess reaction-based method has been demonstrated, achieving a detection limit of 20 nM. [28]

A flow-injection system has been developed based on the use of a zinc-filled reduction column and a bulk acoustic wave impedance sensor (BAWIS) as detector. Both nitrate and nitrite are converted on-line to ammonia with water as a carrier stream, but only nitrate is converted to ammonia with sulfamic acid as a carrier. The formed ammonia diffuses across a PTFE membrane and is trapped in an acid stream, causing a change in the solution conductance. At a throughput of approximately 60 h^{-1}, the system achieves a detection limit of 1.8 μM for nitrite. [95]

Few inorganic impedimetric nitrite electrodes have been investigated with few RSD and stability data acquired. As shown in

Table 2, a similar detection limit as voltammetric electrodes and even lower can be achieved.

3. SPECTROSCOPIC METHODOLOGIES

Spectroscopic methods for nitrite detection operate generally by measuring the radiation or absorption intensity of a particular wavelength affected by nitrite. Spectroscopy is a detection method that can be cooperated with other separation and enrichment methods, such as capillary electrophoresis [100], chromatography [101] and liquid-liquid extraction [102], to improve detection accuracy and decrease the detection limit. Flow injection analysis [30], sequential injection analysis [103], reverse flow injection analysis [37] and microfluidic analytical devices [32] have also been employed for reagent injection, mixture and reaction as a cooperated automation technology.

3.1. Fluorescence spectrometry

In the spectrofluorimetric detection of nitrite, the light emitted by a reagent that absorbed light or other energy can be detected. Fluorescence spectroscopy detection was first reported in 1972 by Gen-Ichiro Oshima and Kinzo Nagasawa, employing benzidine for detection. [104] Fluorescence spectroscopy detection can be divided into two categories: turn-on and turn-off type. Nitrite dissolved in solution can enhance the fluorescence intensity of turn-on indicators, while the fluorescence intensity of turn-off indicators is typically reduced, also known as fluorescence quenching detection. A large variety of indicators have been investigated for nitrite detection, including cerium [105], 2,3-diaminonaphthalene (DAN) [106], 2'7'-dichlorofluorescein [107], tetra-substituted amino aluminum phthalocyanine (TAAlPc) [108], rhodamine 3GO [109] and rhodamine 110 [110].

3.1.1. Turn-on indicator-based methods

Chemiluminescence assays require an expensive and bulky apparatus and are interfered by NG-nitro-L-arginine and some nitroso compounds. In addition, the fluorometric method cannot easily detect trace amounts of nitrite due to high blank values and fluorescence quenching. Additional

preparative steps to remove interfering substances may cause variable recovery and introduce contamination in detection. Therefore, rapid determination of nitrite by reversed-phase high-performance liquid chromatography with fluorescence detection was developed to perform detection at picomole levels of nitrite, including the reaction of nitrite with 2,3-diaminonaphthalene (DAN) to form 2,3-naphthotriazole (NAT), the chromatographic separation of NAT, and the fluorescence detection of NAT. [111]

For an ultra-low detection limit, separation and extraction methods have been employed. Akyuez and Ata proposed a method for nitrite detection in which aqueous nitrite was reacted with 2,3-diaminonaphthalene (DAN) under acidic conditions to form 2,3-naphthotriazole (NAT) and extracted with toluene. The toluene layers were then analyzed by gas chromatography–mass spectrometry (GC–MS) and liquid chromatography with fluorescence detection (LC-FL). A detection limit of 0.29 pg/ml on S/N=3 has been achieved. [112]

Luminol chemiluminescence (CL) detection is a commonly used method for nitrite detection. Accompanied with a Cu–Cd reductor column, luminol CL can also be used for nitrate detection. Nitrite is oxidized to peroxynitrous acid by H_2O_2 in an acidic medium, which is converted to the peroxynitrite anion in an alkaline medium and oxidizes luminol to generate CL emission. [113] Another luminol method, based on ion-exchange separation (HPLC), online photochemical reaction and FIA, has been proposed to implement nitrite and nitrate detection without a Cu-Cd redactor column. Nitrite and nitrate were separated using an anion-exchange column and were then converted to peroxynitrite by UV irradiation using a low-pressure mercury lamp and mixed with a luminol solution to yield chemiluminescence. The key advantage is the employment of a photochemical reaction instead of a copperized cadmium column, thereby eliminating the production of harmful effluents. [114]

Rhodamine has also been used as a fluorescent indicator to detect nitrite. Kumar et al. developed a rhodamine-based fluorescent probe for the detection of trace amounts of nitrite ions in water. The probe operates by the diazotization of its amino group, followed by opening of the spirocyclic ring, intra-molecular rearrangement and fragmentation to produce rhodamine B in an acidic solution (pH 1). Extremely high sensitivity and selectivity were obtained over many other anionic species. [115] Rhodamine B hydrazide was employed as a fluorescence indicator to detect nitrite under acidic pH [116] but is not applicable in natural water at neutral pH. Rhodamine B phenyl hydrazide is sensitive to acid and undergoes ring-opening in acidic media without addition of any ions or oxidizing agents in solution; thus, the compound was synthesized and has been reported as an indicator for NO^{2-} with remarkably high sensitivity and selectivity in aqueous methanol at pH 7.0 over other common ions and oxidants (Cl^-, ClO^-, ClO^{2-}, ClO^{3-}, ClO^{4-}, SO_4^{2-}, SiO_3^{2-}, NO_3^{2-}, CO_3^{2-}). [31]

For nitrite detection out of the library, microanalysis devices have been developed. Nitrite is sensed by the chemiluminescence (CL) reaction of luminol with ferricyanide, which is the product of the reaction of ferrocyanide with nitrite in an acidic medium. He et al. developed a microflow injection analysis system on a chip for the determination of nitrite. [117] In addition to this on-chip analysis system, a microfluidic device with optical fibers has also been proposed in which N-(9-acridinyl)maleimide (NAM) is used as the indicator. [118]

3.1.2. Turn-off indicator-based methods

A number of reagents have been employed as fluorescence quenching indicators, and some of these detection methods cooperate with separation methods. Constantine D. Stalikas and coworkers investigated an ion chromatographic method for the simultaneous determination of nitrite and nitrate by post-column indirect fluorescence detection. The method uses an enhanced fluorescence mobile phase containing tryptophan, and suppression of fluorescence caused by the elution of the target ions was detected. A highly induced fluorescence quenching effect of tryptophan was observed by the presence of phosphate ions, which are utilized as buffer solution components in the flow stream for the post-column reaction. [119]

A notable enhancement of fluorescence response was obtained when a conjugated polyelectrolyte was used in the sensory scheme. Fe^{2+} can easily be oxidized to Fe3+ in the presence of NO^{2-} and H^{+}; the ferric ion dramatically quenches the fluorescence of $PPESO_3$. Thus, anionic conjugated polyelectrolytes and $PPESO_3$ (poly[2,5-bis(3-sulfonatopropoxy)-1,4-phenylethynylene-alt-1,4-poly(phenyleneethynylene)]) have been employed for nitrite detection based on fluorescence quenching effects. [120]

The photochemical reduction of nitrite to NO and generation of peroxynitrite have also been achieved via UV irradiation instead of a cadmium-copper column, and subsequent chemiluminescent detection was employed based on luminol chemiluminescence for nitrite detection. [121]

As modifiers can detach from modified probes, a stability problem is encountered. Silica nanoparticles covalently grafted with a rhodamine derivative of p-hydroxybenzaldehyde, rhodamine 6G hydrozone (Rh 6G-OH), on the surface was fabricated for nitrite detection based on the nitrosation reaction, and high selectivity for nitrite ion in the presence of interference ions was obtained. More importantly, organic dye leakage can be effectively prevented by covalent-grafting of Rh 6G-OH to the surface of SiO_2 nanoparticles. [122]

Spectrofluorimetric microdetermination of nitrite in water was reported after derivatization with 4-methyl-7-aminocoumarin. [123] However, the method involved several steps, including synthesis of the diazonium salt of coumarin and two cumbersome liquid–liquid extraction procedures requiring nearly an hour. A fast and simple method was developed by the use of 6-aminocoumarin (L) without derivatization of the aminocoumarin. The result is an efficient nitrite ion-selective fluorescent sensor in which interference from other common anions is almost negligible. [6]

Lanthanide-based hybrid materials have attracted great attention in sensing systems [124, 125] due to their quite strong photoluminescence performances with specific analytes. However, their applications have been greatly restricted due to their human toxicity and the difficulty of recycling and collecting powder hybrid materials. Therefore, two luminescent cellulose hydrogel films have been synthesized that have high flexibility and can be used to detect nitrite via a simple and green process based on luminescence quenching effects. Nitrite addition resulted in efficient quenching effects of photoluminescence intensity, in contrast to the stable emissions upon exposure to other comparative ions (SO_4^{2-}, CO_3^{2-}, ClO_3^{-}, NO_3^{-}, AcO^{-}, OH^{-}, F^{-}, Cl^{-}, Br^{-}, I^{-}, K^{+}, Na^{+}, Fe^{2+}, Mn^{2+}, Pd^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+} and Fe^{3+}). [126]

Quantum dots have attracted much attention for analytical applications because of their excellent fluorescence properties, high photochemical stability and excellent resistance to chemical degradation relative to organic dyes. [127, 128]

The electrochemiluminescence (ECL) behavior of Si nanocrystals (NCs) was first studied by Bard in 2002 [129], and NCs have been extensively investigated as a new type of ECL emitter, with many NC-based ECL sensing strategies reported [130]. NCs were also employed for nitrite detection based on the ECL quenching of dual-stabilizer-capped CdTe QDs. Experiments have been conducted by Xunxun Yin, achieving a detection limit of 1.4 nM. [131]

To increase CL intensity and system selectivity, Hb was introduced to a nitrite detection system based on a CdTe CL system, which resulted in significant enhancement of the CL signal. Hb reacts with H_2O_2 to produce a large number of hydroxyl radicals that then interact with the QDs, leading to the injection of holes into the 1Sh quantum-confined orbitals of the CdTe QDs with great enhancement of chemiluminescence intensity. Additional nitrite in the system reacts with ferrous Hb to form ferric Hb and NO, then NO binds to ferrous Hb to generate iron nitrosyl Hb, resulting in the quenching of the CL from the CdTe QDs-based CL system [30]

Table 3. Parameters and performances of fluorescence spectrometric methods.

Method type	Material	Working pH	emission	Detection limit	Detection range	RSD	Reference
Turn-on	Rhodamine B phenyl hydrazide	7.0	584 nm	N/A	N/A	N/A	[31]
Turn-on	Dipodal-cobalt(II)	7.4	395 nm	N/A	N/A	N/A	[132]
Turn-on	Luminol	12.0	425 nm	0.01 μgN	0.01-50 μgN	2.0%	[113]
Turn-on	Rhodamine	1.0	585 nm	4.6 ppb	8-40 ppb	N/A	[115]
Turn-on	Luminol	10.0	540 nm	2.0 nM	2.0×10^{-9}-2.5×10^{-6} M	2.6%	[114]
Turn-on	2,3-diaminonaphthalene (GC-MS)	N/A	416 nm	0.02 ng	2.5-100 ng	1.0%	[112]
Turn-off	CdTe quantum dots (QDs), hemoglobin (Hb)	N/A	607 nm	3.0×10^{-10}M	1.0×10^{-9}-8.0×10^{-7} M	2.84 %	[30]
Turn-off	Gold nanoclusters (GNC)	6.0	622 nm	30 nM	0.1-50 μM	3.1%	[133]
Turn-off	Dual-stabilizer-capped CdTe quantum dots	7.4	522 nm	1.4 nM	4.2-207 nM(L)	N/A	[131]
Turn-off	Water-soluble CdSe quantum dots (QDs)	7.0	511 nm	0.2 μM	1μM-0.5 mM(L)	1.72 %	[134]
Turn-off	AuNCs (BSA–AuNCs)	7.4	670 nm	1.0 nM	2.0×10^{-8}-5.0×10^{-5} M(L)	3.5%	[135]
Turn-off	Terbium silica xerogels (Ha and Hb)	5.0	540 nm	N/A	1×10^{-5}-1×10^{-4} M	N/A	[126]
Turn-off	Rh 6G-functionalized silica nanoparticles	N/A	551 nm	1.2 μM	3-60 μM	N/A	[122]
Turn-off	Conjugated polyelectrolytes, $PPESO_3$	N/A	530 nm	0.62 μM	0-70 μM	4.2%	[119]

Xun Yao and coworkers have prepared CdSe quantum dots (QDs) for nitrite detection based on the quenching effect of nitrite, achieving a detection limit of 0.2 μM. Water-soluble CdSe QDs have been fabricated with L-cysteine as the stabilizer, which has low toxicity compared with traditional hydrosulfonyl reagents, for electrochemiluminescence determination of nitrite. The ECL emission of CdSe QDs is greatly enhanced by sulfite and is gradually quenched by nitrite at an indium tin oxide (ITO) electrode. [134]

With quantum dots, encouraging developments have been achieved in analytical applications, but inherent compositional toxicity limits their applications [136, 137]. Gold nanoclusters (AuNCs), whose advantages include low toxicity, excellent biocompatibility, stability, good solubility, strong fluorescence emission and excellent photostability [138-140], have attracted much attention as a fluorescent probe. [141-144] Because of their attractive advantages, near-infrared (NIR)-emitting bovine serum albumin-stabilized AuNCs (BSA-AuNCs) have been prepared via sonochemical methods by Hongying Liu and coworkers for construction of the first nitrite sensor based on the selective fluorescence quenching effect towards nitrite, with a detection limit of 1.0 nM. [135] In similar work by Yue et al., a detection limit of 30 nM was obtained under optimal conditions. [133]

As shown in

Table 3, fluorescence spectrometric methods can achieve a very low detection limit, and their wavelength range is in the scope of visible light. A pH range of 1.0 to 10.0 is suitable for these indicators, and some are optimal in neutral solution.

3.2. Absorption spectrometry

The absorption of a specific is measured to quantify the amount of a specific substance, as the substance can absorb energy (photons) from radiation of a specific wavelength. The absorption spectrum is usually measured by detecting the intensity of the radiation that passes through the substance upon irradiation with a specific wavelength. Light with different wavelengths has been employed for nitrite detection.

3.2.1. Colorimetric spectrophotometry

The complementary color of visible light absorbed by an analyte is usually detected in colorimetric spectrophotometry. A chromogenic reagent is usually needed, as well as reagents to preprocess the analyte and remove impurities and interfering ions. For colorimetric nitrite detection, the Griess diazotization reaction is widely used.

Gong Weidong and coworkers reported an optical detection system of a prototype nitrite sensor based on the Griess reaction with a green light-emitting diode (LED) light source and two integrated photo detectors. A limit of detection of 0.1 μM was obtained. [145] A primary amine that is produced on polyurethane foam by hydrolysis of the terminal urethane groups with hydrochloric acid has also been investigated for nitrite detection. The primary amine reacts with nitrite to form a diazonium ion in the foam matrix, which couples with α-naphthylamine, α-naphthol, β-naphthol, 8-hydroxyquinoline,

resorcinol, or catechol. A purple azo dye produced in the foam membranes is then used for quantitative spectrophotometric determination of nitrite. [146]

For a lower detection limit, preprocess methods have been introduced, such as separation and enrichment. Gapper et al. have introduced ion exchange liquid chromatography (LC) for spectrophotometric detection of nitrite using Griess reagents. [147] Polyetherimide (PEI)-composed membranes have also been employed for nitrite enrichment in samples with an on-line dialysis preconcentration nitrite determination system based on injection methods. The PEI method resulted in high dialyzing yield and analytical signal and low blank signal without membrane clogging. Nitrite penetrated from the PEI membrane is diazotized with sulfanilamide to form an active diazonium in the recipient (acceptor) stream that subsequently couples with N-(1-naphthyl)-ethylenediamine dihydrochloride to form a stable purple azo dye with measured absorbance at 525 nm. [148]

Solid-phase enrichment techniques are another type of preconcentrate method employed to improve the detection limit before Griess reaction-based colorimetric detection. [149] On-line solid-phase extraction (SPE) and liquid waveguide capillary cell (LWCC) spectrophotometric detection have been combined to construct a flow analysis system that can monitor nanomolar levels of nitrite and nitrate simultaneously. The azo compound formed from nitrite will be quantitatively extracted on an HLB SPE cartridge and then eluted and detected in a 16-cm path length LWCC detector. Experiments have been conducted with a detection limit of 0.3 nmol/L. [150]

The Griess reagent has been used as a commercial nitrite sensor. However, special attention is required for the preparation and storage of this reagent because of the usage of high concentrations of three different components and complexity of the operating procedure. A novel aza-BODIPY probe has been developed for sensitive colorimetric detection of the nitrite ions by a simple and direct method. A distinct visual color change from bright blue to intense green appears as nitrite contacts the probe. This probe is reportedly the simplest probe that can be used in the form of strips or dipsticks for on-site analysis of nitrite. [33]

For simultaneous automated detection, sequential injection analysis (SIA) has been employed in a fiber-optic spectrophotometer based on the Griess method. The formed azo dye was measured at 540 nm. [103, 151]

Due to its large physical size, power consumption and large amounts of reagent consumed, the conventional FIA system is unsuitable for long-term, on-site and remote detection. Reagent consumption as well as size and power requirements can be reduced by microfluidic platforms. Some microchip absorption cells with small path lengths result in reduced sensitivities and high LODs. A continuous-flow, microfluidic tinted PMMA absorption cell and detection system has been designed with integrated optical illumination and detection. The system detects nitrite based on the Griess reaction, with a limit of detection of 14 nM. [152]

In addition to the microfluidic platform, a wireless, portable, integrated microfluidic analytical platform for in situ monitoring and quantitative determination of nitrite in freshwater samples was also designed. The miniaturized gold-standard Griess assay is employed for detection of nitrite within a poly-(methylmethacrylate) (PMMA) microfluidic device in which a biomimetic photo-switchable phosphonium ionogel microvalve functionalized with spiropyran was used to control and manipulate flows in microchannels. The microvalve can be actuated by illumination with a light-emitting diode,

and the nitrite concentration is determined by a highly sensitive, low-cost wireless PEDD detector, ensuring inexpensive fabrication and functioning of the whole platform. However, the PSPNIPAAm ionogel-based valves require exposure to acidic solution to induce swelling, and the shrinking mechanism of the gel results in the release of protons into the external solution around the gel. Thus, the pH requirement restricts its application to enzyme- or antibody-based methods or the handling of cells and proteins, which typically require neutral pH. In such cases, the acidic solution must be pushed through the microfluidic system in front of the assay reagents. [32]

In addition to the Griess reaction, there are other methods proposed for absorption detection of nitrite. Daniel et al. have prepared two types of gold nanoparticle (Au NP) probes for nitrite detection based on spectrophotometry. The first one features aniline Au NPs modified with 5-[1,2]dithiolan-3-yl-pentanoic acid [2-(4-amino-phenyl)ethyl]amide (DPAA). The second type features naphthalene Au NPs modified with 5-[1,2]dithiolan-3-yl-pentanoic acid [2-(naphthalene-1-ylamino)et-hyl]amide and MTA. The solution containing aniline and naphthalene Au NPs is red due to intense surface plasmon resonance at 520 nm. When nitrite is added, the amine groups on the aniline Au NPs convert to a diazonium salt under acidic conditions. The diazonium salt then couples with the naphthalene Au NPs to form covalently interconnected nanoparticle probes. Finally, precipitate crosslinked particle networks will form, causing the solution to become colorless. However, the detection limit is somewhat high. [153]

Table 4. Parameters and performances of absorption and Raman spectrometric methods.

Method	Materials	Working pH	Absorbance	Detection limit	Detection range	RSD	Reference
Absorption spectrometry	Griess reagent (microfluidic analytical platform)	3	540 nm	34.0 μg	N/A-1.2 mg	1.93 %	[32]
Absorption spectrometry	Aza-BODIPY (dipyrromethene boron difluoride)	0.2	570 nm	20 ppb (0.5μM)	0-2 ppm	N/A	[33]
Absorption spectrometry	(Ion chromatography)	5	225 nm	0.6 μg	0-2.5 mg	1.81 %	[154]
Absorption spectrometry	Griess-Ilosvay reagent (sequential injection analysis)	N/A	540 nm	0.0022 mg N	0.01-0.42 mg	0.46 %	[103]
Absorption spectrometry	Poly(vinyl chloride) (PVC) particles, quaternary ammonium salt (detection by color band length and number of colored zebra-bands)	N/A	474 nm 514 nm	N/A	0.5-45.3 mg N	N/A	[155]
Absorption spectrometry	Griess reagent (microfluidic analysis system)	1-2	525 nm	14 nM	50 nM-10 μM	N/A	[152]
Absorption spectrometry	(Solid-phase extraction)	N/A	540 nm	0.3 nmol	2-100 nmol	3.6%	[150]
Raman spectrometry	Gold nanoparticle core with an ultrathin silica shell (based on diazotization-coupling reaction)	N/A	N/A	0.07 mg	0.5-6.0 mg	14.5 %	[34]
Raman spectrometry	Poly(4-aminostyrene), 2-naphthol and single-walled carbon nanotubes	N/A	785 nm	5 μM	5-1000 μM	N/A	[35]

Another method to detect nitrite concentration is to read the color band length and number of colored zebra-bands. A detecting tube packed with poly(vinyl chloride) (PVC) particles coated with a quaternary ammonium salt into a mini-column has been developed. Nitrite solution is treated with sulfanilic acid and 1-naphthol; the resulting colored solution is drawn into the detecting tube by suction with a syringe, and a color band then forms in the tube. The color band length (CBL) corresponds to nitrite concentration. Another type of detecting tube has been prepared by alternately packing adsorbent and uncoated PVC particles in a mini-column. In this column, colored zebra-bands are formed whose number is proportional to nitrite concentration. However, the accuracy obtained with these methods is somewhat low, and preparation of the detecting tube to produce colored zebra-bands is difficult. [155]

3.2.2. Ultraviolet spectrophotometry

In addition, ultraviolet radiation has been used as an absorption photometric method for nitrite detection. Different ions have different absorption peaks at a corresponding wavelength. Therefore, a specific analyte can be detected by measuring the absorbance at a certain wavelength. Other wavelengths are needed to distinguish or detect interfering ions.

Ultraviolet spectrophotometry has been employed for nitrite detection in combination with anion chromatography, which was used for anion separation. This measurement does not require pretreatment of samples and reagents yet still achieves nanomolar detection limits and requires <100 ml of samples. [156] Chromatography (IC) and ultraviolet (UV) spectrophotometry have also been used for nitrite detection with the assistant of dilauryldimethylammonium-coated monolithic ODS columns and sodium chloride as an eluent. [154]

An existing UV spectrophotometer was adapted for on-line detection of nitrite with a sequential batch reactor (SBR). Samples react sufficiently in an SBR, and a UV spectrophotometer detects specific ions. The detection system also has a filtering module that is developed to provide particle-free fluids to the sensor. The system has run for five months with a detection range of 0 to 18 mg/L for nitrite and, except for the filtering module, is nearly non-consumable. [157]

As shown in

Table **4**, absorption spectrometry also results in a very low detection limit. Most of these methods work in acidic solution, and the detection wavelength varies from ultraviolet to visible light. Similar to fluorescence spectrometry, reagents are needed for absorption spectrometry.

3.3. Raman spectrometry

Raman spectroscopy has also been employed to measure nitrite by detecting the scattered light. A photon striking a molecule excites it from its ground state to a virtual energy state and interacts with the electron cloud and bonds of that molecule. The molecule emits a photon upon returning to a different rotational or vibrational state. The sample may then be quantitatively measured by measuring the intensity of inelastically scattered light.

However, spontaneous Raman scattering is very weak, making it difficult to separate weak inelastically scattered light from intense Rayleigh-scattered light. Thus surface-enhanced Raman spectroscopy (SERS) [158, 159] was proposed, with tremendously enhanced Raman scattering obtained. This method has been employed for nitrite detection with the use of 4-aminobenzenethiol (4-ABT) on Au, with a detection limit of 5 μM. [160]

Additionally, when the excitation wavelength matches the electronic transition of the molecule, the molecule experiences resonance Raman scattering (RRS), in which the vibrational modes associated with the excited electronic state are greatly enhanced. Based on this finding, UV resonance Raman spectroscopy has been investigated to monitor nitrite. [161]

To improve the selectivity and stability of SERS substrates, shell-isolated nanoparticle-enhanced Raman spectroscopy (SHINERS) [162, 163] was developed. This method has been used to detect trace nitrite based on the diazotization-coupling reaction of nitrite with p-nitroaniline in the presence of diphenylamine in acidic media, where Au/SiO2 nanoparticles with pinholes were used as the SHINERS substrate. The concentration of nitrite can be detected indirectly from azo dye. [34]

In addition, surface resonance Raman scattering (SERRS), which combines SERS with RRS, has also been investigated; this method can provide nondestructive and ultrasensitive detection down to the single-molecule level [164].

4. BIOSENSORS

Biosensors used to perform nitrite detection are typically voltammetric, potentiometric and impedimetric [29] electrodes. As biosensors usually show higher sensitivity and specificity, there is emerging interest in their investigation for direct detection of nitrite.

A variety of biosensors have been developed for nitrite detection that use a number of modifiers, such as copper-containing nitrite reductase (Cu-NiR) and viologen-modified sulfonated polyaminopropylsiloxane (PAPS-SO_3H-V) [165], copper-containing nitrite reductase (Cu-NiR, from Rhodopseudomonas sphaeroides forma sp. denitrificans) and viologen-modified chitosan (CHIT-V) [166], cytochrome c (Cyt c) [167], single-layer grapheme nanoplatelet (SLGnP)–protein [168], myoglobin (Mb) [169] and a (Mb)-L-cysteamine (Cys)-AuD biological hybrid [170].

In addition to the variety of modifiers, many substrates have also been investigated, such as a gold electrode modified with Nafion and a Cu-Mg-Al layered double hydroxide (Cu-LDH) [167], LaF_3-doped CeO_2 (LaF_3-DP-CeO_2) [169] and a glassy carbon electrode [165].

The irreversible denaturation of proteins in a rigid environment and difficult contact between the prosthetic group and the electrode result in a slow DET between cytochrome c and conventional unmodified electrode materials. [171] Several modification strategies and immobilization methodologies have been employed to provide biologically favorable microenvironments for proteins such as ITO electrodes modified with polyaniline derivatives [172], platinum electrodes modified with fully sulfonated polyaniline nano-networks [173] and GCE modified with hybrid poly-(3-methylthiophene) (P3 MT) and multiwalled carbon nanotubes (MWCNT) [174].

Hb as a bio-modifier has been immobilized on a number of substrates, such as a carboxyl-functionalized multiwalled carbon nanotubes/polyimide composite [175], a gold nanoparticles/polythionine/platinum nanoparticles-modified glassy carbon electrode [176] and a pencil lead electrode [177]

However, the deep burying of heme groups in the large three-dimensional structure of the proteins and the denaturation of Hb when immobilized onto the electrode surface make it difficult to transfer electrons from hemoglobin (Hb) to conventional electrodes. The additional diffusion resistance offered by entrapment materials or the mesopores usually results in lower sensitivity and a higher detection limit. Therefore, Hb was directly electrospun onto the surface of a glassy carbon (GC) electrode with a highly porous structure, which significantly reduces the additional diffusion resistance of analytes without the use of an entrapment matrix. [178] Biological incompatibility can also make the DET difficult when biomolecules are directly composited on an electrode surface. To improve the biosensor performance, Shaghayegh Saadati et al. fabricated a glassy carbon electrode modified with a covalently attached amine-terminated ionic liquid and titanium nitrite nanoparticles used as support for immobilization of hemoglobin protein with direct electron transfer and achieved excellent bioelectrocatalytic nitrite reduction activity. [39]

Table 5. Parameters and performances of biosensors.

Material	Working pH	Detection limit	Detection range	RSD	Stability	Reference
Hemoglobin on glassy carbon electrode	3.0-11.0	0.1μM	N/A-2 mM	2.7%	Stored 5 days, 88% remained	[39]
Hydroxylamine oxidase (HAO) and electrode modified by zirconia nanoparticles (ZrO2 NPs)	7.0	N/A	3-117 μM	N/A	21 days, 87% remained	[179]
Copper, zinc superoxide dismutase (SOD1) on carbon nanotubes (CNT)–polypyrrole (PPy) nanocomposite-modified platinum electrode	7.0	50 nM	100 nM-1 mM	N/A	Stored at 4℃ for 1 month, 92% remained; for 2 months, 83% remained	[40]
Hemoglobin-modified pencil lead electrode (Hb/PLE)	7	5 μM	10-220 μM	2%	N/A	[177]
Hemoglobin immobilized on gold nanoparticles/polythionine/platinum nanoparticles-modified glassy carbon electrode	6.0	20 nmol	70 nmol-1.2 mmol	5.2%	Suspended above 0.1 mol/L pH 6.0 PBS at 4℃ for a month, 90% remained	[176]
Hemoglobin immobilized on carboxyl-functionalized multiwalled carbon nanotubes/polyimide composite	7.0	0.63 μM	3-68 μM	N/A	N/A	[175]
Gold dendrites (AuD) and myoglobin (Mb)-L-cysteamine (Cys)-AuD	7.0	0.3 μM	0.5-400 μM	2.3%	Stored 4 weeks, 95% remained	[170]
Myoglobin on LaF3-doped CeO2 and ionic liquid composite film	7.0	2 μM	5-4650 μM	4.2%	Stored at 4℃ in 0.1 M pH 7.0 PBS for 2 weeks, 95% remained; for a month,	[169]

					87% remained	
Catalase on gold electrode	7.3	8×10^{-11} M	N/A	N/A	N/A	[29]

Electron donors and acceptors are usually needed to activate the nitrite redox enzyme, which can transport electrons to or from the enzyme. However, the donors or acceptors are often expensive and not economically feasible for use in industrial processes. As an improvement, biosensors without electron donors and acceptors have been designed. The latest such sensor was fabricated based on a carbon paste electrode and zirconia with hydroxylamine oxidase enzyme by Hamideh Dehghani and coworkers. [179]

For simultaneous measurement of nitrite and nitrate in biological samples, a bienzymatic biosensor using copper, zinc superoxide dismutase (SOD1) and nitrate reductase (NaR) co-immobilized on a carbon nanotubes (CNT)–polypyrrole (PPy) nanocomposite-modified platinum electrode was developed. Two enzymes were co-immobilized on an electrode surface, with biological activity completely retained. To provide a porous host matrix for the immobilization of SOD1 and NaR, the electrode surface was modified with polypyrrole (PPy) and a well-ordered conductive polymer chain with good environmental stability [180] was also provided. CNT–PPy nanocomposites with additional surface area to immobilize more SOD1 and NaR also act as molecular wires to accelerate electron transfer between underlying electrode and active sites. To eliminate possible interferences during measurements in biological samples, a cellulose acetate (CA) membrane was also used. The electrocatalytic activity of SOD1 towards nitrite was observed at +0.8 V with a detection limit of 50 nM and sensitivity of 98.57±1.7 nA $mM^{-1}cm^{-2}$. [40]

An obvious feature of biosensors is that they usually work in neutral solution, as shown in

Table 5. So that it is convenient to perform nature water detection. And as shown in Table 5, biosensors also have a low detection limit due to the high activity of the protein or enzyme toward the analyte.

5. CONCLUSION AND FUTURE PERSPECTIVES

Electrochemical sensors and biosensors, which are simple, inexpensive and easily miniaturized, have been investigated for many years to improve their selectivity and sensitivity. These sensors are suitable for miniaturization and long-term monitoring. Compared with spectroscopy, their detection limit is somewhat higher. But they are easily used and require no reagents or complex instruments. Spectroscopic methodologies can get very low detection limits and can be used to detect trace amounts. At the same time, reagents are required by spectroscopic methods to perform detection. Reagent consumption have been observably reduced by microfluidic systems.

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