

Review

Heavy Metal/Toxins Detection Using Electronic Tongues

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Received: 29 June 2019; Accepted: 31 July 2019; Published: 2 August 2019



Abstract: The growing concern for sustainability and environmental preservation has increased the demand for reliable, fast response, and low-cost devices to monitor the existence of heavy metals and toxins in water resources. An electronic tongue (e-tongue) is a multisensory array mostly based on electroanalytical methods and multivariate statistical techniques to facilitate information visualization in a qualitative and/or quantitative way. E-tongues are promising analytical devices having simple operation, fast response, low cost, easy integration with other systems (microfluidic, optical, etc) to enable miniaturization and provide a high sensitivity for measurements in complex liquid media, providing an interesting alternative to address many of the existing environmental monitoring challenges, specifically relevant emerging pollutants such as heavy metals and toxins.

Keywords: electronic tongue; heavy metals; toxins; multivariate statistical techniques; information visualization

1. Introduction

The massive global contamination of the atmosphere, water, and soil is a direct consequence of anthropogenic activities (industrial, wastewater, and domestic effluents) in the last decades. Moreover, the management of water resources in large urban centers faces an overall decline in the quality of potable waters, with the most common contaminants being heavy metals, pesticides, bacteria, fertilizers, and textile dyes. Unfortunately, the list of emerging pollutants only increases with over 700 substances recognized nowadays [1,2], including drugs, hormones, nanoparticles, and toxins. Most of the contaminants are non-biodegradable, putting at risk living organisms and human health due to bioaccumulation [3,4]. Within this context, European Union monitoring programs have currently included three groups of toxins: Diarrhetic shellfish toxins (DSTs), paralytic shellfish toxins (PSTs), and amnesic shellfish toxins (ASTs), and some other lipophilic contaminants [5].

Generally, the detection of pollutants is performed with spectroscopic and chromatographic techniques that require laborious sample pretreatment and trained personnel. Here, we focus on an interesting methodology that addresses many of the existing challenges in the detection of heavy metals and toxins, the so-called electronic tongue (e-tongue) systems. An e-tongue is a multisensory array based on non-specific or low-selective sensing units, taking advantage of their cross-sensitivity to identify a liquid medium, mostly using electroanalytical methods. Usually, an elevated amount of data is acquired, demanding multivariate statistical techniques for qualitative and/or quantitative analysis to facilitate information visualization from both simple and complex liquid media. Despite pioneering works in the 1990s [6–8], the term was coined in 2005 by the International Union of Pure and Applied

Chemistry (IUPAC) [9], with different detection methods reported in the literature, commonly based on voltammetric, potentiometric, impedimetric, and biosensing detection [10–14]. Here, we will focus on e-tongue devices devoted to heavy metal/toxin detection in liquid systems.

2. Heavy Metals

Within the wide range of environmental contaminants, heavy metal ions have received paramount concern owing to their persistence in ecosystems and severe effects on the human metabolic system due to bioaccumulation at trace levels. Notwithstanding, these contaminants are from anthropogenic activities, being also natural components in the earth's crust, with some of them (iron, selenium, copper, cobalt, manganese, and zinc) essential in minute amounts for particular biochemical processes and, without exceptions, harmful at high concentrations [15,16]. In short, a disorder in metal homeostasis can cause neurodegenerative diseases (Alzheimer's, Parkinson's, anemia, and arteriosclerosis) and seriously affect neuronal functions [17,18]. On the other hand, when accumulated in the human body, heavy metals may induce cancer and chronic or acute diseases in the kidneys, skin, lungs, bones, cardiovascular, and immune system [15,16,18].

Consequently, their non-biodegradability amplifies risks and concerns, as heavy metals can be accumulated in the food chain and bio-transformed, demanding higher attention toward finding efficient detection methods to avoid environmental and health problems. That led the search for better monitoring and management of natural resources using sensitive, rapid, simple, and selective methods for the detection of heavy metal ions, in order to achieve a sustainable solution to improve their trace-level monitoring in drinkable water, foodstuffs, and natural resources. The most traditional techniques for the detection of heavy metal ions are high performance liquid chromatography (HPLC) coupled with electrochemical- or UV-Vis-detectors, atomic absorption spectroscopy (AAS), inductively coupled plasma mass spectroscopy (ICP-MS), electrothermal atomic absorption spectrometry, flame atomic absorption spectrometry, wet chemical methods such as colorimetry, titrimetry, and gravimetry, and electrochemical techniques [19–28]. Despite the high accuracy and sensitivity reached in these methods, most of them require expensive, complex, and sophisticated equipment that needs trained staff, making them difficult to use in on-site measurements for portable and easy-to-use detection [19,26,29,30].

In this context, electrochemical methods are preferable due to their high sensitivity, fast response, low power cost, simpler approach, and ease of adaptability in order to be integrated into portable, disposable devices for the in-situ multi-element analysis of heavy metals. Nanomaterials have been used as an interesting strategy to enhance the sensitivity of the sensors due to easy functionalization and high electrochemical activity enabled by the electron-transfer process derived from unique electronic, physical, and chemical properties [31]. Screen-printed electrodes modified with mercury, bismuth, gold, selenium, tin, carbon, and conducting polymers in voltammetric systems were used for the simultaneous detection of heavy metals at residual levels, displaying a low limit of detection (LOD) and a large linearity range [32–35]. Similarly, Yang et al. used glassy carbon electrodes (GCE) chemically modified with bismuth nanoparticles [36] in square-wave anodic stripping voltammetry (SWASV) for the simultaneous detection of Pb^{2+} and Cd^{2+} in natural waters, with detection limits of 0.2 gL^{-1} and 0.6 gL^{-1} for Pb^{2+} and Cd^{2+} , respectively. The responses of very similar sensors were improved by Lee et al. by using graphene/bismuth nanocomposite films electrochemically deposited onto GCE [27]. They were able to simultaneously detect Zn^{2+} , Cd^{2+} , and Pb^{2+} , displaying detection limits of $1.80 \text{ }\mu\text{gL}^{-1}$, $0.18 \text{ }\mu\text{gL}^{-1}$, and $0.11 \text{ }\mu\text{gL}^{-1}$, respectively. Jung et al. developed a reusable polymer chip based on the silver working electrode and microfluidic channels for the continuous environmental monitoring of Pb^{2+} on-site [37]. The chip sensor was characterized through forty-three consecutive measurements inside the microchannels using SWASV, with results displaying high reproducibility and linearity over a wide concentration range (1 to 1000 parts per billion (ppb)), leading to a low cost, environmentally friendly sensor.

Despite the good results achieved, there still challenges to overcome in order to improve heavy metals detection. One of them is better reproducibility and stability in complex liquids, which can be

achieved by sensors based on nanomaterials [38]. Furthermore, detecting multiple heavy metals is a hard task, as in most cases the sensor presents specific sensitivity to only one or two heavy metals. Therefore, an elegant solution can be found with the use of a sensing array such as e-tongues, as will be discussed in the next section.

2.1. E-Tongues Applied in Heavy Metals Detection

It is well-known that the use of several electrodes having no selectivity, or low-selectivity in a sensor array has been more efficient to perform complex liquid analysis than sensors having high specificity [39]. Thus, the concept of an electronic tongue system has become an interesting alternative to detect heavy metal ions in complex liquid media. Vlasov and Legin developed a series of ion-selective chalcogenide glass sensors with outstanding chemical stability and sensitivity [7,8,40,41]. In 1997 they published a seminal paper using a potentiometric e-tongue to explore the cross-sensitivity of an array comprised by 33 sensing units composed of distinct chalcogenide vitreous and crystalline membranes, for the evaluation of heavy metal ions (Ni^{2+} , Cu^{2+} , Zn^{2+} , Cd^{2+} , and Pb^{2+}) in a concentration range of 10^{-7} – 10^{-3} mol L^{-1} [42]. Later, they also demonstrated the integration of a potentiometric e-tongue with flow injection analysis (FIA). Seven chalcogenide glass sensors were employed for on-line measurements at a waste incineration pilot plant for Pb^{2+} , Cr^{6+} , Cu^{2+} , and Cd^{2+} ions. Linear (partial least squares, PLS) and non-linear (artificial neural network, ANN) multivariate analysis were assessed, and PLS presented the lowest average errors in the determination of metal content [43].

Despite the use of organic membranes in e-tongues since 2000 [44], their use for heavy metal detection was only assessed in 2008 by Rudnitskaya et al. [45] through a potentiometric sensor array for the rapid assessment of ultra-low activities of copper, lead, zinc, and cadmium in seawater. It comprised 5-polymeric and 6-chalcogenide glass membranes as sensing units, presenting high sensitivity (nmol L^{-1}) and good linearity in both buffer and non-buffered solutions. Authors could detect copper down to 0.2 nmol L^{-1} , lead at 0.4 nmol L^{-1} , cadmium at 0.6 nmol L^{-1} , and zinc at 30 nmol L^{-1} in individual buffer solutions. The sensor array was capable of simultaneously detecting all ions that were mixed into 0.5 mol L^{-1} sodium chloride buffer solutions (seawater conditions), with a 20% average relative error. In mixed solutions, copper and zinc were detected at 1 nmol L^{-1} , and lead and cadmium down to 2 nmol L^{-1} , in accordance with the chronic seawater criteria. Spelthahn et al. developed a sensor array formed by electrodes covered with polymeric- and chalcogenide glass-membranes for the simultaneous detection of Ag^{+} , Cu^{2+} , Cd^{2+} , and Pb^{2+} [46]. Potentiometric experiments with the multisensory array immersed in heavy metal ion solutions (from 10^{-9} to 10^{-3} mol L^{-1}) displayed a low detection limit (10^{-7} – 10^{-8} mol L^{-1}) and a short response time (>1 min). Authors suggested at that time that future developments could combine both organic/inorganic materials in a chip-based electronic tongue.

The use of conducting polymer or organic small molecules as sensing units were first introduced by Riul et al. [47,48] in an impedimetric e-tongue system. Natural lignin films deposited onto gold interdigitated electrodes through the Langmuir–Blodgett technique were used as sensing units in an impedimetric e-tongue setup for the detection of heavy metal ions in tap water. Authors combined Fourier transform infrared spectroscopy (FTIR) and Langmuir isotherms (surface pressure vs. area) to explore the physical interactions formed between lignin phenyl groups and Cu^{2+} ions dispersed in an aqueous solution to explain the observed differences in impedance measurements [49]. Multi-walled carbon nanotubes (MWCNT) and polylactic acid (PLA) nanofiber nanocomposites were explored in a similar impedimetric e-tongue integrated into a flow injection analysis system to analyze potable waters contaminated with trace levels of heavy metals (Ba^{2+} (1.0 ppm), Cd^{2+} (0.001 ppm), Cu^{2+} (0.01 ppm), Pb^{2+} (0.01 ppm), Ni^{2+} (0.025 ppm), Mn^{2+} (0.1 ppm), and Fe^{3+} (0.3 ppm)) [50], enabling the distinction of contaminants through principal component analysis (PCA). Later, Teodoro et al. explored ternary nanocomposites based on electrospun nylon nanofibers, cellulose nanowhiskers, and silver nanoparticles as the sensing layers. The synergy between materials enabled the detection

of heavy metals (Pb^{2+} , Cd^{2+} , Cu^{2+} , and Ni^{2+}) at nmol L^{-1} concentration, assessed by information visualization techniques combined to feature selection protocol, as depicted in Figure 1 [51].

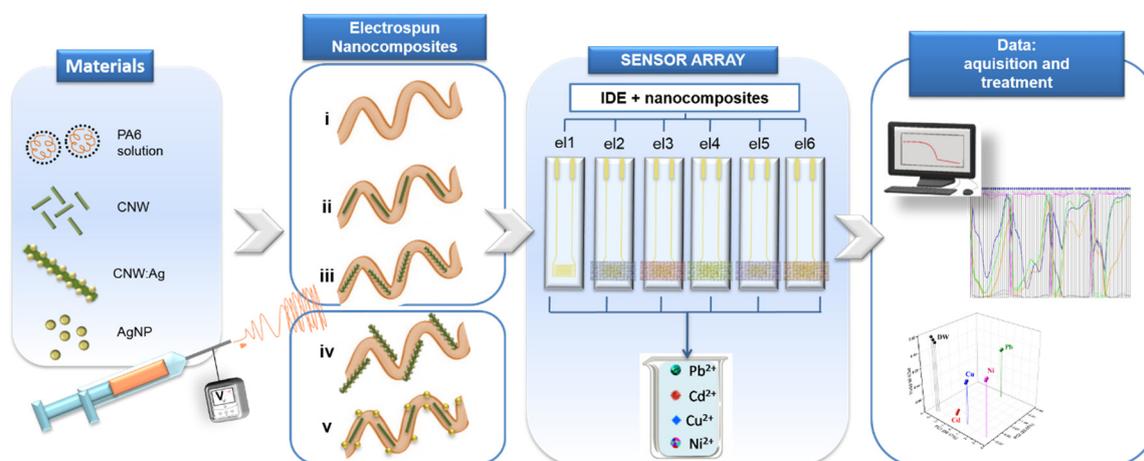


Figure 1. Experimental setup employed for ternary nanocomposites fabrication. Samples (i–iii) represent architectures fabricated by incorporation of nanostructures in the bulk of electrospun fibers, whereas samples (iv) and (v) represent electrospun fibers that were surface modified by immersion into the nanostructure solutions. PA6: nylon; CNW: cellulose nanowhiskers; AgNP: silver nanoparticles. Reproduced with permission from [51]. Copyright 2019 Elsevier.

The growing demand for miniaturized and integrated sensors led to the development of diverse e-tongues as follows. Mourzina et al. [39] proposed all-solid-state thin-film ion-selective microelectrodes (ISEs) based on chalcogenide glass-sensitive membranes through the use of silicon planar technology and pulsed laser deposition techniques. The simultaneous multicomponent analysis of Pb^{2+} , Cd^{2+} , and Zn^{2+} ions was performed by a potentiometric e-tongue, with the collected data modeled by a multilayer feed-forward artificial neural network using a back-error propagation training algorithm, resulting in an average accuracy of 15%–30% for the simultaneous detection of Pb^{2+} , Cd^{2+} , and Zn^{2+} ions. Another miniaturized e-tongue based on stripping voltammetry, also integrated into an FIA system was developed using all-solid-state planar electrodes for the analysis of residual contaminants in the water on the International Space Station (ISS), achieving an average detection limit of $10 \mu\text{mol L}^{-1}$ for Zn^{2+} , Pb^{2+} , Cu^{2+} , and Mn^{2+} [52]. One year later, Wang et al. proposed a flow injection analysis system integrated into a hybrid e-tongue, combining stripping voltammetry and multiple light-addressable potentiometric sensors (MLAPS), efficiently detecting mixed solutions of Fe^{3+} , Cr^{6+} , Mn^{5+} , and As^{3+} in wastewater/seawater. Since chalcogenide thin-film electrodes were not sensitive to Zn^{2+} , Cd^{2+} , Pb^{2+} , and Cu^{2+} ions, samples were measured with a silver-based mercury film working electrode in a conventional electrochemical cell that was also integrated to a FIA system, displaying the limit of detection at $\mu\text{g L}^{-1}$ [41]. Authors overcome the miniaturization problems by using a gold microelectrode array (MEA) prepared using planar silicon technology, in a light-addressable potentiometric sensor (LAPS) miniaturized multisensory chip [53] that was able to quantify zinc, lead, and copper. This device was further improved with a renewable gold nanoband electrode array (NEA-LAPS) [54], allowing the detection of Pb^{2+} and Cu^{2+} ions in ppb level.

A low-cost approach was studied by Pérez-Ràfols et al. that modified screen-printed electrodes with carbon nanofiber (SPCE-CNF), ex-situ antimony (ex-situ-SbSPCE-CNF), glutathione (GSH-SPCE-CNF), and cysteine (Cys-SPCE-CNF), to form the sensing units of a voltammetric e-tongue schematically shown in Figure 2A. This system was applied in the analysis of tap water contaminated with heavy metals, using differential pulse anodic stripping voltammetry (DPASV) as illustrated in Figure 2B. The voltammograms were modeled by PLS using the design depicted in Figure 2C, with the root mean square error (RMSE) values varying from 10.7 to $12.3 \mu\text{g L}^{-1}$ during the training subset. The simultaneous determination of Cd^{2+} , Pb^{2+} , Tl^{+} , and Bi^{3+} in tap water in the presence of Zn^{2+} and

In^{3+} ions, presented root square deviation (RSD) from 1.1% to 13.6%, which is high if compared to those obtained by inductively coupled plasma mass spectrometry (ICP-MS), RSD $\sim 0.6\%$ [28]. The same group later proposed a multivariate standard addition calibration method that basically consists of eliminating the preconcentration step to simulate a true blank solution. It is a strategy developed to solve complex matrices and overlapped peaks issues in tonic water samples spiked with Tl^+ and In^{3+} . A relative error calculated from the PLS model varied from 29.7% to 45.3% using external calibration, which fallen sharply to 0.5%–2.3% for the proposed multivariate standard addition [55]. This postulate glimpses to solve situations in which the overlapping of peaks occur in complex matrices that cannot be simulated nor externally calibrated.

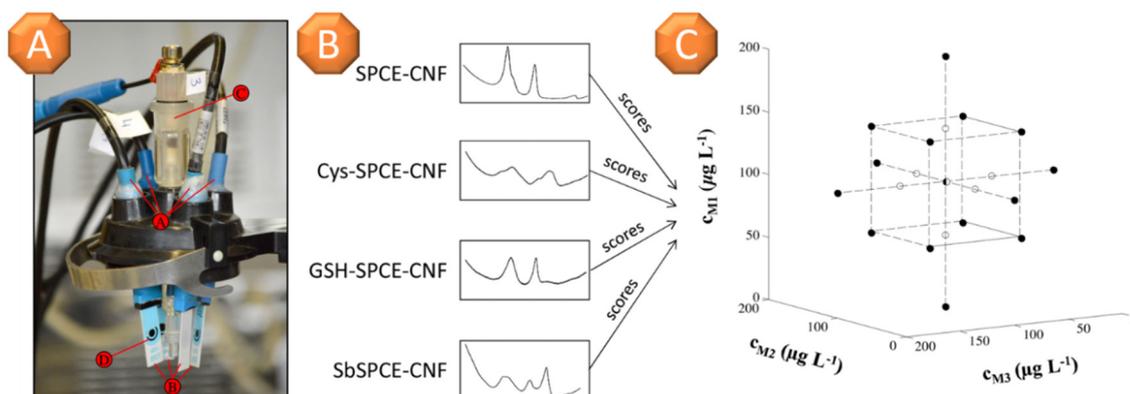


Figure 2. Schematic diagram of the experimental setup for voltammetric electronic tongue (e-tongue) measurements (A) using four different screen-printed electrodes, (B) differential pulse anodic stripping voltammetry (DPASV) voltammograms and (C) partial least squares (PLS) design used for training (●) and testing (○) subsets. M1, M2, and M3 represent any possible combination of three metals among Zn^{2+} , Cd^{2+} , Tl^+ , Pb^{2+} , In^{3+} , and Bi^{3+} . Reproduced with permission from [28]. Copyright 2017 Elsevier.

2.1.1. Computational Analysis Assisting E-Tongues in the Detection of Heavy Metals

Overall, e-tongues generate a massive amount of data and, consequently, data analysis has become an increasingly important tool for pre-processing, improvement of signal-to-noise ratio, and extraction of information. Multivariate methods such as PCA, linear discriminant analysis (LDA) and PLS are usually employed. In the last decade Oliveira et al. have used multivariate projection techniques to facilitate information visualization through interactive document maps (IDMAP), Sammon's mapping (SM), and parallel coordinates (PC) techniques that, when combined, allow feature data selection [56–58]. As demonstrated in [51], the feature selection protocol applied during statistical analysis of the whole capacitance data using parallel coordinates (Figure 3A) and least square projection (LSP) techniques enabled the extraction of the most relevant sensing units and frequencies positively contributing to the discrimination of heavy metal ions in concentrations $< 10 \text{ nmol L}^{-1}$, (Figure 3B,C). The blue boxes in Figure 3A provide information about the dimensions (frequencies in that case) that mostly contribute to the sample discrimination, separated in Figure 3B. In Figure 3C the silhouette coefficients [56] were plotted, e_{l_2} and e_{l_3} being the sensing units that least contributed to the analysis. Figure 3D,E depicts, respectively, the pattern recognition of Pb^{2+} , Cu^{2+} , Cd^{2+} , and Ni^{2+} ions in aqueous solutions, and lead solutions from 10^{-8} to $10^{-3} \text{ mol L}^{-1}$.

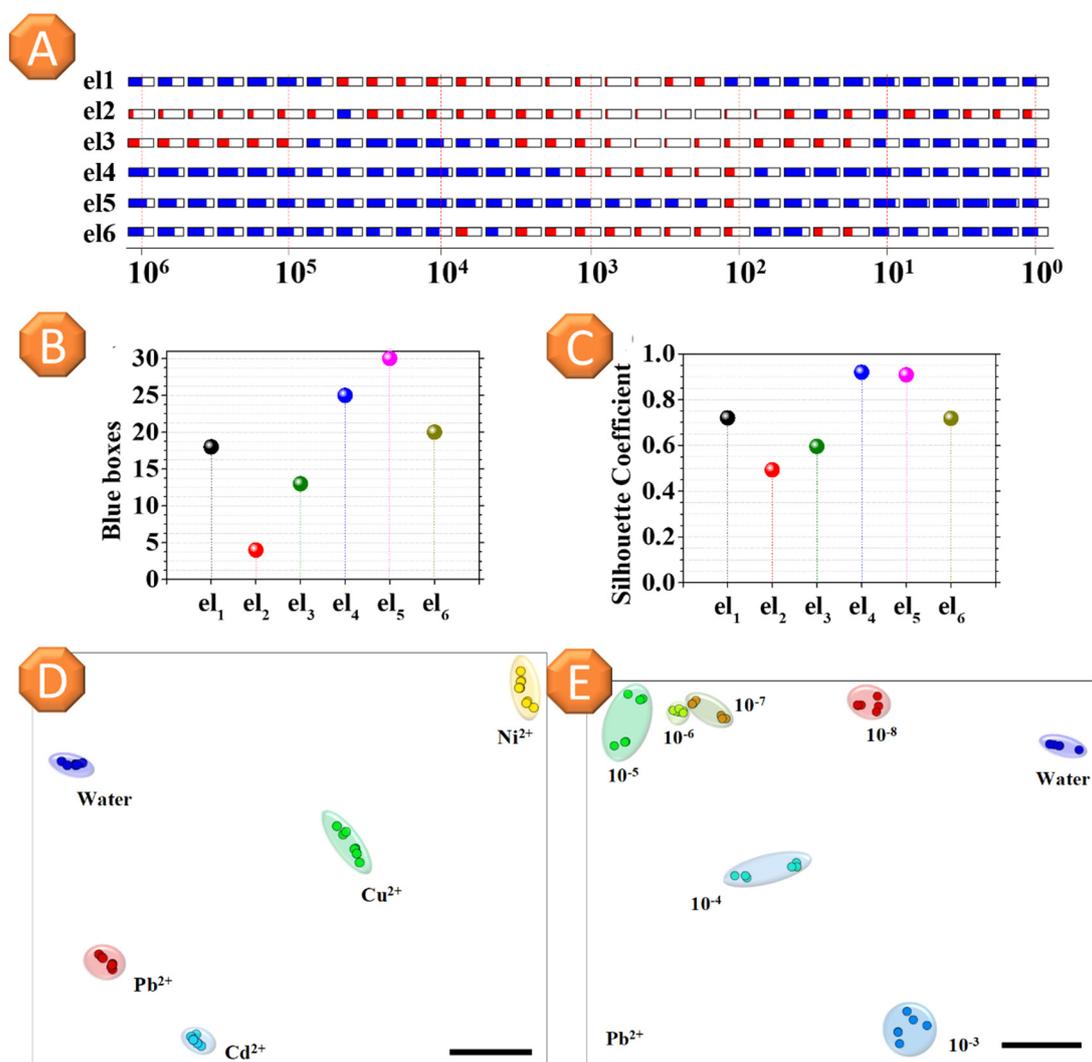


Figure 3. (A) Blue boxes collected from Parallel Coordinate plot for the different metal solutions at a concentration of 1 mmol L^{-1} , using the six sensing units. (B) Data plot of blue boxes and (C) silhouette coefficient of each sensing unit (for interpretation of the references to color in this figure legend, the reader is referred to the web version of this article). LSP plot for (D) different metal ions solution at a concentration of 1 mmol L^{-1} , and (E) different concentrations (10^{-8} to $10^{-3} \text{ mol L}^{-1}$) of lead solutions obtained by excluding sensing units number 2 and 3 and using the whole capacitance spectra. The black bar is only a guide to measure distances between data points. Reproduced with permission from [51]. Copyright 2019 Elsevier.

Advanced supervised methods such as artificial neural networks (ANNs) and genetic algorithms (GA) have been used in more challenging analysis to maximize the information achieved [28,57]. That in part transforms the complex sensor development into a software improvement, as demonstrated by del Valle et al. [59]. The use of ANNs proved to be suitable for building up response models for highly non-linear cases and used to determine multicomponent species. They demonstrated the ability of a potentiometric e-tongue based on polyvinyl chloride (PVC) membranes in the determination of low levels of Cu^{2+} , Pb^{2+} , Zn^{2+} , and Cd^{2+} ions from quaternary mixtures in open-air waste streams and rivers heading down the Gulf of Mexico. Despite the simplicity of this e-tongue, an ANN based on feed-forward and back-propagation, with multiple outputs configured with Bayesian regularization successfully modelled the data. To solve the matrix effect problem during e-tongue analysis, authors proposed an ANN model that corrects this effect through the multiple species response. The results for Cd^{2+} were not good, but the simultaneous detection of Pb^{2+} , Cu^{2+} , and Zn^{2+} ions in road soil samples

were satisfactorily modeled by ANNs and validated with atomic absorption spectroscopy, exhibiting low root mean squared error values ($\sim 1 \text{ mmol L}^{-1}$) [60]. Still, concerning the presence of heavy metals in soils, an automatic titration method was proposed employing an e-tongue integrated to an automatic microburette, used as an endpoint detection method in titration to resolve ternary mixtures of Pb^{2+} , Cd^{2+} , and Cu^{2+} ions at mmol L^{-1} level. An ANN model afforded a high accuracy in the determination of Pb^{2+} , with a reproducibility of 3.0% for Pb^{2+} , 4.1% for Cd^{2+} , and 5.2% for Cu^{2+} [61].

According to Florido et al. a simple, low-cost solution to remove partial heavy metals from liquid wastes is the use of natural sorbents such as grape stalk wastes generated in the wine production process. Therefore, an automated e-tongue integrated into a flow injection analysis system was used in the on-line monitoring of the biosorption process of Cu^{2+} ions in grape stalk waste [62]. The mechanism of metal ion uptake is ionic exchange due to the substantial release of Ca^{2+} and alkaline metals (K^+ and Mg^{2+}) during Cu^{2+} sorption process. Further studies were developed to monitor both Cu^{2+} ions (from removal) and Ca^{2+} ions (from exchanged and released process) in effluent solutions of grape stalk wastes [63]. Data were modeled by an ANN, and RMSE values at $\sim 0.07 \text{ mmol L}^{-1}$ could be determined. The system was also adapted to monitor in real-time binary ($\text{Cu}^{2+}/\text{Pb}^{2+}$), ($\text{Cu}^{2+}/\text{Zn}^{2+}$) and ternary ($\text{Cu}^{2+}/\text{Pb}^{2+}/\text{Zn}^{2+}$), ($\text{Cu}^{2+}/\text{Zn}^{2+}/\text{Cd}^{2+}$) mixtures, simultaneously releasing Ca^{2+} ions in the effluent solution [64]. This task was only possible due to a more elaborated algorithm employed in the ANN modeling that was applied using the Fourier transform during model optimization, establishing the affinity order $\text{Pb}^{2+} > \text{Cu}^{2+} > \text{Zn}^{2+} > \text{Cd}^{2+}$.

A patented method named ICA (independent component analysis) was utilized to improve the prediction accuracy of ANNs. An orthogonal experiment design (OED) was employed to reduce the number of training samples without losing any characteristics of specific ions. This methodology offered rapid and accurate results, without disturbing the natural speciation. The robustness and appropriateness of the approach were assessed using mean relative error (MRE). When optimized, the e-tongue system could quantify the concentration of four selected metals and chloride with an average MRE lower than 0.10 [65]. Genetic algorithms could optimize the impedance response of gold, platinum, glassy carbon, and silver nanoparticle electrodes in the detection of eight different heavy metals (Cd, Co, Zn, Ni, Cu, Cr, Ar, and Pb) in 24 water samples. The impedance data were recorded as single-electrode multi-frequency, single-frequency multi-electrode, and multi-electrode multi-frequency. Assisted by GA, authors could improve the cross-sensitivity of electrodes by selecting the best frequency and electrode combination [66,67].

A fuzzy logic system proposed by Turek et al. overcomes both calibration and laborious data pre-treatment problems faced in PCA, PLS, or ANN analysis. Fuzzy-logic minimized an experiment to 18 measurements for one- and two-component solutions of Ag^+ , Pb^{2+} , and Cu^{2+} ions that were validated as unknown, single-, and multi-component heavy metal solutions, with $\sim 80\%$ hit rate [68]. Such improvements in algorithm analysis will speed-up the use of e-tongues on analytical tasks because it may increase the analytical frequency analysis by decreasing the number of required sensing units, measurements, and need of recalibration.

2.1.2. Optical Multisensory System in the Detection of Heavy Metals

According to Vlasov et al., numerous sensing mechanisms can be employed in e-tongues [9] and that includes optical sensors. Despite the lower limits of detection achieved by electroanalytical techniques, optical systems are still attractive due to their simplicity of operation and fast response times. Within this context, some researchers developed hybrid devices operating with both light and electricity, such as the light-addressable potentiometric sensor (LAPS) or the multiple light-addressable potentiometric sensor (MLAPS) that have been successfully applied in e-tongue systems [41,53,54,69,70]. Lvova et al. [19] explored the fluorescent properties of macrocyclic fluorophore-modified PVC membranes to quantify the concentration of Cd^{2+} , Zn^{2+} , Pb^{2+} , and Cu^{2+} ions on fountains, rivers, and seawater of Rome and region. PCA and PLS multivariate analysis were performed to evaluate the precision of the proposed method. Low root mean square error of calibration and validation (RMSEC and RMSECV) were

observed, 0.47 and 0.64 for Cd^{2+} ; 0.057 and 0.064 for Cu^{2+} , 0.216 and 0.315 for Zn^{2+} , respectively. Regarding to the polluting species of interest, some samples were contaminated only with Cd^{2+} and a recovery of 90.5% to 106.6% was attained, with exception to seawater solutions that affected the measurements due to its high salinity. An interesting optical e-tongue multisensory array based on nine dye sensitive materials containing either pyridylazo or porphyrin chromophores, printed on an ABS membrane, was used in the detection of toxic heavy metal residues (Pb^{2+} , Cd^{2+} , and Hg^{2+}) in fish samples [71]. Samples were prepared with muscle tissue from the crucian carp fish and artificially digested for further colorimetric measurements. The images captured by the scanner produced red (R), green (G), and blue (B) values from 0 to 255, comparing the results with blank measurements. Extreme learning machine (ELM) exhibited superior prediction results 0.854, 0.83, and 0.84 when compared with PLS modeling that predicted 0.579, 0.594, and 0.538, for Pb^{2+} , Cd^{2+} , and Hg^{2+} ions, respectively. The entire process followed by the authors is summarized in Figure 4 as a flow chart.

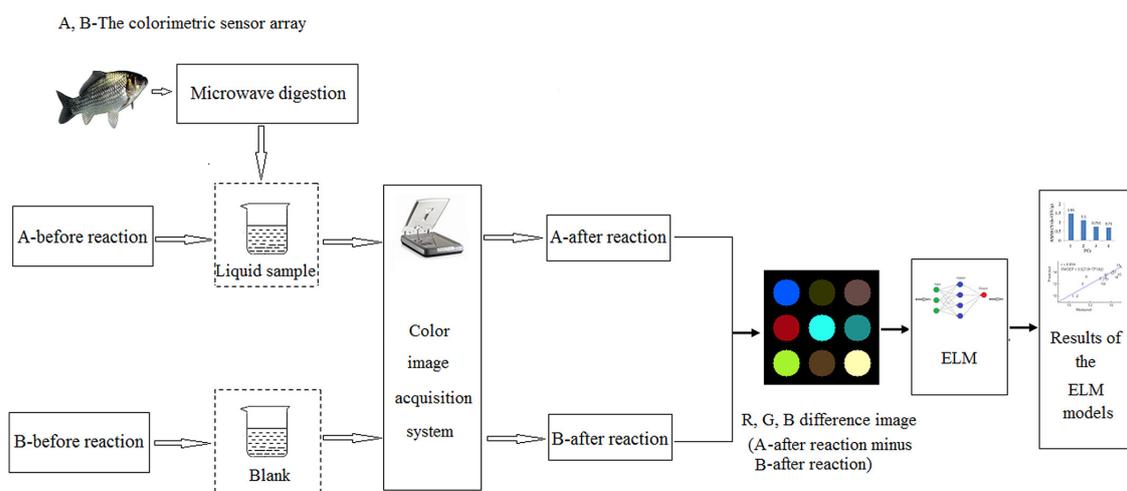


Figure 4. Schematic diagram of the colorimetric sensor array system for heavy metal detection in raw fish, from sample extraction to quantitative prediction models. Reproduced with permission from [71]. Copyright 2019 John Wiley & Sons, Inc.

We can also find interesting developments on paper-based microfluidic devices devoted to heavy metal detection, such as the chemically patterned microfluidic paper-based analytical device (C- μ PAD) used for multiplex heavy metal detection [24]. In this work, three chromogenic reagents having distinct reactions with Ni^{2+} , Cr^{6+} , and Hg^{2+} were covalently attached to functionalize each arm of the C- μ PADs. Afterward, a drop of mixed heavy metals solution was spread, and then flowed via capillarity to the detection zone. Such a simple system achieved detection limits of 0.24 ppm for Ni^{2+} , 0.18 ppm for Cr^{4+} and 0.19 ppm for Hg^{2+} . Despite the dependence of colorimetric devices on high sensitive indicators, Feng et al. [72] increased the sensitivity of a paper-based sensor array by enrichment using a pyridylazo compound. Their system was able to distinguish eight different heavy-metal ions (Hg^{2+} , Cd^{2+} , Pb^{2+} , Ag^{+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , and Co^{2+}) in sewage water below $\mu\text{mol L}^{-1}$ concentration. The identification of heavy metal ions was possible using pattern recognition methods, such as the hierarchical clustering analysis (HCA) and PCA [72]. Table 1 summarizes the performance of e-tongues regarding the detection of heavy metals reported by some studies presented in this review.

Table 1. Summary of e-tongues applied to heavy metals detection.

Heavy Metals	Sample	Sensing Units	Principle of Detection	Limit of Detection	Concentration Range	Computational Analysis	Ref.
Ni ²⁺ , Cu ²⁺ , Zn ²⁺ , Cd ²⁺ , Pb ²⁺	natural water	thirty-three chalcogenide glass and crystalline chemical sensors: based on Ag ₂ S, As ₂ S ₃ , AgI, SbS ₃ , GeS, GeS ₂ , CdI ₂ , PbI ₂ , Cu, Ag, As, Se, Te, Sb, Ge, CdS, PbS, CuS, AgBr, AgCl, LaF ₃ , Sb _{metal} .	POT	-	10 ⁻⁷ –10 ⁻³ mol L ⁻¹	3D simulation of sensor cross-sensitivity	[42]
Pb ²⁺ , Cr ⁶⁺ , Cu ²⁺ , Cd ²⁺	waste gases from incineration in pilot plant	seven chalcogenide glass sensors: PbAgAsS, CdAgAsS, TlAgAsS, CuAgAs-SeTe, CuAgAsSe, AgBrAsS, AgAsSe	POT/FIA	3 μmol L ⁻¹ Pb ²⁺ ; 1 μmol L ⁻¹ Cr ⁶⁺ ; 1 μmol L ⁻¹ Cu ²⁺ ; 1 μmol L ⁻¹ Cd ²⁺	2 × 10 ⁻⁷ – 2 × 10 ⁻⁴ mol L ⁻¹	PCA; PLS; ANN	[43]
Cu ²⁺ , Pb ²⁺ , Zn ²⁺ , Cd ²⁺	seawater	six chalcogenide glass sensors: Cu-Ag-As-Se; Cd-Ag-As-S; Pb-Ag-As-S; Ag-As-Se-Te; Cu-Ag-As-Se-Te; Ag-As-S. 5 PVC membrane based on: trioctylphosphine oxide; potassium tetra-phenyl borate + trioctylphosphine oxide; potassium tetra-phenyl borate; potassium tetra-phenyl borate + octylphenyl-N,N'-di-isobutylcarbamoylmethylphosphine oxide; potassium tetraphenyl borate + tetrabutylmethylenediphosphine dioxide	POT	0.2 nmol L ⁻¹ Cu ²⁺ ; 0.4 nmol L ⁻¹ Pb ²⁺ ; 30 nmol L ⁻¹ Zn ²⁺ ; 0.6 nmol L ⁻¹ Cd ²⁺	10 ⁻¹⁰ –10 ⁻² mol L ⁻¹	PLS	[45]
Cd ²⁺ , Cu ²⁺ , Pb ²⁺	81 samples of combined portions of three stock solutions (one for each considered metal)	chalcogenide glass: CdI ₂ -Ag ₂ S-As ₂ S ₃ ; Cu-Ag-As-Se) and PVC membrane: octylphenyl-N,N'-di-isobutylcarbamoylmethylphosphine oxide	POT/FIA	5.5 pmol L ⁻¹ Cd ²⁺ ; 6.2 pmol L ⁻¹ Cu ²⁺ ; 5.6 pmol L ⁻¹ Pb ²⁺	0–3.2 ppm Cd ²⁺ ; 0–95 ppb Cu ²⁺ ; 0–3 ppm Pb ²⁺	ANN; FFT	[73]
Ag ⁺ , Cu ²⁺ , Cd ²⁺ , Pb ²⁺	aqueous solutions	four chalcogenide glass: CdSAgIAs ₂ S ₃ , PbSAgIAs ₂ S ₃ , AgIAs ₂ S ₃ , CuAgAsSe; and 2 polymeric membranes: N,N'-diethyl-N,N'-di- <i>p</i> -tollyldipicolinic diamide, N,N'-diethyl-N,N'-diphenyl-2,2'-dipyridyl-6,6'-dicarboxylic diamide	POT	10 ⁻⁸ –10 ⁻⁷ mol L ⁻¹	10 ⁻⁹ –10 ⁻³ mol L ⁻¹	-	[46]
Cu ²⁺	aqueous solutions	lignin LB films	CV; EIS	-	>10.0 mg L ⁻¹	Curve fitting with an equivalent electric circuit	[49]
Ba ²⁺ , Cd ²⁺ , Cu ²⁺ , Pb ²⁺ , Ni ²⁺ , Mn ²⁺ , Fe ³⁺	potable water	MWCNT and PLA nanofiber nanocomposites	EIS/FIA	-	μg L ⁻¹	PCA	[50]
Pb ²⁺ , Cd ²⁺ , Cu ²⁺ , Ni ²⁺	aqueous and lead solutions	ternary nanocomposites based on electrospun nylon nanofibers, cellulose nanowhiskers and silver nanoparticles	CV; EIS	<10 nmol L ⁻¹	10 ⁻⁸ –10 ⁻³ mol L ⁻¹	PCA; PLS; IDMAP; PC	[51]
Pb ²⁺ , Cd ²⁺ , Zn ²⁺	Synthetic aqueous solutions of Pb(NO ₃) ₂ , Cd(NO ₃) ₂ , Zn(NO ₃) ₂ and Fe(NO ₃) ₃	eight chalcogenide glasses: CuAgAsSeTe, CuAgAsSe, PbAgAsI, CdAgAsI, TlAgAsI, AgIAsS, AgIAsSe, AgAsTeSe	POT	1 × 10 ⁻⁷ mol L ⁻¹ Cu ²⁺ and Pb ²⁺ ; 4 × 10 ⁻⁷ mol L ⁻¹ Cd ²⁺ ; 3 × 10 ⁻⁵ mol L ⁻¹ Ti ²⁺	10 ⁻⁵ –10 ⁻³ mol L ⁻¹	ANN	[39]
Zn ²⁺ , Pb ²⁺ , Cu ²⁺ , Mn ²⁺	water of the International Space Station	nine ceramic-based REDOX and conductivity sensors onto gold SPE	ASV/FIA	10 μmol L ⁻¹	100 μmol L ⁻¹	-	[52]
Fe ³⁺ , Cr ⁶⁺ , Mn ⁵⁺ , As ³⁺ , Zn ²⁺ , Cd ²⁺ , Pb ²⁺ , Cu ²⁺	wastewater/seawater	chalcogenide glass Cr/Au silver-based mercury film electrode	MLAPS with SV	60 μg L ⁻¹ Zn ²⁺ ; 1 μg L ⁻¹ Cd ²⁺ ; 2 μg L ⁻¹ Pb ²⁺ ; 8 μg L ⁻¹ Cu ²⁺ ; 60 μg L ⁻¹ Mn ⁵⁺ ; 30 μg L ⁻¹ As ³⁺ ; 280 μg L ⁻¹ Fe ³⁺ ; 26 μg L ⁻¹ Cr ⁶⁺	μg L ⁻¹	-	[41]

Table 1. Cont.

Heavy Metals	Sample	Sensing Units	Principle of Detection	Limit of Detection	Concentration Range	Computational Analysis	Ref.
Pb ²⁺ , Cu ²⁺	standard solutions of zinc, lead, and copper in acetate buffer	gold MEA in a LAPS	POT	ppb	-	SCM; MNLR	[53]
Pb ²⁺ , Cu ²⁺	sulfuric acid and acetate buffer	gold NEA-LAPS	SWASV	ppb	20 ppb–100 ppb	-	[54]
Cd ²⁺ , Pb ²⁺ , Tl ⁺ , Bi ³⁺	spiked tap water	SPCE-CNF; ex-situ-SbSPCE-CNF; GSH-SPCE-CNF; Cys-SPCE-CNF	DPASV	µg L ⁻¹	0–200 µg L ⁻¹	PLS	[28]
Tl ⁺ , In ³⁺	tonic water samples spiked with Tl ⁺ and In ³⁺	sensor array based on a SeCyst-SPCNFE and an ex-situ-BiSPCE	DPASV	µg L ⁻¹	19.9–174.9 µg L ⁻¹ Tl ⁺ ; 20.2–174.9 µg L ⁻¹ In ³⁺	PLS	[55]
Cu ²⁺ , Pb ²⁺ , Zn ²⁺ , Cd ²⁺	natural water waste streams (Gulf of Mexico)	eleven PVC membranes: N,N',N'-tetrabutyl-3,6-dioxaoctanedi (thioamide), <i>o</i> -xylylenebis (N,N-diisobutylidithiocarbamate), S,S'-methylenebis (N,N-diisobutylidithiocarbamate), <i>tert</i> -butylcalix[4]arene-tetrakis (N,N-dimethylthioacetamide), tetrabutylthiuram disulfide, 3,7,12,17-tetramethyl-8,13-divinyl-2,18-porphinedipropionic acid disodium salt, tri-N-dodecylamine, tetrabenzyl pyrophosphate, [2,2']-Furildioxime monohydrate	POT	-	5.2 × 10 ⁻⁸ – 2 × 10 ⁻⁶ mol L ⁻¹ Cd ²⁺ and Pb ²⁺ ; 5.2 × 10 ⁻⁷ – 2 × 10 ⁻⁵ mol L ⁻¹ Cu ²⁺ and Zn ²⁺	ANN	[59]
Pb ²⁺ , Cd ²⁺ , Cu ²⁺ , Zn ²⁺	road soil	nine PVC membranes: 1,3-bis(N-benzoylthioureido)benzene, S,S'-methylenebis(N,N-diisobutylidithiocarbamate), <i>tert</i> -butylcalix[4]arene-tetrakis (N,N-dimethylthioacetamide), tetrabutylthiuram disulfide, 3,7,12,17-tetramethyl-8,13-divinyl-2,18-porphine-dipropionic acid (disodium salt), N,N',N'-tetrabutyl-3,6-dioxaoctane di(thioamide), <i>o</i> -xylylene bis(N,N-diisobutylidithio-carbamate), tetrabenzyl pyrophosphate, [2,2']-furildioxime monohydrate	POT	-	10 ⁻⁶ –10 ⁻² mol L ⁻¹	ANN	[60]
Pb ²⁺ , Cd ²⁺ , Cu ²⁺	contaminated soil	eight PVC membranes: S,S'-methylenebis (N,N-diisobutylidithiocarbamate), <i>tert</i> -butyl-calix[4]arene-tetrakis (N,N-dimethylthioacetamide), 1,3-bis(N-benzoylthioureido)-benzene, N,N',N'-tetrabutyl-3,6-dioxaoctane di(thioamide), <i>o</i> -xylylene bis (N,N-diisobutyl-dithiocarbamate), tetrabenzyl pyrophosphate, [2,2']-furil-dioxime monohydrate, triethylphosphineoxide	POT	1 mg L ⁻¹	-	ANN	[61]
Cu ²⁺	grape stalk waste	Cu(II)-selective electrodes	POT/FIA	-	µg L ⁻¹	Thomas' model	[62]
Cu ²⁺ , Ca ²⁺	effluent solution of grape stalk wastes	5-sensor array with Cu ²⁺ and Ca ²⁺ -selective electrodes; electrodes with generic response to heavy-metals	POT/FIA	µmol L ⁻¹	-	ANN	[63]
binary (Cu ²⁺ /Pb ²⁺), (Cu ²⁺ /Zn ²⁺) and ternary (Cu ²⁺ /Pb ²⁺ /Zn ²⁺), (Cu ²⁺ /Zn ²⁺ /Cd ²⁺) heavy metal mixtures, simultaneously to the release of Ca ²⁺ ions in the effluent solution	vegetable wastes	crystalline membranes based on a composite of Ag ₂ S-CuS in epoxy resin used in the preparation of the Cu ²⁺ -selective sensors; polymeric membrane with mobile carrier	POT/FIA	µmol L ⁻¹	-	optimized Fourier-ANN coupling	[64]

Table 1. Cont.

Heavy Metals	Sample	Sensing Units	Principle of Detection	Limit of Detection	Concentration Range	Computational Analysis	Ref.
Ca ²⁺ , Cd ²⁺ , Cu ²⁺ , Pb ²⁺	multiple free ions dissolved in solutions	ISE array of six commercial electrodes: Ca ²⁺ ; Cd ²⁺ ; pHoenix Cl-ISE; Cu ²⁺ ; Pb ²⁺ ; orion double junction Ag/AgCl reference electrode	-	0.01 μmol L ⁻¹ Cu ²⁺ ; 0.1 μmol L ⁻¹ Pb ²⁺ and Cd ²⁺ ; 1 μmol L ⁻¹ Ca ²⁺	0.1 μmol L ⁻¹ – 10 mmol L ⁻¹ Cu ²⁺ ; 1 μmol L ⁻¹ – 10 m mol L ⁻¹ Pb ²⁺ and Cd ²⁺ ; 10 μmol L ⁻¹ – 0.1 mol L ⁻¹ Ca ²⁺	PCA; ANN; genetic ICA; OED	[65]
Cd ²⁺ , Co ²⁺ , Zn ²⁺ , Ni ²⁺ , Cu ²⁺ , Cr ⁶⁺ , Ar ²⁺ , Pb ²⁺	24 water samples containing 8 different heavy metal ions	gold, platinum, glassy carbon and silver nanoparticle electrodes	EIS	-	-	PCA; GA	[66,67]
Ag ⁺ , Pb ²⁺ , Cu ²⁺	single- and multi-component heavy metal solutions	miniaturized chalcogenide glass sensors	POT	-	10 ⁻⁶ mol L ⁻¹ – 10 ⁻³ mol L ⁻¹	fuzzy logic	[68]
Cd ²⁺ , Cu ²⁺ , Zn ²⁺	fountains, rivers and seawater (Italy)	macrocyclic fluorophore-modified PVC membranes	FLUO	0.0013 mg L ⁻¹ Cd ²⁺	-	PCA; PLS	[19]
Pb ²⁺ , Cd ²⁺ , Hg ²⁺	muscle tissue from crucian carp fish species and artificially digested	nine dye sensitive materials, containing either pyridylazo or porphyrin chromophores	COL	0.05 mg kg ⁻¹ Pb ²⁺ ; 0.02 mg kg ⁻¹ Cd ²⁺ and Hg ²⁺	-	PCA; ELM; PLS	[71]
Ni ²⁺ , Cr ⁶⁺ , Hg ²⁺	lake-water	C-μPAD immobilized with silane compounds terminating in amine (NH ₂), carboxyl (COOH), and thiol (SH)	COL	0.24 ppm Ni ²⁺ ; 0.18 ppm Cr ⁶⁺ ; 0.19 ppm Hg ²⁺	-	-	[24]
Hg ²⁺ , Cd ²⁺ , Pb ²⁺ , Ag ⁺ , Ni ²⁺ , Cu ²⁺ , Zn ²⁺ , Co ²⁺	sewage water	paper-based microfluidic device modified with pyridylazo	COL	50 μmol L ⁻¹	-	PCA; HCA	[72]
Zn ²⁺ , Cu ²⁺ , Ni ²⁺	standard solutions in water	two polymeric membranes that change color by complexation with chromogenic reagents	OPT	10 ⁻⁷ mol L ⁻¹	-	ANN	[74]

Anodic stripping voltammetry (ASV); artificial neural network (ANN); cathodic stripping voltammetry (CSV); chemically patterned microfluidic paper-based analytical device (C-μPAD); colorimetry (COL); cyclic voltammetry (CV); differential pulse anodic stripping voltammetry (DPASV); electrochemical impedance spectroscopy (EIS); extreme learning machine (ELM); fast Fourier transform (FFT); flow injection analysis (FIA); fluorimetry (FLUO); genetic algorithms (GA); hierarchical clustering analysis (HCA); independent component analysis (ICA); interactive document map (IDMAP); ion selective electrode (ISE); least square projection (LSP); light-addressable potentiometric sensor (LAPS); mean relative error (MRE); microelectrode array (MEA); multi-electrode multi-frequency (MEMF); multiple light-addressable potentiometric sensors (MLAPS); multivariate nonlinear regression (MNLRL); multi-walled carbon nanotubes (MWCNT); nanoband electrode array (NEA-LAPS); orthogonal experiment design (OED); optical (OPT); parallel coordinates (PC); partial least squares (PLS); poly(lactic acid) (PLA); potentiometry (POT); principal component analysis (PCA); screen-printed electrodes (SPE); screen-printed electrodes modified with carbon nanofiber (SPCE-CNF); screen-printed electrodes modified with ex-situ antimony (ex-situ-SbSPCE-CNF); screen-printed electrodes modified with cysteine (Cys-SPCE-CNF); screen-printed electrodes modified with glutathione (GSH-SPCE-CNF); sequential injection analysis (SIA); single-frequency multi-electrode (SFME); single-electrode multi-frequency (SEMF); standard curve method (SCM); square wave anodic stripping voltammetry (SWASV); stripping voltammetry (SV).

3. Toxins

Although the major impact on pollution of aquatic environments originates from human activities, contamination caused by naturally occurring microorganisms, i.e., marine toxins, is also a major concern. The main groups affecting aquatic systems are mycotoxins, algal, bacterial, and plant toxins [75]. Among them, the most relevant toxin groups found in freshwater are anatoxin-A (ATX), cylindrospermopsin (CYN), and microcystins (MCs); while marine toxins are classified into brevetoxin (BTX), okadaic acid (OA), palytoxin (PTX), saxitoxin (STX), cyclic imine (CI), domoic acid (DA), pectenotoxin (PTX), yessotoxin (YT), azaspiracid (AZA), and ciguatoxin (CTX) [76]. According to the European Union legislation, the official reference method for the detection of paralytic shellfish toxins (PST) is liquid chromatography with fluorimetric detection (FLD) [77]. As LC-FLD is a laborious technique involving expensive apparatus that must be operated by highly skilled human resources, e-tongues are a rapid, simple, and interesting alternative to detect marine toxins, that have been slightly explored in the literature as follows.

Lvova et al. presented a potentiometric e-tongue system for the detection of cyanobacteria microcystin toxins (MCs) [78], with chemical structures of two isomers presented in Figure 5A. The system was formed by PVC-plasticized sensors, platinum (Pt), and stainless-steel bar electrodes. It was successfully used to distinguish toxic and non-toxic *Microcystis aeruginosa* strains added into potable water (Figure 5B). A few years later the system was successfully applied in the analysis of water samples collected in two different areas in Italy that were spiked with MC solutions [79]. Figure 5C shows the responses of the potentiometric sensor for toxic *Microcystis aeruginosa* strains grown in an inorganic bold basal medium. The results obtained in different water matrices were compared with those obtained by standard chromatography ultra-high-performance liquid chromatography with diode array detector (UHPLC-DAD) and colorimetric enzymatic analysis. The root mean square error (RMSE) of calibration and validation and the correlation coefficient of predicted versus measured data were used to evaluate the efficiency of partial least squares (PLS) models (Figure 5D). The obtained values were close to $1 \mu\text{g L}^{-1}$ (guideline value for MC content in potable water), indicating the great success of the e-tongue system in the monitoring of an environmental area.

E-tongue applications usually require frequent recalibration of the multisensory array [80]. In this context, Legin et al. proposed an interesting alternative based on a mathematical sensor drift correction [81]. The univariate single sensor standardization approach significantly improved the precision of both regression and classification models, with the calibration lifetime extended when compared to raw uncorrected data. As a proof of concept, authors studied two microcystin strains of cyanobacteria *M. aeruginosa* (toxic and non-toxic) in water samples using a potentiometric e-tongue for 74 days. Data were statistically analyzed with LDA, logistic regression, and partial least squares-discriminant analysis (PLS-DA), using a single sensor standardization algorithm to correct the drift, thus increasing the classifiers accuracy from ~60% to 100%.

Ferreira et al. developed chemical sensors using plasticized polyvinyl chloride membranes for the detection of paralytic shellfish toxins (PST) [82]. Plasticized PVC membranes containing ionophores in nine distinct compositions were drop-casted on screen-printed electrodes to form a potentiometric multisensory system. Authors focused on the detection of four PST, saxitoxin, decarbamoyl saxitoxin, gonyautoxin 5 (GTX5), and C1&C2, found in Portuguese coastal waters. The sensors were not suitable for the selective detection of PST due to their inherent cross-sensitivity and low selectivity to PST, and high selectivity to interferents (sodium, potassium, and calcium). However, it makes them suitable for e-tongue systems due to their low selectivity that many chemical sensors display in the multicomponent analysis. Cruz et al. applied a potentiometric e-tongue system to evaluate PST in extracts of naturally contaminated mussels [83] collected from four sites in the Portuguese coast in 3 distinct years. PST free mussels were collected as a control group during absence periods of *Gymnodinium catenatum* blooms. PCA and PLS analysis were employed as calibration methods and were in good agreement with results obtained from chromatography. In addition, one of the sensors succeeded in the selective detection of decarbamoylsaxitoxin (dcSTX) in acidic bivalve extracts [82]. Therefore, specific single sensors combined in an e-tongue system are promising tools for rapid screening of PST in bivalves.

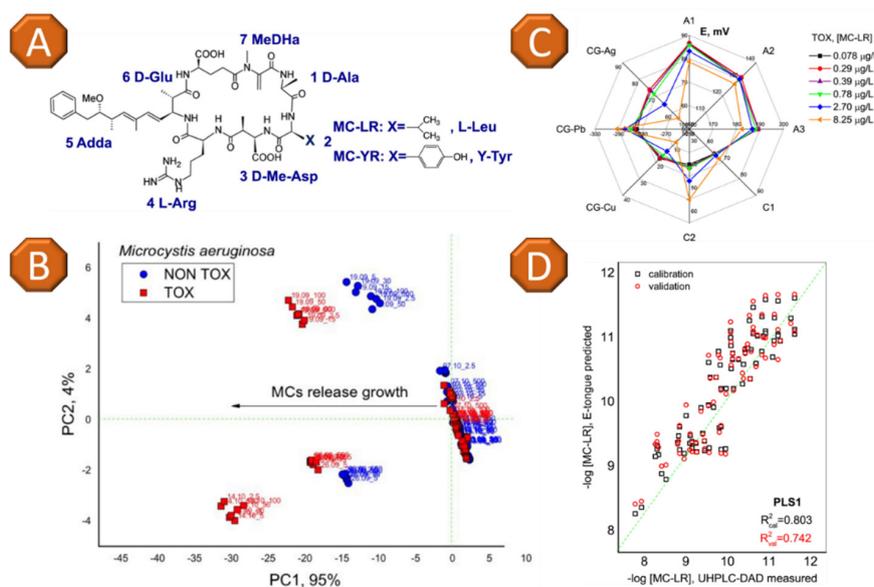


Figure 5. (A) Chemical structures of two microcystin isomers. (B) Principal component analysis (PCA) plot for e-tongue data of local potable water samples contaminated by toxic (TOX) and non-toxic (NON-TOX) *Microcystis aeruginosa* strains. (C) Potentiometric responses for distinct sensors in tap water spiked with toxic *Microcystis aeruginosa* strains. (D) PLS correlation results for microcystin content determined by means of potentiometric e-tongue system and standard chromatographic technique (UHPLC-DAD method). Reproduced with permission from [78,79]. Copyright 2014 and 2016, Elsevier.

Besides the contamination in aquatic environments, naturally occurring toxins in foodstuffs are also a great problem for public health. Staple foods like corn or cereals may contain high levels of mycotoxins produced by mold on grains, such as aflatoxin and ochratoxin [84]. Samanta et al. used nanocrystalline silicon oxide (nc-SiO₂) immunosensors in the detection of trace quantities of common mycotoxins in food samples obtained from distinct geographical locations in India [85]. Corn sample extracts were obtained in a methanol/water mixture, followed by filtration. Three types of mycotoxins were detected: Aflatoxin B1 (AFB1), aflatoxin B2 (AFB2), and ochratoxin A (OTA). They used an array composed of 18 sensors (six for each toxin) immobilized with specific monoclonal antibodies commercially available for each individual toxin (anti-AFB1, anti-AFB2, and anti-OTA). Impedance spectroscopy measurements were performed in a two-electrode configuration, with the sensitivity calculated as the fractional change in the impedance values before and after the toxin exposure. According to the authors, the total impedance of a single nanopore is the combination of ionic conductance within the pore and the capacitive impedance at the bottom of the pore. The corresponding data was processed with an incremental fuzzy algorithm, which enabled the learning of new patterns without losing prior trained knowledge. Authors reached a detection limit down to 0.1 fg mL⁻¹, with 93% accuracy even considering large quantities of non-target toxins. Ghosh et al. improved the nc-SiO₂ immunosensor array optimizing the pore geometry as a figure of merit to evaluate toxins in food samples [86]. Regular 200 nm diameter pores were produced on silicon substrates by electrochemical etching in five different thicknesses (from 65 to 135 nm). The oxidized substrates formed pores in distinct dimensions, followed by monoclonal anti-AFB1 immobilization to produce functionalized sensors. Non-infected corn seeds were selected as a food sample, and their extract was spiked with different mixtures of AFB1 and OTA. The obtained data were processed by PCA and PLS-DA. The optimized nc-SiO₂ immunosensor e-tongue was capable of successfully detecting 0.1 fg mL⁻¹ AFB1 and OTA, with 10% and 20% errors, respectively. The approach presented by them to enhance the performance of e-tongue systems using nc-SiO₂ immunosensors is interesting and can be easily extended to different molecules for food toxin detection. Table 2 summarizes the performance of e-tongues regarding the detection of toxins reported by some studies presented here.

Table 2. E-tongues applied in toxins detection.

Toxins	Sample	Sensing Units	Principle of Detection	Limit of Detection	Concentration Range	Computational Analysis	Ref.
microcystin released by <i>Microcystis aeruginosa</i> strains	potable water	six PVC-plasticized sensors based on ion-exchangers and ligands of various structure, platinum (Pt) and stainless-steel bar electrodes	POT	-	10^{-10} – 10^{-8} mol L ⁻¹	PCA; PLS	[78]
microcystin released by <i>Microcystis aeruginosa</i> strains	mineral and tap water, river and lake water (Italy)	PVC-based solvent polymeric membranes doped with Co(TPP)Cl and nonactin ionophores, and ion-exchangers TpClPBK and TDANO3; chalcogenide glass sensors (CG-Cu, CG-Pb, CG-Ag) and polycrystalline sensor based on LaF3	POT	0.014 µg L ⁻¹	0.078–8.25 µg L ⁻¹	PLS-DA	[79]
microcystin released by <i>Microcystis aeruginosa</i> strains	tap water	PVC-based solvent polymeric membranes doped with Co(TPP)Cl and nonactin (sensor C1) ionophores, and ion-exchangers TpClPBK and TDANO3; chalcogenide glass sensors (CG-Cu, CG-Pb) and polycrystalline sensor based on LaF3	POT	-	-	LDA; LR; PLS-DA	[81]
saxitoxin (STX), decarbamoyl saxitoxin (dcSTX), gonyautoxin GTX5 and C1&C2	extracts of bivalves found in marine water (Portugal)	nine PVC membranes: Calix[6]arene, Calix[4]arene-25,26,27,28-tetrol, 1,4,7,10,13-pentaoxa-16-azacyclooctadecane, 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, Calix[6]arene-hexaacetic acid hexaethylester, Octadecyl 4-formylbenzoate, 4,6,11,12-tetrahydro-3-methyl-1-phenyl-1H-pyrazolo[3',4':4,5]pyrimido[1,2-b]quinazolin-5-ium tetrafluoroborate, Octadecyl 4-formylbenzoate, 4,6,11,12-tetrahydro-3-methyl-1-phenyl-1H-pyrazolo[3',4':4,5]pyrimido[1,2-b]quinazolin-5-ium tetrafluoroborate	POT	0.25–0.9 µmol L ⁻¹ STX and dcSTX; 0.08–1.8 µmol L ⁻¹ GTX5 and C1&C2	0.1–6.8 µmol L ⁻¹	-	[82]
saxitoxin (STX), decarbamoyl saxitoxin (dcSTX), GTX5 and C1&2 released by <i>Gymnodinium catenatum</i> blooms	extracts of naturally contaminated mussels found in marine water in distinct years (Portugal)	plasticized PVC membranes containing ionophores in 6 distinct compositions: calix[6]arene, calix[4]arene-25,26,27,28-tetrol, 1,4,7,10,13-pentaoxa-16-azacyclooctadecane, 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, octadecyl 4-formylbenzoate and 4,6,11,12-tetrahydro-3-methyl-1-phenyl-1H-pyrazolo[3',4':4,5]pyrimido[1,2-b]quinazolin-5-ium tetrafluoroborate	POT	0.19–1.5 µmol L ⁻¹ STX and dcSTX; 0.24–2.5 µmol L ⁻¹ GTX5; 0.63–7.2 µmol L ⁻¹ C1&2	0.19–1.5 µmol L ⁻¹ STX and dcSTX; 0.24–2.5 µmol L ⁻¹ GTX5; 0.63–7.2 µmol L ⁻¹ C1&2	PCA; PLS; JY-PLS	[83]
aflatoxin B1 (AFB1), aflatoxin B2 (AFB2) and ochratoxin A (OTA)	extract of non-infected corn seeds (India)	eighteen nanocrystalline silicon oxide immunosensors (six for each toxin) immobilized with specific monoclonal antibodies commercially available for each individual toxin (anti-AFB1, anti-AFB2 and anti-OTA)	EIS	0.1 fg mL ⁻¹	0.1 fg mL ⁻¹ –100 ng mL ⁻¹	incremental fuzzy logic	[85]
aflatoxin B1 (AFB1) and ochratoxin A (OTA)	extract of non-infected corn seeds	nine nanocrystalline silicon oxide immunosensors with different pore dimensions immobilized with anti-AFB1	EIS	0.1 fg mL ⁻¹	0.1 fg mL ⁻¹ –1 pg mL ⁻¹ (AFB1); 0.1 fg mL ⁻¹ –100 ng mL ⁻¹ (OTA)	PCA; PLS-DA	[86]

Electrochemical impedance spectroscopy (EIS); joint-Y partial least square regression (JY-PLS); linear discriminant analysis (LDA); logistic regression (LR); partial least squares (PLS); partial least squared - discriminant analysis (PLS-DA); potentiometry (POT); principal component analysis (PCA).

4. Conclusions and Future Trends

We have reviewed the pragmatic aspects of multisensory systems when used in for the control, measurement, and processing of information related to the detection of heavy metals and toxins in water, soil, and food. Despite the successful application of innovative e-tongue systems in the simultaneous detection of pollutants, there are still some challenges (sensor replacement, frequent recalibration of the multisensory array, drift correction) defying the production of commercially available instruments for accurate on-site analysis. Further investigation towards the development of more reliable, durable, and miniaturized sensors is encouraged. Additional integration to the Internet of Things (IoT) would enable the inception of a broad sensing network, thus providing continuous, real-time information on the environmental health of water resources throughout the globe. In addition, the use of computational analysis has led to better e-tongue performances in both sample classification and quantification. These are important findings pointing to promising future trends in e-tongue sensing combined with computational resources.

Author Contributions: All authors have participated and contributed equally in all stages of this work.

Funding: This research was funded by the Sao Paulo Research Foundation (FAPESP) and the National Council for Scientific and Technological Development (CNPq).

Acknowledgments: The authors thank the financial support from the Brazilian agencies FAPESP (2015/14836-9) and CNPq (308570/2018-9).

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

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