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*Review*

# Biosensing Strategies to Monitor Contaminants and Additives on Fish, Meat, Poultry and Related Products

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**Abstract:** Biosensors have emerged as highly sensitive, rapid, and specific tools for detecting food safety hazards, particularly in perishable products such as fish, meat, and poultry. These products are susceptible to microbial contamination and often contain additives intended to improve shelf life and flavor, which may pose health risks to consumers. Recent advances in biosensor technologies integrated with smartphones, artificial sensing systems, 3D printing, and the Internet of Things (IoT) offer promising solutions for real-time monitoring. This review explores the types, mechanisms, standardization approaches, and validation processes of biosensors used to detect contaminants and additives in animal-based food products. Furthermore, the paper highlights current challenges, technical limitations, and future perspectives regarding the broader implementation of biosensors in modern food safety monitoring systems.

**Keywords:** biosensor; fish; meat; quality; monitoring; standardization

## 1. Introduction

Many types of contaminants interns of physical, allergenic, environmental, chemical and biological components present in fish, meat, poultry and related products. At present, about 600 million due to foodborne illnesses and 420,000 annual food-related deaths are reported by World Health Organization [1]. Quality and safety deteriorated fish, meat, poultry and related product could cause foodborne illnesses on consumers. Chemical and biological contaminants such as antibiotics residues, toxic chemicals, additives, heavy metals, pathogens and pesticides present in food products have been reported. For instance, nitrate in meat sample [2], chloramphenicol (antibiotics residue) in beef and pork meat samples [3], *Salmonella enterica*, *Listeria monocytogenes*, and *Escherichia coli* in ready-to-eat beef, chicken and turkey breast meat [4], adulteration of donkey meat in cooked sausages [5], fish spoilage bioamines like hypoxanthine in fish samples [6] etc. have been reported. Rapidly and accurate detection of these food contaminants that solve the traditional (culture-based techniques) are getting emphasis to the current food quality and safety adminstration system. Labor-intensiveness, expensive (required cost of chemicals), time-consuming, requirement

of trained personnel, and very limited to onsite detection (laboratory based) are constraints of culture-based, antibody-based immunoassays, fatty acid and protein profiling, chromatographic separations, and spectroscopic techniques of food contaminant detection [1]. Target analytes in meat and fish samples types of bioreceptors and means of measurement is illustrated in Figure 1.

Biosensors are analytic devices employed to analyse, record, and transform biochemical information by controlling the interaction of immobilized bioreceptors and chemical components from pathogenic or naturally produced, or additives used in foods [7,8]. Food biosensors applications in intelligent packaging like labeling, microbial spoilage, time-temperature integrators, biosensors, nanosensors, Radio Frequency Identification tags, barcodes, etc. are being familiar at industrial or commercial levels [9]. Based on their measurement techniques and type of transducers use during real-time monitoring, biosensors are classified as physical (measure changes in mass as pressure, strain or fors), electrical (measure changes in electric distribution), calorimetric (measure changes in heat), optical (measure changes in light), magnetic (measure changes in magnetic field). and ion channel switch (measure changes in functional molecular interaction) [1]. Other classifies biosensors based on the type of biorecognition element employ to detect target analytes in fish, meat and poultry- related products quality and safety monitoring. Enzyme-based biosensors, immunosensors and DNA-based biosensor are known in these type as described by Nami, *et al.* [7]. Readout mechanisms of biosensors are also means of classification into acoustic wave, surface plasmon resonance-SPR, and mass spectrometry, and label-based like fluorescence and chemiluminescence bioreceptors as designated by Nanda *et al.* [9].

Standardization and validation of biosensors in fish, meat, poultry and related product quality and safety monitoring for better reliability, reproducibility, and regulatory acceptance is mandatory at commercial and industrial levels. Complexity of food matrices and interference of environmental and biochemical changes could reduce reliability and reproducibility of biosensors. Hence, calibration and standardization should be regular approaches to establish   For instance, calibrating heat-transfer biosensor employed to detect trace levels of chemical additives in dairy for assurance of consistent sensitivity and reproducibility was conducted [10]. Although many types of biosensors to monitor fish and meat samples are being developed to date, due to standardization and validation limitations incorporating into regulatory and commercial systems, such as HACCP, ISO 22000:2018, or Codex Alimentarius frameworks are not yet realized. This review is intended to share insights on biosensing strategies of biosensors to monitor contaminants and additives in fish, meat, poultry and related products. Moreover, a brief discussion on standardization and validation of biosensors in real-time quality analysis as well as current challenges, technical limitations, and future perspectives of biosensor utilization have been addressed.
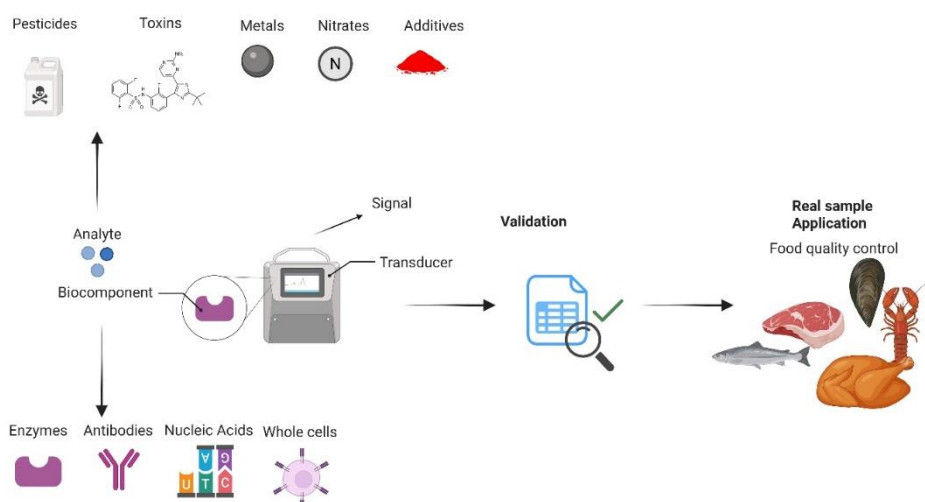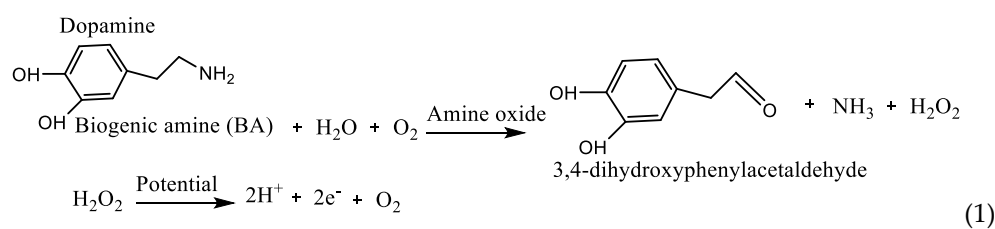


**Figure 1.** Schematic representation of meat and fish sample target analytes, biorecognition elements and an analytical method.

## 2. Biosensors and Monitoring Strategies of Fish, Meat, Poultry and Related Product Quality Parameters

*2.1. Biosensor Development Strategies and Mechanism of Sensing*

Biosensors are analytic devices employed to analyse, record, and transform biochemical information by controlling the interaction of immobilized bioreceptors and chemical components from pathogenic or naturally produced, or additives used in foods [7]. Bioreceptors are incorporated into biosensor as reversible and irreversible immobilization strategies [1]. The presence of chemical components such as xanthine, histamine in fish and fishery products, pathogens like Salmonella species in poultry products and *Echerichia* coli (*E. coli*) in ground beef are mainly sources of food-borne diseases [7]. Hence, monitoring their availability and standardizing their permissible limit is very crucial. Bioreceptors developed by reversible immobilization employing proteins and enzymes are applicable for generating biorecognition elements. These biorecognition elements easily detach from the sensing surface so that to be linking and binding agents during reuse of biosensor [1,11]. However, the biorecognition element (bioreceptors) made by irreversible immobilization has strong crosslinking, entrapment, and covalent bonding mechanisms [11,12]. Irreversible immobilization of bioreceptors help to develop highly stable biorecognition element though have significant limitations such as loss of enzyme activity, toxicity of linkers used, and demand of high purity of enzymes [1]. Figure 2 shows detection of biogenic amines in meat samples with different measurement techniques. Moreover, Figure 3 illustrates the strategies of glucose biosensor preparation process and electrochemical measurement glucose reduction in fresh meat.

Biosensors contain a bioreceptor and a transducer as two major parts for accurate detection of chemical components and transform biochemical information into electrical or optical signals. These bioreceptors are immobilized with nucleic acids, antigens, or hormones, or enzymes, molecularly imprinted polymers (MIP), or chemoresponsive dyes such as chemical/natural pH dyes, conjugated polymers, colorimetric sensor arrays, and fluorophores for recognizing and identifying each target element. Whereas, the transducer helps to transform the biochemical information into electrical or optical signals later measured employing colorimetric or electroanalytical devices [7]. The sensing mechanism of these biosensors are based on the reaction of active site with the bioreceptor (immobilized biorecognition) as biological or organic material) and the substrate from the tested food material. The electrons produced due to the chemical reaction create a medium of electron flow on the surface of the electrode so that the transducer transform them as response signals. A typical sensing mechanism of biogenic amine to monitor the quality and safety of meat is presented by Nami, *et al.* [7]. First, biogenic amine present in a meat product is oxidized into hydrogen peroxide ($H_2O_2$), $NH_3$, and aldehyde in the presence of oxygen and water using amine oxides as a catalyst (Equation 1). Next, by applying a high potential, the produced hydrogen peroxide ($H_2O_2$) is dissociated into 2 hydrogen ions, oxygen creating and 2 electrons. Then, 2 electrons are formed which use as electron flow providing response signals by the surface of the electrode.



$$\text{Biogenic amine (BA)} + H_2O + O_2 \xrightarrow{\text{Amine oxide}} \text{3,4-dihydroxyphenylacetaldehyde} + NH_3 + H_2O_2$$

$$H_2O_2 \xrightarrow{\text{Potential}} 2H^+ + 2e^- + O_2$$

$$(1)$$

Similar sensing mechanism of histamine to monitor the histamine in the fish spoilage is presented in Equation 2 [13]. First, histamine is oxidized into imidazole acetaldehyde, $NH_3$, and $H_2O_2$ using diamine oxidase (DAO). Then, the produced hydrogen peroxide (($H_2O_2$) is dissociated into 2 hydrogen ions, oxygen and creates 2 electrons which use as electron flow providing response signals by the surface of the electrode.

$$H_2O_2 \xrightarrow{\text{Potential}} 2H^+ + 2e^- + O_2 \tag{2}$$
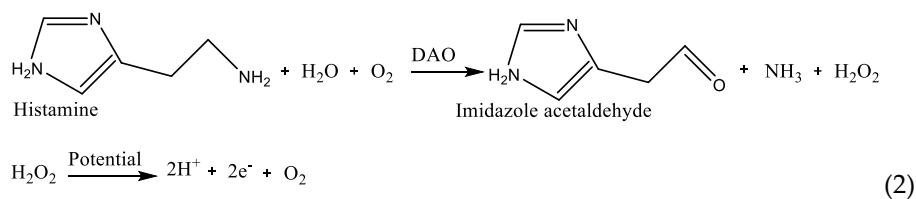
Omanovic-Miklicanin and Valzacchi [14] developed chemiluminescence biosensors to detect the presence of putrescine (Put) and cadaverine in beef, pork, chicken, turkey and fish meat samples. They used putrescine oxidase or diamine oxidase as biorecognition elements (bioreceptors) and microplate luminometer as detection device. The enzymatic reaction and biosensing mechanism are explained in Equation 3. Since the putrescine does not show chemiluminescence characteristic its concentration in meat samples cannot be determined directly during the chemiluminescence reaction. However, it can be measured indirectly by measuring $H_2O_2$. Hence, first, the putrescine is oxidized into $H_2O_2$, 4-aminobutanal and $NH_3$ in the presence of oxygen and water and using putrescine oxidase or diamine oxidase enzymes (Equation 3). Then, $H_2O_2$ is reacted with luminol in an alkaline solution and using cobalt (II) chloride hexahydrate as chemiluminescence catalyst. At last, this catalyzed chemiluminescence reaction of luminol with hydrogen peroxide create 3-aminophthalate with light and the created light is measured employing microplate luminometer (Equation 3). The produced light intensity due to this reaction is proportional to the concentration of hydrogen peroxide.



$$\tag{3}$$
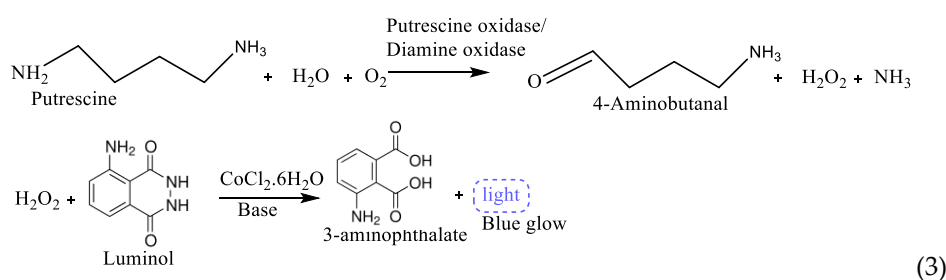
Availability of xanthine in chicken meat can be sensed using an optical biosensor developed employing guanine deaminase and xanthine oxidase as bioreceptors [15]. Briefly, xanthine oxidase and dye phenol red indicator were co-immobilized into sol-gel based circular plastic discs to develop the biosensor. The mechanism for this biosensing is: first, xanthine is converted into uric acid and $H_2O_2$ in the presence $H_2O$ and oxygen and xanthine oxidase as an enzymatic catalyst (Equation 4). The produced uric acid change pH range of the medium in range of 7.5 - 6. Then, using phenol red as absorptive dye the change in colour can be visualized.



$$\tag{4}$$
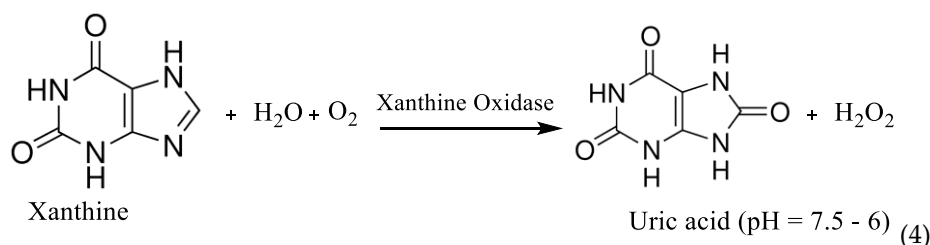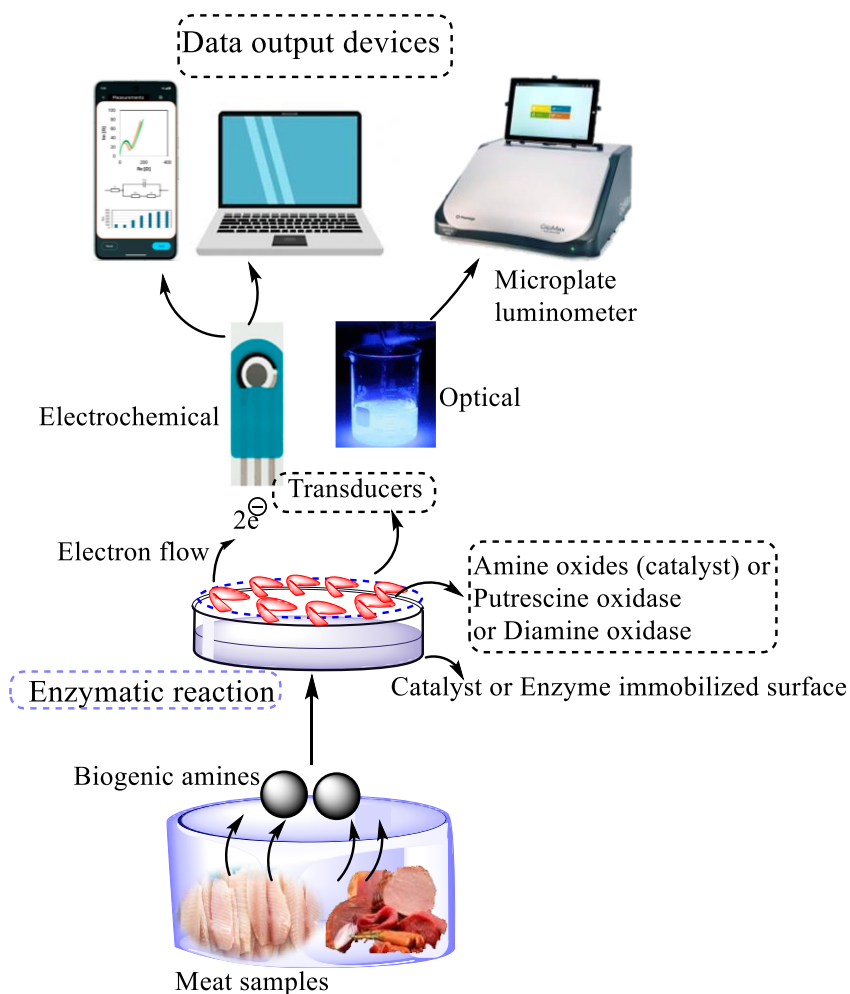
**Figure 2.** Diagram illustrating the detection of biogenic amines in meat samples.
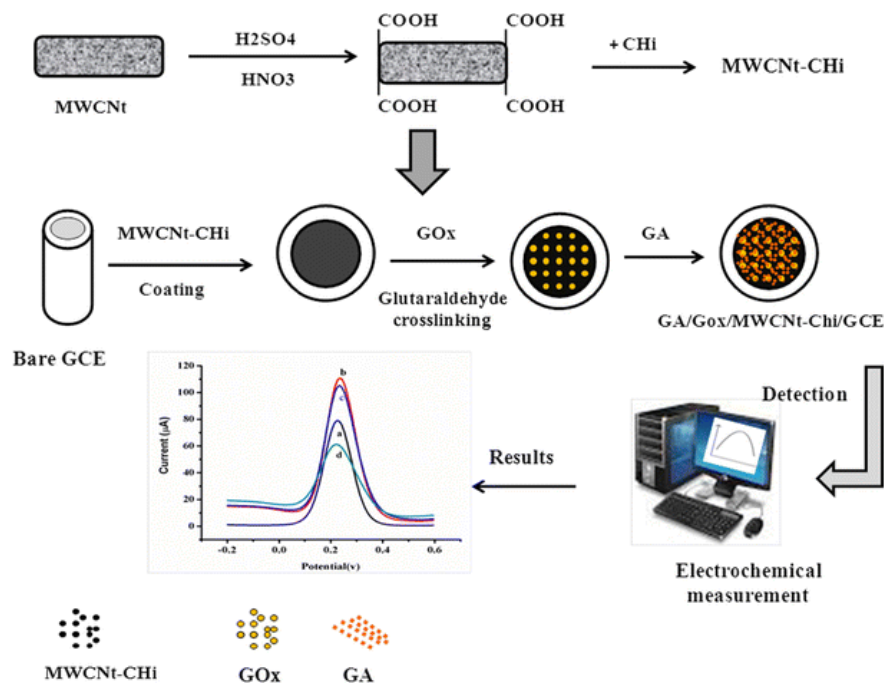


**Figure 3.** Illustration of stepwise glucose biosensor preparation process and electrochemical measurement of glucose reduction in fresh meat (reproduced from Uwimbabazi, et al. [16] with permission from the Journal of Food Analytical Methods, copyright 2017).

*2.2. Types of Biosensors Employed to Monitor Fish, Meat, Poultry and Related Product Quality Parameters*

Several biosensors have been developed and introduced to the current world. These biosensors have different applications based on the target analyte intended to be determined. These have been employed for fish, meat, poultry and related product quality and safety monitoring. Nami, *et al.* [7] classified particular biosensors based on the type of bioreceptor (biorecognition Element) utilize into enzyme-based biosensors, immunosensors and DNA-based biosensor. Enzyme-based biosensors employ enzymes to create contact with sample analyte and produce signal for measurement. Immunosensors use antibodies as a bioreceptor which are applicable for the detection of pathogens or toxins in meat samples. These antibodies contact with pathogen or toxin and create signal for measurement. However, DNA-based biosensors are applicable to detect particular DNA of meat samples using DNA as biorecognition element. Here, the bioreceptor DNA interact with the target DNA in the particular analyte. Some of the enzyme-based biosensors, immunosensors and DNA-based biosensor and their bioreceptor employed for monitoring fish, meat, poultry and related product quality and safety are summarized in Table 1.

Nanda, *et al.* [9] on the other hand classified biosensors based on the immobilization of biorecognition elements, types of transducers use, and detection techniques apply as label-free and label-based. Bioreceptor based biosensors are developed by immobilizing enzyme, aptamer, whole cell, nano, immunosensors, and antibody. Electrochemical, optical, mass-based/gravimetric biosensors are based on their transducers use during real-time analysis of target analytes. Some transducers and electrode employed with biosensors for fish and meat quality monitoring are presented in Table 1. On the other hand, label-free such as acoustic wave, surface plasmon resonance-SPR, and mass spectrometry, and label-based like fluorescence and chemiluminescence bioreceptors are grouped based on their detection techniques.

Emerging biosensor technologies such as smartphones, artificial sensing, 3D printing, and Internet of Things (IOT) are being applicable for detection techniques of fish, meat, poultry and related product quality and safety monitoring. Using machine learning models are applicable in optical sensor-based methods considering color changes and water loss to predict beef quality [17].

**Table 1.** Type of biosensor employed for fish, meat, poultry and related product quality and safety monitoring.

| Type of biosensor | Target Analyte | Source of analyte | Bioreceptor | Transducer / Electrode | Data visualization device | Measured value | Reference |
|---|---|---|---|---|---|---|---|
| Enzyme-based biosensors | Histamine | Fish | Diamine oxidase (DAO) or monoamine oxidase (MAO) enzymes | Electrochemical Screen printed carbon electrodes | cyclic voltammetry (CV), chronoamperometry and electrochemical impedance spectroscopy (EIS) | $8.957 \times 10^{-2}$ mM | [18] |
| | Hypoxanthine | Pork meat | Xanthine oxidase | Electrochemical Platinum wire as counter electrode | Thermogravimetric Analysis | 111.3 µM at 7 days | [6] |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Putrescine | Beef, pork, chicken, turkey and fish meat | Putrescine oxidase | Electrochemical | Chemiluminescence Microplate luminometer | 0.8 – 2 mg/L | [14] |
| | Xanthine | Chicken meat | Guanine deaminase and Xanthine oxidase | Electrochemical with fibre optic probe | Spectrometer (OceanOptics) | 44 $\mu$M at 5 days | [15] |
| | Nitrate | Meat sample | Nitrate reductase | Ag/AgCl reference electrode and platinum auxiliary electrode and working electrode glassy carbon (GCE) | Voltammetric analysis | Detection limit: 2.2 × $10^{-9}$ M and limit of quantification: 5.79 x$10^{-9}$ M | [2] |
| | Glucose reduction | Glucose oxidase | Beef meat | Glassy carbon electrode modified with multi-walled carbon nanotubes and chitosan | Cyclic voltammetry (CV), differential pulse voltammetry (DPV), and electrochemical impedance spectroscopy (EIS) | Reduction in glucose from 0.01-0.06 mmol/L | [16] |
| Immunosensors | Chloramphenicol | Beef and pork meat samples | Monoclonal antibody to CAP (anti-CAP) | Electrochemical immunosensor; Electrochemical impedance spectrosco | Electrochemical impedance spectroscopy (EIS | Detection limit: 0.06 ng/mL | [3] |

| | | | | py technique | | | |
|---|---|---|---|---|---|---|---|
| | *Salmonella enterica, Listeria monocytogenes,* and *Escherichia coli* | Ready-to-eat beef, chicken and turkey breast meat | Alexa Fluor 647-labeled monoclonal antibodies | Streptavidin coated optical waveguides | Fluorometer | Detection limit: $10^3$ CFU/mL | [4] |
| | Calpastatin | Beef meat | Primary anti-calpastain antibody and secondary enzyme-labelled antibody | Potentiostat–galvanostat with Gold working (W.E.) and counter (C.E.) electrodes silver pseudo-reference electrode | Amperometric detection | 481 ng/mL | [19] |
| | Tetracycline | Poultry muscle samples | Lyophilized reconstituted sensor cells | Cell-biosensor | Bioluminescence with SynergyTM HT Multi-detection Microplate Reader | Sensitivity: 10 µg/kg | [20] |
| DNA-based biosensors | DNA (Donkey meat) | Donkey adulteration in cooked sausages | DNA | Multi-parameter SPR device with gold chips | Surface plasmon resonance (SPR) | Detection limit: 1.0 nM | [5] |
| | Dopamine Adulterant | Beef meat | Anti-dopamine substance | - | Colorimetric sensor | Detection limit: 0.13 mM | [21] |
| | Bacteria (Campylobacter spp.) | Chicken meat | Genomic Campylobacter DNA | Paper membrane, and biotinylated-DNA | Chemiluminescent read-out | 3 pg/µL of DNA Detection limit | [22] |

| | | | | detection probe | | | |
|---|---|---|---|---|---|---|---|

## 3. Applications of Biosensors in Real-Time Food Quality Monitoring In Fish, Meat and Meat Products

*3.1. Biosensor-Based Detection of Freshness Indicators in Fish, Meat and Meat Products*

In order to measure the qualitative and quantitative characteristics of meat and meat products freshness, the visual appearance, pH, and meaty aroma are the major ones. In this line, metabolites, synthesized by chemical oxidation and microbial proliferation, could modify the quality of muscle foods freshness. Throughout storage, metabolites produced by from microbial development and chemical oxidations change the muscle foods quality and freshness.

### 3.1.1. Hypoxanthine

In the fish/meat industry, the xanthine (XA) is exploited as a freshness indicator because of its accumulation in the tissues after died. In order to monitor the freshness of pork, a $TiO_2$ and graphene composite has been established [6]. The biosensor assesses the oxidation activity of xanthine oxidase (XOD) and hypoxanthine (Hx) during seven days at refrigerated condition [6]. The Hx existence provoked a sour taste that is facile to detect the fish and meat sample degradation. Pierini, et al. [23] developed an electroanalytical tool (edge plane pyrolytic graphite electrode (EPPGE)) to determine the Hx, Xa and UA content in Argentinian fish samples. Similarly, to control the Hx content in pork meat freshness at several post-mortem periods, Guo, et al. [24] developed an enzyme sensor by joining $O_2$ electrode and XOD. These authors reported that the produced biosensor displayed heightened sensitivity to Hx compared to HPLC analysis. Through grafting reduced expanded graphene oxide (REGO) with $Fe_3O_4$ nanoparticles, Dervisevic, et al. [25] produced a new amperometric xanthine biosensor and applied it to control fish freshness till 20 days. The xanthine concentration was detected at a range between 2 and 36 mM, at 3 seconds at detection limit equal to 0.17 mA/M. Interestingly, after 25 days of old fish samples, biosensor held 70% of its activity. In order to assess the fish freshness with color marking by the unaided eye, XOD was employed in enzyme-mediated AuNRs oxidation [26]. In this study, the color of the sensing system has a good link with Hx level at a range between 0.05 and 0.63 mM. Chen, et al. [27] proposed a fluorescence sensor derived from platinum nanoparticles (Pt NPs) to perceive Hx in aquatic products. At a [Hx] ranged between 8-2500 μM, the new biomaterial possesses a linear connection and detection limit at 2.88 μM. In meat samples, a μPAD biosensor was developed to Hx detection. The detection and quantitative limits were registered at 1.8 and 6.1 mg/L, respectively. The proposed assay exhibited a linear dynamic in the range of 5–40 mg/L. The analysis time was 5 min for triplicate measurement [28]. To assess the meat freshness by Hx detection, Görgülü, et al. [29] fabricated multi-enzyme biosensors. In this study, Polypyrrole–polyvinyl sulphonate (PPy–PTS) films were synthesized on the platinum electrode surface by electropolymerization. The indicator enzymes, XOD and uricase, were immobilized within the polymer matrix. The registered amperometric response, at a potential of +400 mV, was attributed to the current resulting from the enzymatic oxidation of $H_2O_2$. The established biosensor displayed a minimum detection limit of 2.5 μM, a concentration range with a linear response of 2.5 to 10 μM. After 33 days of storage, the biosensor maintained 65% of its initial performance, demonstrating acceptable long-term stability for practical applications. For the evaluation of HX in beef, chicken fish, and pork meat, Devi, et al. [30] evolved a biosensor designed with Au/Fe nanoparticules, and XOD was covalently grafted onto the electrode surface. At an optimal response within 3 s at pH 7.2 and 30°C, the biosensor showed linearity in the range of 0.05 μM to 150 μM for Hx, with a detection limit of 0.05 μM. By employing an absorption transmission approach, Garg and Verma [15] fabricated an optical biosensor to detect Hx. The assay operates on the enzymatic reaction catalyzed by XO, which transforms xanthine into uric acid and $H_2O_2$. Owing to

the uric acid formation, this reaction provokes a pH reduction, characteristically from 7.5 to 6.0. These investigated the xanthine content in chicken meat during 5 days of storage. As projected, xanthine concentrations augmented eventually, representing deteriorating of meat quality, from ~5 μM on day 1 to 44 μM on day 5. The method's reliability was established within spiked samples; display a recovery % between 94.2 and 96.5%. Zhang, et al. [31] developed a new tool named electrochemiluminescence (ECL) of CdS quantum dots (QDs), combining electrochemistry and chemiluminescence. This technique indicated that electrical energy was used to launch a chemical reaction that generates light. These authors assembled and synthesized the new material onto poly (diallyldimethylammonium chloride)-functionalized carbon nanospheres (PFCNSs) and leading to an increase of ECL intensity by dissolved O2 as a coreactant. The sensor established a fast response with a linear range from $2.5 \times 10^{-8}$ -$1.4 \times 10^{-5}$ M and a detection limit of 5 nM (S/N = 3), and the obtained findings from fish sample analysis were closely matched to those from standard amperometric methods.

### 3.1.2. Biogenic Amines and Volatile Amines

Biogenic amines, small organic compounds comprising one or more amino groups, are categorized into aliphatic, aromatic, and heterocyclic amines. These amines are mainly synthesized by enzymatic decarboxylation of free amino acids or by amination and transamination of aldehydes and ketones [32].

The most prevalent biogenic amines present in aquatic and meat products are tyramine, cadaverine, putrescine, histamine, and trimethylamine [33]. Throughout the muscle food deterioration, the formation of histamine, putrescine, and cadaverine are generally used as freshness indicators and could be monitored. Zhai, et al. [34] created an amine-responsive bilayer films by using agar (AG), anthocyanins (AN), gellan gum (GG), and $TiO_2$ nanoparticles for visual monitoring of meat spoilage. The AG-AN layer served as the detecting layer for volatile amines, while tThe AG-AN/GG-2%$TiO_2$ film noticed trimethylamine (TMA) at a limit of 0.018 mM, a typical gas from meat spoilage. During silver carp and pork spoilage, the film exhibited a range color variation between the rose-red and green, stress its possible use in intelligent food packaging.

Based on the peroxidase-like activity of (Fe and Co) codoped-CDs, Li, et al. [35] developed a colorimetric tool to detect the cadaverine and the putrescine. With the enzymatic hydrolysis by diamine oxidase, biogenic amines were disintegrated to generate H2O2 which reacts with tetramethyl-benzidine with the catalysis of (Fe,Co)-codoped CDs. The colorimetric method was used to perceive of cadaverine and the putrescine in various fish samples with a limit of 0.06 mg/kg. Checked by HPLC, the recoveries of the colorimetric method were confirmed by standards, signifying that the established colorimetric method was sensitive and accurate.

In order to monitor biogenic amines (BAs), Luo, et al. [36] developed a hydrogel composed of β-d-glucose pentaacetate (β-D-GP), silver ions, and agarose. Under alkaline conditions, in contact with BAs, β-D-GP could be hydrolyzed to form β-d-glucose, which decreases silver ions to silver nanoparticles, and generate visible color variations. These changes can be analyzed with the naked eye or quantified using smartphone-based RGB (red/green/blue) analysis in fish samples. Polyaniline (PANI) synthesized via in situ chemical oxidative polymerization was spray-coated onto flexible interdigitated electrodes (IDEs) for noticing ammonia gas and have been employed for checking food quality. The sensor's electrical response augmented linearly with increasing ammonia concentrations. It confirmed a constant linear response in the 50–150 ppm range and effectively evaluated the meat and sheep liver freshness in real-time[37]. Chang, et al. [38] produced a detecting system provided with an ultrasensitive amine gas sensor to perceive volatile amines from raw fish. Remarkably, the sensor offers an electrical response within 1 min that meticulously links with TVB-N values. The sensor's ppb-level sensitivity and integrated humidity control enable fast and accurate detection. These findings support the development of real-time, on-site freshness monitoring in fish processing environments. The amine gas sensor is able to detect ammonia, dimethylamine (DMA), and trimethylamine (TMA) at ppb levels, permitting it to monitor volatile compounds released from raw

fish and indicate spoilage. The method truthfully releases the effects of storage temperature and a fish portions viz. ventral, dorsal, and lateral on spoilage development. For beltfish and mackerel, the sensors displayed robust correlation with TVB-N values.

Through in-situ polymerization, Shi, et al. [39] deposited the TiO2-PANI- into Silk Fibroin Fiber (SFF). The novel composite (TiO2-PANI/SFF) played the role of an excellent micro sensor exhibiting sensing capability, with a response value equal to 0.82 and a response time of 10 seconds to 100 µg/L of NH3. In pork samples, when utilized to evaluate freshness, the sensor's was powerfully interrelated with TVB-N levels ($R^2$ = 0.99). In order to measure the TVB-N in pork by combing 2 non-destructive sensing methods: colorimetric sensors and HIS: hyperspectral imaging [40]. For data fusion and modeling, these authors proposed a BP-AdaBoost which corresponds to an effective backpropagation adaptive boosting algorithm. The performance of model was examined relative to PCA-BPANN: backpropagation artificial neural network model. Test results revealed that the data fusion model outdid the single-sensor models, with BP-AdaBoost proposing superior capability in handling complex data fusion compared to PCA-BPANN. In pork meat, this investigation revealed the possible integrating of HIS and colorimetric sensors, and the BP-AdaBoost algorithm for non-destructive TVB-N.

### 3.2. Biosensor-Based Detection of Microbial Hazards in Fish, Meat and Meat Products

The occurrence of pathogenic microorganisms in food caused significant dangers to general health safety and can also affect the environment. The biosensors expansion has importantly improved food safety [41]. Conventional microbiological methods characteristically comprise enrichment, filtration, and incubation phases, requiring a time frame of from 2 - 10 days to obtain [42]. Contrarily, modern biosensor-based tools proposed earlier and more precise detection, with the further advantage of on-site pertinence. For pathogens, their toxins, and metabolites, their low detection limits highpoint the importance of highly sensitive analytical tools for guaranteeing the fish, meat and meat products safety.

Across different optical sensing methods, colorimetric, fluorescence, Chemiluminescence Surface Plasmon Resonance (SPR) and Localized Surface Plasmon Resonance (LSPR), are usually employed [43]. In the SPR-based biosensing, normally engages reflectance spectroscopy for the detection of target pathogens, the bioreceptors are fixed to a metal transducer surface. Where specific wavelengths of electromagnetic radiation act towards the metal's electron and generate resonance. When bacterial cells attach to this surface, they induce quantifiable variations in the refractive index [41]. In order to detect pathogenic microorganisms in different meat and meat products, optical biosensors were employed.  As an illustration, a fiber-optic immunosensor, fortified with immunomagnetic separation, certainly perceived *Listeria monocytogenes* in meat at levels as < 3 × 10² CFU/mL [44]. Another method employed an aptamer-based fiber-optic biosensor to select *L. monocytogenes* in artificially infected ready-to-eat (RTE) meat, effectively identifying it specifically among other microbial strains [45]. Oh, et al. [46] engaged LSPR to detect *Salmonella Typhimurium* in pork at 4 log CFU/mL within 30 min. To synchronize detect the *E. coli* O157:H7, *Salmonella enteritidis*, and *Listeria monocytogenes*, Zhang, et al. [47] established an SPR biosensor combined to an enrichment broth. In order to simplify selective recognition, polyclonal antibodies which are special for each pathogen were anchored on separate channels of SPR chip. After an enrichment step, chicken meat were analyzed using the SPR system, efficaciously perceiving target microorganisms at 14, 6, and 28 CFU/25 g for *E. coli* O157:H7, *Salmonella enteritidis*, and *Listeria monocytogenes*, respectively. Liang, et al. [48] produced a smartphone-based biosensor to detect microbial spoilage on ground beef. In this study, le lower limit of detection was between 10 and 100 CFU of *Escherichia coli* K12. Morant-Miñana and Elizalde [49] produced an electrochemical genosensor for the *Campylobacter* spp detection. This new material, developed from thin-film gold electrodes dropped onto Cyclo Olefin Polymer (COP), displayed high sensitivity, robust linear response observed for *Campylobacter* spp, and positively authenticated by real poultry meat samples. It displayed similar findings to those obtained with purified PCR products with a concentration ranged between 1 - 25 nM, and a LOD equal to 90 pM.

Ohk and Bhunia [4] developed and optimized a multiplex fiber optic sensor able to detect simultnesouly *L. monocytogenes*, *E. coli* O157:H7, and *S. enterica* in food samples. Streptavidin-coated optical sensors were equipped with biotinylated polyclonal antibodies and treated with bacterial suspensions or supplemented food samples for 2 hours. In this study, turkey, ready-to-eat beef, and chicken samples were inoculated with ~$10^2$ CFU of each pathogen /25 g was enriched during 18 hours in a selective enrichment medium SEL broth and tested by the biosensor. The sensor positively recognized each pathogen individually or in combination and the detection limit was $10^3$ CFU/mL for all three pathogens. This new approach, multiplex fiber optic biosensor, could be proper to detect simultaneously *Listeria*, *E. coli*, and *Salmonella* in food, decreasing the necessity for separate single-pathogen detection systems. By virtue of its excellent characteristics like ultra-rapid electron transfer aptitude, great surface/volume ratio, suitability for biological applications, and its single connections with DNA bases of the aptamer, Muniandy, et al. [50] fabricated an rGO-azophloxine nanocomposite (rGO-AP) aptasensor to detect foodborne pathogens. The contact of the label-free single-stranded deoxyribonucleic acid (ssDNA) aptamer with *S. Typhimurium* was examined by variance pulse voltammetry exploration, and this aptasensor indicated high selectivity and sensitivity for the detection of intact bacterial cells. rGO-AP revealed a linear detection range between 10 to $10^8$ CFU/mL and a good linearity ($R^2 = 98\%$). Furthermore, rGO-AP could detect, bacterial concentration ranging from 10-$10^4$ CFU/g in the inoculated chicken sample with *S. Typhimurium*. Rasooly [51] evaluated the potential of Surface plasmon resonance (SPR) biosensors to detect staphylococcal enterotoxin B (SEB), engaging 2 antibodies, in foods. A capturing antibody, covalently enclosed to the biosensor chip surface was performed to the initial binding of the antigen and a second antibody sticks to the captured antigen. Initially, the whole assessment cycle taked 5 minutes when using a single antibody or 8 minutes when two antibodies are employed. Interestingly, SPR biosensor could detect SEB in meat at 10 ng/ml, with initial binding < 2 min. On another study conducted byLiu, et al. [52], a fast detection of *Salmonella* serotypes B and D in ready-to-eat (RTE) turkey has been explored. These authors proved that a concentration of *Salmonella* < $3 \times 10^2$ cells/mL at1 hour was attained. Additionally, the findings displayed that the sensor is able to distinguish low concentration of live *Salmonella* cells from high levels of dead *Salmonella* cells.

*3.3. Biosensor-Based Detection of Contaminants, Antibiotics, and Drug Residues in Fish, Meat And Meat Products*

Food quality valuation includes perceiving impurities *viz.* drug residues, pesticides, toxins and heavy metals. Conventional tools like mass spectrometry and capillary electrophoresis are costly and taking considerable time. To guarantee consumer security, biosensors offer a closer and a gainful alternative with adequate perception. For instance, for heavy metals as As, Cd, Hg, biosensors employed enzymes (e.g. glucose oxidase, urease, cholinesterase, alkaline phosphatase) and genetically modified microorganisms [53]. By developing a chemiluminescence sensor called MIP (molecularly imprinted polymer (MIP), Cai, et al. [54] recognized eight benzimidazoles in beef and mutton, establishing ultrafast sensitivity. In fact, these authors confirmed that the detection limits were ranged between 1.5 and 21 pg/mL, with 18 minutes, and High recovery efficiency (66-91%). In order to identify or fungal or bacterial toxins existing in meat products, electrochemical biosensors are used. As an example, trichothecene (T-2 toxin) was detected inn swine meat [55]. By employing an electrochemical and SPR biosensors, Staphylococcal enterotoxin B were sensed in pork [56], in potted meat [51], respectively. By amperometric biosensor, Dinçkaya, *et al.* [2] appraised the nitrate concentrations in meat and confirmed that LOD was $2.2 \times 10^{-9}$ M with a response time equal to 10 s. On the other hand, some studies employed SPR as biosensors to identify drug residues. In several meat species like pork, beef, and chicken, SPR technique was able to detect sulphonamides and chloramphenicol have been quantified [57–59]. In order to detect the SDM: sulfadimethoxine in beef and chicken meat, Mohammad-Razdari, et al. [60] established electrochemical biosensor based on pencil graphite electrode (PGE) and adapted with a reduced graphene oxide (RGO) and Au nanoparticles for sulfadimethoxine (SDM). In the best-performing trials, the proposed biosensor

showed a linear range from $10-10^{-5}$ M, LOD at $3.7 \times 10^{-16}$ M towards SDM. For meat sample applications, the aptasensor was applied to fish, chicken, and beef and showed acceptable recovery rates across the tested concentration range, demonstrating dependable performance and accuracy in analytic quantification between 92 and 103%. For the label-free detection of ceftiofur residues in meat trials, Stevenson, et al. [61] developed an affinity-based electrochemical biosensor. These authors validated a platform that can detect ceftiofur within 15 min of using the sample at levels down to 0.01 ng/mL in phosphate-buffered saline and 10 ng/mL in 220 mg ground turkey meat samples. The Table 2 summarizes some examples of biosensors to monitor the quality and safety of fish, meat and meat products.

**Table 2.** Biosensors to monitor the quality and safety of fish, meat and meat Products.

| Analyte | Employed electrode and material of detection | Immobilization Technique | Food product | LOD | Sensitivity/linear range/detection time | References |
|---|---|---|---|---|---|---|
| Some examples for biosensors detecting freshness of fish, meat and meat products. | | | | | | |
| Hx | **XOD within a Nafion matrix** on a graphene–titanium dioxide | Entrapment | Pork | 9.5 μM | Sensitivity: 4.1 nA/μM<br><br>Linear range 20–512 μM | [6] |
| | XOD and horseradish peroxidase | Adsorption | Raw and treated meat samples | 1.8 mg/L | Quantitative limit: 6.1 mg L$^{-1}$ | [28] |
| | XOD and polyvinylferrocenium perchlorate matrix on a platinum | Adsorption | Fish | 0.6 μM, | Linear range 2.1–103 μM | [62] |
| | XOD and platinum electrode with single-walled carbon nanohorns (SWCsNH) and gold nanoparticles (AuNP) | Covalent | Fish | 0.61 | Linear range 1.5–35.4 | [63] |

| | XOD and uricase within a polypyrrole-paratoluenesulfonate composite film | Entrapment | Fish | 5 | 5-500 Linear range | [64] |
|---|---|---|---|---|---|---|
| | XOD on carbon film electrodes and carbon nanotube | Cross-linking | Fish | 0.77 | 10-130 | [65] |
| | XOD onto a modified platinum electrode surface. | Entrapment | Seafood | 0.0023 | 0.01–10 | [64] |
| | XOD onto paper substrate | Adsorption | Fish | 4.1 | 4–35 | [66] |
| Calpastatin | Capillary and optical fiber biosensor | Covalent | Longissimus muscle from beef | | Calpastatin activity (R2 = 0.6058) | [67] |
| Cadaverine | Receptor molecules onto the surface of thiol-gold | Covalent | Beef, chicken, or pork | | | [68] |
| Putrescine | **Casein** onto the **electrode surface** using **glutaraldehyde** | Covalent | Beef, pork, chicken, turkey meat samples | LOD: 0.8 mg/L–1.3 mg/L | Linearity range: 1–2 mg/L | [69] |
| TVB-N | **pre-fabricated responsive dyes**, **embedded** onto a **paper or polymer film** | Adsorption | Pork meat | | Correlation coefficient (R$^2$ = 0.932) | [40] |
| Some examples for biosensors detecting pathogen microorganisms and toxins in meat and meat products | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| *Campylobacter* spp. | **Amino-modified DNA probes** onto a **nylon membrane** | Covalent | Chicken meat | LOD: 3 pg/µL of DNA | - | [22] |
| *Salmonella enterica, Listeria monocytogenes,* and *Esc herichia coli* O157:H7 | **antibodies** onto the **optical fiber surface** using **carbodiimide** | Covalent | Beef, turkey breast and chicken | LOD: $10^3$ CFU/ mL | - | [4] |
| *Salmonella Typhimurium Staphyloccocus aureus* | **Thiol-modified aptamers** onto **gold nanoparticles** | **Non-covalent** | Pork | 15 CFU/mL 35 CFU/mL | Recovery rate: 94.12%–108.33% | [47] |
| *S. enterica* serovar *Typhimurium* | Amine-terminated DNA aptamers onto a carboxyl-functionalized graphene-modified electrode employing carbodiimide | Covalent | Chicken meat | LOD: 1 CFU/mL | Linear range (detection): 1–8 log CFU/mL | [50] |
| *Salmonella pullorum* | **specific antibodies** onto the **electrode surface** using **glutaraldehyde** | Covalent | Chicken meat | LOD: 100 CFU/mL | Detection time: 1.5 to 2 h | [70] |
| *E coli* K-12 | **specific antibodies** onto the **gold electrode surface**. | Adsorption | Chicken meat | LOD: 3 log CFU/mL | - | [71] |
| *Listeria monocytogenes* | **thiol-modified DNA aptamers** | Covalent | Meat samples | LOD: 2 log | Linear detection | [45] |

| Analyte | Immobilization | Method | Matrix | LOD | Detection range / time | Ref |
|---|---|---|---|---|---|---|
| | onto **gold nanoparticles** | | | CFU/g | range : From **10² to 10⁷ CFU/m** Detection time <30 minutes | |
| *L. monocytogenes* toxin *S. aureus* enterotoxin B | **live mammalian cells** onto the surface of **gold interdigitated microelectrodes** | Adsorption | Salami | 10⁴ CFU/mL 100 ng/mL | Detection time <1 hour | [72] |
| Staphylococcal enterotoxin B | **anti-SEB antibodies** onto a **gold-coated SPR** | Covalent | Meat | 0.5 ng/mL | 0.5 ng/mL to 20 ng/mL Detection time <20min | [51] |
| Trichothecene T-2 toxin | **Anti-T-2 toxin antibodies** onto a modified electrode surface using **glutaraldehyde** | Covalent | Swine meat | 0.04 ng/mL | 0.05 – 20 ng/mL Detection time = 30 min | [55] |
| Some examples for biosensors detecting antibiotics, drug residues, and additives in meat products | | | | | | |
| Tetracyclines | *E. coli* **cells** in **agarose gel** on the surface of microplates or membrane | Entrapment | Poultry muscle samples | **2–5 µg/kg** | 2 **to 100 µg/kg**. Detection time = 3Hours | [20] |
| Chloramphenicol (CAP) | **CAP–protein conjugate** onto the **SPR sensor chip** | Covalent | Poultry muscle | 100 ng/kg | to 1 µg/kg detection time <30 min | [73] |
| **Oxytetracycline (OTC)** **Kanamycin (KAN)** **Ampicillin (AMP)** | aptamers onto citrate-stabilized gold nanoparticles | Adsorption | Chicken | **0.42 ng/mL** **0.31 ng/mL0. 28 ng/mL** | 1–100 ng/mL 1–80 ng/mL 1–60 ng/mL | [74] |

| | | | | | Detection time = 15 min | |
|---|---|---|---|---|---|---|
| Ractopamine | **ractopamine–BSA conjugate onto a carboxymethylated dextran chip** | Covalent | Pork | 0.09 ng/mL | 0.1 – 10 ng/mL Detection time = 10 min | [75] |

## 4. Standardization and Validation of Biosensors in Real-Time Food Quality Monitoring

The standardization and validation of biosensors are indispensable processes for ensuring their reliability, reproducibility, and regulatory acceptance in the food industry. Unlike conventional chemical assays, biosensors often demonstrate significant variability due to differences in biological recognition elements, sensor fabrication, and susceptibility to environmental factors such as temperature, pH, and matrix complexity. This variability makes necessary robust calibration and method validation protocols to ensure consistent performance across food matrices and operational environments [76,77].

Calibration and standardization are foundational steps for establishing accuracy and consistency in biosensor output. The calibration process typically involves the use of matrix-matched reference standards, ideally certified, to reflect real-world food conditions in terms of composition, viscosity, and potential interferents [78]. Biosensors must exhibit predictable and linear responses across a defined concentration range of the target analyte. For example, a heat-transfer biosensor used for detecting trace levels of chemical additives in dairy was calibrated using milk samples with varying fat contents to ensure consistent sensitivity and reproducibility [10].

### 4.1. Validation

Although harmonized guidelines for validation of biosensor-based methods do not exist, a valid text is represented by the International Council for Harmonisation (ICH) "Bioanalytical Method Validation and Study Sample Analysis – M10 guideline, 2022". This document was adopted also by the European Medicines Agency (EMA) and the Food and Drug Administration (FDA). Method validation, as defined in the ICH M10 guideline, requires comprehensive evaluation of analytical performance. Key parameters include accuracy, precision (repeatability and intermediate precision), selectivity, sensitivity, linearity, limit of detection (LOD), limit of quantitation (LOQ), carryover, and analyte stability (EMA - European Medicines Agency, 2024; ICH Expert Working Group, 2022; U.S. Department of Health and Human Services Food and Drug Administration, 2022).

#### 4.1.1. Specificity and Cross-Reactivity Challenges

In biosensor-based ligand binding assays (LBA), specificity refers to the sensor's ability to detect only the target analyte without interference from structurally similar compounds, such as analogues, metabolites, or co-formulated substances. This becomes critical when detecting contaminants like veterinary drug residues or pesticide metabolites. Specificity is typically evaluated by spiking blank matrix samples with structurally related compounds at their expected maximal concentrations. A well-validated biosensor should show negligible response to these analogues and maintain accuracy for the primary analyte within ±25% at the extremes of its dynamic range. In cases where specificity is compromised, adjusting the quantification range or employing alternative recognition elements (e.g., more selective antibodies or aptamers) may be necessary.

### 4.1.2. Selectivity in Complex Food Matrices

Selectivity addresses the biosensor's performance in distinguishing the analyte from endogenous matrix components that may interfere with detection. This is especially challenging in samples like milk, eggs, or processed foods, where proteins, fats, and enzymes can cause non-specific binding or signal suppression. To ensure selectivity, the assay must be tested in at least 10 different blank food matrix samples, with analyte spiked at both low and high concentrations. The signal from unspiked samples should fall below the lower limit of quantification (LLOQ) in at least 80% of the matrices tested. Selectivity testing should also consider lipemic and hemolyzed conditions, as well as matrices derived from diseased or stressed animal populations when relevant.

### 4.1.3. Calibration Curve and Reportable Range

Accurate quantification with biosensors depends on the establishment of a calibration curve, relating analyte concentration to signal response. The curve should span from the LLOQ to the upper limit of quantification (ULOQ), ideally covering at least six concentration points plus a blank. Many biosensor platforms use a logistic fit (4- or 5-parameter models) to accommodate non-linear signal responses, especially near saturation zones. A robust calibration curve requires consistency across multiple runs (minimum of six), with at least 75% of calibration points meeting accuracy criteria (±25% at LLOQ/ULOQ; ±20% at other levels).

### 4.1.4. Accuracy and Precision Requirements

Validation of accuracy (closeness to the true value) and precision (repeatability) is conducted using quality control (QC) samples at multiple concentration levels, typically LLOQ, low, medium, high, and ULOQ. Within-run and between-run performance should be assessed over at least six analytical runs using independently prepared QCs. Acceptable accuracy and precision limits are ±20% (±25% for LLOQ and ULOQ). A total error (sum of bias and variability) threshold of ≤30% (≤40% at extremes) is often applied as an overall acceptance criterion.

### 4.1.5. Dilution Linearity and High-Dose Hook Effect

Due to the limited dynamic range of many biosensors, dilution of samples with high analyte concentrations is necessary. Dilution linearity must be verified to ensure that sample dilution does not introduce bias. This is also critical for identifying the hook effect, a phenomenon where excessive analyte saturates binding sites, leading to signal suppression. Dilution series should be tested in at least three independent preparations, demonstrating linearity across the measured range, with ≤20% deviation from expected values.

### 4.1.6. Stability Under Analytical Conditions

Stability testing ensures that storage, processing, and handling conditions do not compromise the biosensor's performance. This includes assessments of freeze-thaw stability, bench-top stability, and long-term storage. For each condition, QCs at low and high concentrations should be evaluated, and analyte recovery should remain within ±20% of nominal values. This step is particularly important for biosensors using biologically active components (e.g., enzymes or antibodies), which are prone to degradation under suboptimal storage.

These criteria ensure the biosensor ability to generate reliable results for target contaminants such as pesticides, preservatives, or industrial pollutants [79]. These validation criteria should be tailored depending on whether the biosensor detects contaminants, chemical additives, toxins, or other analytes. A critical point is also food matrices, in fact the ICH M10 Guideline underlines that other pivotal parameters are matrix effects, incurred sample reanalysis (ISR), and inter-batch reproducibility; all of which are particularly relevant for biosensors deployed in complex food matrices like oils, processed meats, lipid-reach sea foods (e.g., shellfish) [80,81]. In Table 3 a summary of these parameters as well as a brief description is reported.

**Table 3.** Summary of Key Validation Parameters for Biosensor-Based Methods according to ICH M10 guideline.

| Parameter | Definition | Regulatory Expectation | Biosensor-Specific Considerations |
|---|---|---|---|
| **Specificity** | Ability to detect only the target analyte, not structurally similar compounds | Interference from related compounds should result in <LLOQ signal; accuracy ±25% at extremes | Biosensors using antibodies/aptamers must be screened against analogs, metabolites, and additives |
| **Selectivity** | Differentiation of analyte in presence of matrix components | ≥80% of blank matrices should show <LLOQ signal; accuracy within ±25% at LLOQ | Must account for interference from fats, enzymes, or proteins common in food matrices |
| **LOD (Limit of Detection)** | Lowest concentration distinguishable from blank with confidence | typically signal/noise (S/N) ≥3 | Important for contaminant detection; impacted by sensor noise and baseline stability |
| **LOQ (Limit of Quantification)** | Lowest concentration quantifiable with acceptable accuracy & precision | S/N typically ≥10 | Defines lower end of calibration; matrix effects often limit LOQ in real food samples |
| **Calibration Curve** | Relationship between analyte concentration and sensor response | ≥6 levels + blank; logistic fit often used; 75% points within ±20–25% of nominal value | Non-linear response at low/high ranges often requires 4/5-parameter modeling |
| **Accuracy** | Closeness of measured value to true value | Within ±20% (±25% at LLOQ/ULOQ); evaluated within- and between-runs | Challenging when sensor drift or matrix effects occur; needs robust QC planning |
| **Precision** | Repeatability of results under same conditions | CV ≤20% (≤25% at LLOQ/ULOQ); across ≥6 runs and 5 QC levels | Signal variability from biorecognition elements (e.g. enzyme-based biosensors) must be managed |
| **Total Error** | Sum of bias (accuracy) and variability (precision) | Should not exceed 30% (40% at LLOQ/ULOQ) | A helpful global indicator of biosensor method performance |
| **Dilution Linearity** | Consistency of measurement across diluted samples | Mean ±20% of expected after correction; ≥3 dilutions tested | Needed for samples exceeding range; verifies absence of hook effect |

| Hook Effect | Signal suppression at high analyte concentrations | No signal drop-off in undiluted samples expected above ULOQ | Particularly relevant in immunoassay-based biosensors |
|---|---|---|---|
| Carry-over | Residual analyte signal from prior sample influencing subsequent results | Signal in blank after ULOQ standard must be <LLOQ | Typically minimal in biosensors; confirm with blank after high calibrator |
| Stability | Analyte remains unchanged during storage, preparation, and analysis | Mean ±20% at low/high QC; validated over actual storage conditions | Biosensor reagents (e.g. enzymes, aptamers) and analyte stability must both be validated |

Despite innovative sensor designs, regulatory approval remains a time-intensive process. In fact, often, apart from a validation study, a comparison study with validated chemical reference methods, such as HPLC or mass spectrometry, is preferred. These comparative assessments are crucial for establishing biosensor equivalence in terms of sensitivity, selectivity, and reproducibility. Without this level of validation, biosensors face challenges in gaining acceptance for routine food safety monitoring, despite offering advantages such as portability and real-time readouts [82,83].

Biosensor integration into quality control systems presents operational challenges, including interoperability with digital traceability platforms, training personnel in sensor operation, and upgrading existing laboratories or processing infrastructure. In large-scale manufacturing environments, biosensor data must seamlessly interface with automated decision-support systems for tasks such as batch release or contamination alerts [84,85].

Furthermore, data harmonization is critical. Standardized biosensor outputs must be structured and formatted for compatibility with central databases that consolidate information from inspections, internal audits, and supply chain feedback. As highlighted by Wijayanti, et al. [86], biosensors are increasingly incorporated into the digitalization of food quality frameworks, but effective deployment requires unified validation standards and interoperable data formats to enable real-time risk assessment and traceability [86].

### 4.2. Limits and Challenges for Biosensors Application in in Real-Time Food Quality Monitoring

Achieving high sensitivity and specificity remains a central challenge in the development of biosensors for detecting food additives and contaminants. These parameters determine the biosensor's ability to detect target analytes at trace levels and to discriminate them from structurally similar compounds. In complex food matrices, such as milk or cereals, matrix components can interact with sensor surfaces or recognition elements, leading to background signal noise or false positives [87].

For instance, certain immunoassays for mycotoxins have demonstrated cross-reactivity with masked or metabolized toxin forms, undermining their selectivity. Similarly, surface-enhanced Raman scattering (SERS)-based lateral flow biosensors developed for detecting colistin in milk have shown matrix interference from milk proteins, which reduced analytical clarity despite fast detection times. Such cases highlight the need for advanced recognition elements and sample pre-treatment strategies to mitigate matrix effects and improve signal fidelity. Moreover, the operational stability of biosensors, especially those incorporating biological recognition elements like enzymes or antibodies, is a persistent issue limiting their shelf-life. Enzyme-based biosensors are particularly susceptible to denaturation or leaching during storage, which reduces signal reproducibility and overall reliability [86,88].

Efforts to improve stability have focused on immobilization techniques such as cross-linking, encapsulation in polymeric matrices, or covalent bonding to support materials. These approaches aim to preserve the functional conformation of the biomolecules and enhance resilience to environmental stressors during storage and use. However, long-term validation of such methods under varied food storage conditions remains limited and is critical for regulatory and industrial acceptance. Another critical issue may be represented by environmental factors, including temperature, humidity, and pH, that have a significant impact on biosensor performance. Temperature fluctuations can alter enzyme kinetics, signal generation rates, or the refractive index in optical systems. For example, enzymatic biosensors may show exaggerated signals at elevated temperatures or delayed responses in colder environments. Similarly, pH instability affects the electrochemical response of sensors, especially those incorporating carbon nanomaterials for detecting heavy metals or preservatives [89].

Humidity can degrade sensitive components, particularly in optical biosensors, where uncontrolled moisture introduces signal noise or damages light-sensitive dyes. Moreover, food matrices with variable composition further complicate biosensor operation, reinforcing the need for robust calibration and compensation mechanisms to ensure consistent performance [90].

Some examples of issues in biosensors validation and application for the analysis of food additives and contaminants, along with the study strategies developed for their resolution, are proposed in Table 4.

**Table 4.** Biosensor applications for food additives and contaminants: key challenges and mitigation strategies.

| Analyte | Biosensor Type | Matrix | LOD/ LOQ | Key Challenges | Mitigation Strategies | Study |
|---|---|---|---|---|---|---|
| **Carbendazim** | upconversion-MnO2 luminescent resonance energy transfer | food | LOD: 0.05 ng·mL⁻¹ | specificity | aptamer integration and high fluorescence quenching capability of MnO2 nanosheets | [91] |
| **cadmium (Cd), lead (Pb) and mercury (Hg)** | luciferase-based biosensors | food | LOD: Cd: 0.01 μM Pb: 0.025 nM Hg: 2 nM | decrease of sensitivity | expression of Pb importers or nonspecific modifications | [92] |
| **Nitrate** | Immobilized Nitrate Reductase | dry-cured ham | - | comparison with HPLC | good agreement with standard HPLC method: R 2 = 0.971 | [93] |
| **amnesic shellfish** | Aptamer-Based Biosensor | - | LOD: 13.7 nM | specificity | identification and truncation optimization | [94] |

| | | | | | | |
|---|---|---|---|---|---|---|
| **toxins: domoic acid** | | | | | | |
| **Paralytic Shellfish Poisoning Toxins** | Surface Plasmon Resonance- Based Biosensors | shellfish | - | interferences | comparison of several extraction methods | [95] |

## 5. Challenges, Limitations, and Future Perspectives in Biosensor Applications for Fish, Meat, Poultry, and Related Products Safety Monitoring

Addressing the challenges and limitations in ensuring the safety of fish, meat, poultry, and related products is a fundamental pillar of modern food systems. However, biosensors—despite their transformative potential—still face multifaceted limitations that restrict their scalability and real-world implementation. These challenges span across biological, technical, regulatory, and economic domains, especially in resource-limited settings or small-to-medium-scale enterprises.

One of the most fundamental limitations stems from the complexity of food matrices, which vary widely in moisture content, fat and protein composition, and microbial load. These intrinsic properties can interfere with biosensor readings, especially in systems relying on electrochemical or optical signals [87,96–98]. High-fat samples like beef or lamb may cause signal drift or fouling of the sensing surface, while the high-water activity in fish products may lead to enzymatic degradation or dilution of target analytes [87,96]. Additionally, meat and poultry tissues can contain a mixture of endogenous enzymes and oxidation byproducts that further complicate signal stability [97,98]. In seafood, detection is further complicated by the presence of marine-specific hazards such as tetrodotoxin, okadaic acid, or domoic acid, which require ultra-sensitive detection limits and matrix-adapted recognition elements [96,99,100]. In poultry, early-stage detection of infection is difficult due to low biomarker concentrations during the asymptomatic phases of disease progression, which often fall below the limit of detection (LOD) of many conventional biosensors [97,101].

Cross-reactivity and specificity pose another technical barrier. Biosensors must be able to differentiate between highly similar microbial species or strains, such as *Campylobacter jejuni* versus *C. coli*, or between pathogenic and non-pathogenic *E. coli* strains, which often share structural markers [87,101–103]. The inability of many biosensors to discriminate between viable and non-viable cells may lead to false positives, especially in post-sanitization environments [102,104]. Moreover, many detection platforms still struggle with achieving the necessary selectivity in mixed microbial environments, particularly in raw or minimally processed products [96,105,106].

Furthermore, detection of residues such as tetracyclines or aflatoxins—particularly in trace amounts across different feed types, tissues, or products—requires extremely sensitive and consistently calibrated platforms [106–111]. Small deviations in temperature, pH, or sample handling can cause shifts in biosensor response, making reproducibility a serious concern for both researchers and industry practitioners [87,90,112].

Operational challenges are also significant. Electrochemical biosensors often require external power sources and supporting instruments (e.g., potentiostats), which hinder their portability and real-time usability in field inspections [113–116]. Similarly, colorimetric biosensors, despite their visual simplicity, tend to require multi-step sample preparation and are vulnerable to variations in ambient lighting or subjective interpretation, especially in environments lacking standardized conditions [100,117,118]. Smartphone-based visual readers are being tested to mitigate these issues, but their precision and user-friendliness still vary widely [119,120]. In contrast, SERS-based biosensors, while capable of ultra-sensitive detection, are technically demanding due to their reliance on precision optical components (e.g., Raman lasers, detectors) and the need for specialized substrates such as gold or MOF-coated nanoparticles [100,121–126]. Additionally, there is no

universal SERS substrate that can accommodate all analyte types, necessitating tailored fabrication for each application [121,125,126].

Moreover, optical and surface plasmon resonance (SPR) technologies provide label-free, real-time monitoring capabilities that are especially suited to packaging and food processing environments [127,128], but they require precise optical setups, which limit portability.

From a regulatory and commercial perspective, biosensor platforms are not yet widely incorporated into formal food safety systems such as HACCP, ISO 22000, or Codex Alimentarius frameworks. Validation against gold-standard methods (e.g., culture-based enumeration, ELISA, or qPCR) is still lacking for many sensor formats, which affects their credibility in audits, certifications, and trade compliance [87,112,129–131]. The absence of harmonized validation protocols makes it difficult to compare results across borders or industries, leading to skepticism among food producers and regulatory bodies alike [90,112].

On the economic front, biosensors incorporating nanomaterials, CRISPR technology, or microfluidics often have high development and production costs, especially when coupled with surface functionalization and antibody/aptamer design [97,129,132–136]. This restricts their use in lower-income regions or small-scale food businesses. Scaling up from laboratory prototypes to commercial-grade devices often requires substantial investment in cleanroom facilities, testing, and certification [116,137]. Moreover, concerns regarding the long-term environmental and human health impacts of nanomaterials (e.g., silver nanoparticles, graphene oxide) continue to raise regulatory red flags, necessitating the shift toward green synthesis and biodegradable materials [138–140]. The need for non-toxic, disposable sensor platforms is gaining traction in global sustainability goals [138].

Biosensors also have an emerging role in monitoring cultured (cell-based) meat, a sector with specific challenges related to contamination control during cell cultivation, the composition of growth media, and the use of biochemical additives [141,142].

Finally, while point-of-care (POC) and intelligent packaging biosensors are increasingly being designed, real-world uptake is still slow. High costs, difficulty in integrating sensor data into existing software ecosystems, and energy requirements for continuous operation (especially for cold chains or remote sites) further hinder long-term monitoring applications [104,143,144]. In addition, data security and interoperability challenges persist, particularly when transferring biosensor data to cloud-based regulatory or logistics systems [130,131].

Despite the broad range of challenges, biosensor development is progressing rapidly, supported by innovations in nanotechnology, synthetic biology, electronics, and digital infrastructure. The next generation of biosensors is being engineered to meet not only technical performance benchmarks but also criteria for usability, affordability, and sustainability.

A key design philosophy is alignment with the REASSURED framework—Real-time connectivity, Ease of sample collection, Affordable, Sensitive, Specific, User-friendly, Rapid, Robust, Equipment-free, and Deliverable to end users [5,6]. Recent advancements in lab-on-a-chip (LOC) systems and wearable biosensors now allow continuous monitoring of animal stress biomarkers (e.g., cortisol, IL-6), meat spoilage indicators (e.g., biogenic amines), or microbial contamination in real-world environments [120,145–148]. LOC devices can be used directly in slaughterhouses, packaging lines, or distribution centers, reducing delays between contamination and detection.

Integration of biosensor data with IoT platforms, blockchain-enabled traceability, and AI-driven analytics is revolutionizing food safety by enabling predictive diagnostics and real-time response. For example, blockchain can secure biosensor data logs for traceable certification, while AI algorithms can analyze spectral or electrical patterns to detect anomalies or mixed contaminations [149-154

[149–154]. AI-based decision-support systems can also be trained in biosensor outputs to guide preventive measures in processing plants or farms. Smartphone-enabled biosensors also bridge accessibility gaps by allowing frontline inspectors and small producers to capture and transmit results immediately, often with GPS and timestamp metadata

[119,152]. These solutions support decentralized decision-making and democratize food safety monitoring [85,155,156].

The frontiers of biosensor technology are also being expanded through multiplexing and advanced signal amplification. CRISPR-Cas systems offer unparalleled specificity at attomolar levels, enabling detection of pathogens like *Listeria monocytogenes*, *E. coli* O157:H7, or *Salmonella enterica* in complex matrices [132,133,157,158]. Meanwhile, nanozyme-based colorimetric sensors provide robust alternatives to enzyme-based assays, maintaining stability under diverse environmental conditions and simplifying fabrication [159–162]. Nanozymes also eliminate cold-chain dependence for sensor reagents [161].

Multi-analyte aptasensors are being designed to simultaneously detect microbial pathogens, spoilage indicators, and chemical toxins in a single run—dramatically improving throughput and cost-effectiveness [96,105,163]. Similarly, molecularly imprinted polymer (MIP)-based sensors are showing high selectivity for volatile markers like histamine or trimethylamine, offering practical applications for seafood spoilage detection [164,165]. Such developments are particularly useful in import-exports where spoilage needs to be evaluated rapidly at ports or distribution hubs.

In the realm of packaging, intelligent sensors are now integrated directly into films, labels, or coatings to detect changes in gas composition (e.g., $CO_2$, $NH_3$), humidity, or microbial growth. These include hypoxanthine-sensing films for fish freshness and polymyxin B-aptamer platforms for endotoxin detection in poultry products [166–171]. Emerging solid-state SERS substrates (e.g., paper, elastomers, AuNS-glass composites) also offer durability and reusability in smart packaging applications [170,172,173]. Such features make them attractive for both consumers and regulatory audits.

To overcome energy and maintenance concerns, self-powered biosensors using biofuel cells or photoelectrochemical modules are being tested for autonomous deployment in storage environments with minimal infrastructure [144]. These devices align well with sustainability goals and reduce the carbon footprint of food monitoring [143,144].

Ultimately, the successful integration of biosensor technologies into food safety systems will rely not only on overcoming technical and operational barriers but also on establishing robust regulatory frameworks and fostering international standardization. It is essential that biosensor data be recognized as legally valid and interoperable across digital platforms used in global supply chains. Interdisciplinary collaboration among scientists, technologists, policymakers, and industry stakeholders will be key to accelerating the transition from research prototypes to field-deployable, validated tools.

By addressing current limitations in sensitivity, matrix interference, cost-effectiveness, and data integration, biosensors can be positioned as core components of intelligent, sustainable, and resilient food safety systems for the fish, meat, and poultry industries.

## 6. Conclusions

Biosensors have emerged as transformative tools for ensuring the safety and quality of fish, meat, poultry, and related food products. Their capacity to rapidly and sensitively detect contaminants, pathogens, spoilage markers, and drug residues positions them as viable and often superior alternatives to conventional laboratory-based methods. Recent advancements including the integration of nanomaterials, lab-on-a-chip platforms, smartphone interfaces, and IoT connectivity have significantly enhanced their portability, usability, and real-time monitoring capabilities.

Nevertheless, several critical challenges remain. The complexity of food matrices, environmental variability (such as pH, humidity, and temperature), and the inherent instability of biological recognition elements can affect performance and limit reproducibility. Regulatory acceptance is further constrained by the absence of harmonized validation standards and insufficient comparative assessments with gold-standard analytical techniques. Additionally, high development and implementation costs hinder widespread adoption, particularly in resource-limited settings.

Looking forward, the development of biosensors should prioritize robustness, affordability, and compliance with international regulatory frameworks. Embracing the REASSURED criteria ensuring

devices are real-time, easy to use, affordable, sensitive, specific, user-friendly, rapid, robust, equipment-free, and deliverable to end users will be key to broader deployment. Integration with AI-powered analytics and blockchain-based traceability systems can also unlock new opportunities for predictive diagnostics and transparent supply chain management. With continued interdisciplinary collaboration and innovation, biosensors are well-positioned to become cornerstone technologies in next-generation food safety and quality assurance systems.

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