Fundamentals and application of voltammetric electronic tongues in quantitative analysis

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A R T I C L E I N F O

A B S T R A C T

Electronic tongues (ETs) are bioinspired analytical tools based on the synergies between (bio)sensors and chemometrics. Through the application of chemometrics, it is possible to infer underlying relationships between the measured analytical signals and the chemical properties of the samples, both for descriptive and predictive purposes, otherwise impossible to decipher. Research in voltammetric ETs during the last two decades has demonstrated the benefits derived from the use of sensor arrays with complementary response, together with advanced data treatment methods to enhance their overall performance. In this direction, the different approaches followed when developing voltammetric ETs and some relevant applications in quantitative analysis are reviewed herein.

1. Introduction

Research in electrochemical sensors during the last two decades has demonstrated the advantages that can be obtained from the use of arrays of sensors with complementary response, combined with advanced data treatment methods to enhance their overall performance [1–3]. Such an approach is known as electronic nose (EN) when gas samples are analysed, or electronic tongue (ET) when it is applied to the analysis of liquid samples. More specifically, ETs have been defined by the IUPAC as "an analytical instrument comprising an array of nonspecific, low-selective, chemical sensors with high stability and cross-sensitivity to different species in solution, and an appropriate method of PARC (pattern recognition) and/or multivariate calibration for data processing" [4].

Thus, ETs are based on multi-sensor devices applied to the analysis of liquid samples, that harness chemometric methods to overcome the complex nature of some sensors responses. In this regard, ETs main advantages lie in their ability to provide comprehensive information about complex samples by simultaneously detecting a large spectrum of compounds in a few seconds/minutes, without requiring any pre-treatment step as the data processing stage may offset any matrix effect from the sample itself [1–3,5], and even correct interferences, drifts or non-linearity effects of the sensors [6].

From the definition, it is clear that ETs have two key components: the sensor array and the chemometrics part. Those two are the ones that define the ET and determine the nature of the information obtained. On the one side, the choice of the sensors impacts on which physicochemical parameters of the sample are measured. On the other side, the selection of the multivariate data analysis method determines the task (application) carried out by the ET (e.g. categorical *vs.* regression based models). Obviously, the performance of the sensors has a direct impact on the performance of the system, as their responses have to be related to the parameters being analysed. Nonetheless, the chemometric methods have as much impact as the sensors, as they are responsible to infer the underlying relationships between the measured analytical signals and the chemical properties of the samples.

Among the different types of chemosensors that can constitute the ET sensor array, electrochemical sensors (including

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potentiometric, voltammetric and impedimetric) are the most common ones [5]; although other types of sensors such as optical, gravimetric or piezoelectric might also be used. In this regard, it is possible to combine sensors from different types, an approach that is known as *data fusion*; howbeit this requires further considerations on how to integrate these data consistently [7]. More recently, the incorporation of biosensors has opened a new field of applications [3,8]. Such systems are referred to as bioelectronic tongues (BioETs), and do only differ in the incorporation of one or several biosensors into the array.

The chemometric methods used can be mainly classified according to two parameters: (i) the machine learning task (unsupervised or supervised methods); and (ii) their application (categorical or regression based models). The latter is related to which is the output of the model, namely divided into models used for qualitative (classification) or quantitative purposes, while the former takes into account whether labelled or unlabelled data is provided to the learning system when building the model. That is, in unsupervised methods only the sensors' responses (the predictors) are provided to the system to build the model; whereas in supervised methods, both the predictors as well as the target(s) are provided (training set) and used to build the model, which is later applied to estimate those targets for new samples. However, other authors divide the different analysis methods in three different types: exploratory, classification and calibration. That is, distinguishing visualization or clustering methods such as principal component analysis (PCA) or other cluster analysis techniques from the actual unsupervised categorical methods [9].

Up to date, a wide variety of applications involving the use of ETs has already been reported [1–3]. Among those, agri-food analysis (including beverages) and environmental monitoring are the two more prominent fields, although significant applications have also been developed in the security, pharmaceutical or chemical industry fields, among others. Particularly, in the agri-food analysis, most of the developed applications deal with the classification of food and beverages according to perceptions of food quality (e.g. taste), varieties, geographical origin, etc. in an effort to provide an automated equivalent to sensory panels; whereas in the environmental monitoring side, most of the applications focus on the detection and determination of different contaminants such as heavy metals, pesticides or disinfection-by-products (DBPs), as well as other compounds of agri-environmental interest such as fertilizers or alkaline ions.

This review focuses on the application of ETs based on voltammetric (bio)sensors devoted to quantitative analysis. Instead of providing a comprehensive summary of all of the reported works in the past years, the aim of this review is to highlight the most relevant advances in the field over different scenarios, being an essential introduction to the key concepts for the non-specialist interested to learn on the topic, and at the same time serving as a springboard for all the researchers working with electrochemical sensors.

2. Voltammetric electronic tongues

Among the different types of sensors considered when developing ET applications, voltammetric (bio)sensors are the most common ones. To illustrate this, a bibliometric study was performed making use of the Web of Science database, which results are summarized in Fig. 1.

Although the term "electronic tongue" is the most popular one, and actually the one proposed by the IUPAC, some authors also refer to ETs as "taste sensor", "multisensor system", "sensor array" or "multisensor array" [1], and consequently some of those terms were also used when doing the search. It can be clearly seen how
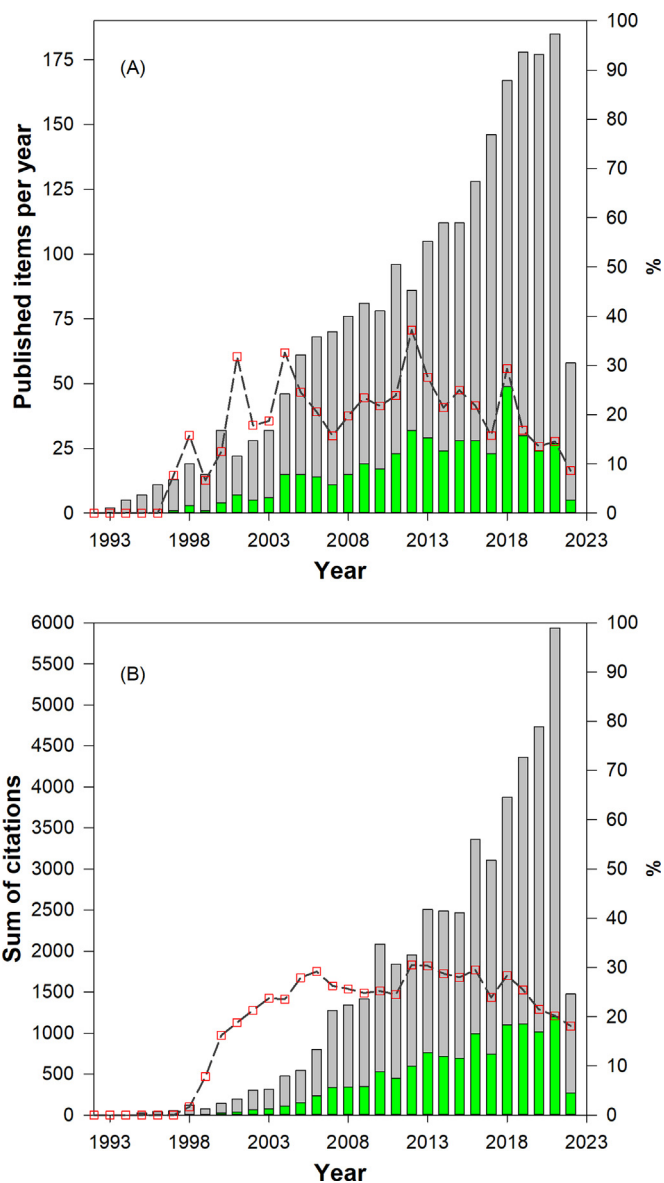

Fig. 1. Citation report created from Web of Science through the searches ("electronic tongue" or "taste sensor") as topic, as well as refining the previous with the topic "voltam*" (green bars). The percentage of the latter with respect to the former is also plotted (red □). Search limited to the following document types: review, article and book chapter. Accessed on 28/03/2022.

both the number of publications, as well as the citations received by those, have steadily increased over the last 20 years after the term was coined. Besides the numbers shown, it is important to highlight that there is also a significant number of publications that do not mention the terms ET or taste sensor, and simply describe the combination of a multi-sensor system and some data treatment approaches. Similarly, there is also a significant number of papers in which ETs' principles are applied, but making use of only one sensor (e.g., Refs. [10–13]); an approach that is possible thanks to the multi-dimensional response of the sensors.

The results from the previous search were refined using the term "voltam*" to consider only the applications involving voltammetric sensors, while ensuring to include all the word variations such as voltammetric, voltametric or voltammetry. Analogously, similar trend can be seen both for the number of manuscripts and citations. If considering the last 10 years, *ca.* 22% of

ETs publications report on voltammetric ETs, whereas in terms of citations, those receive *ca.* 26% of total citations; numbers that confirm the relevance of voltammetric (bio)sensors in the context of ETs.

Over the next sections we will focus on the main parameters that define ETs (Fig. 2): (i) the type of sensors, (ii) the measuring technique, and (iii) the data processing. Finally, an overview of different selected applications will be provided to better illustrate the capabilities of such an approach.

2.1. Voltammetric (bio)sensors

As already stated, the idea behind ETs is to have an array of sensors with cross-response features, capable to provide wide and comprehensive information of the sample, rather than using one sensor with high selectivity and sensitivity towards a specific analyte. Afterwards, through the combination of the sensors' responses and with the aid of chemometric methods, the classification of samples or the actual quantification of specific analytes/indexes is achieved.

This approach presents two main advantages when compared to classical research in chemo- and bio-sensors. On the one side, the difficulties found when developing highly specific sensors are overcome by shifting the complexity from the analytical to the data processing field. On the other side, we are also able to overcome the lack of knowledge of unique characteristic compounds responsible for certain perceptions or that can be used to achieve samples discrimination. For example, it is even possible to estimate an unmeasured variable from other measured variables, what is known as "soft sensor" [14]. This is highly relevant when evaluating complex integral features such as toxicity or perception attributes which depend on numerous chemical components simultaneously.

A wide variety of sensors have been considered when developing ET applications (Fig. 3). The first time a voltammetric ET was reported, it was based on the usage of two bare metallic wires as working electrodes, namely Au and Pt [15]. Next, the use of other noble metals was explored (Au, Pt, Ir, Pd, Rh, Ag, etc.) [16−22], while later on, also other metals such as Re, Cu, Ni, Co, W and Ti have been considered [23−25]. The advantages of those lie in their simplicity and durability in terms of material, whereas the use of different metals leads to different electrochemical behaviour and the low-selectivity required to develop ET applications.

Despite the development of novel sensing platforms is not the ultimate goal of ETs research, it cannot be neglected that ETs nourish from advances in the sensors field. In this direction, the development of composites based on conductive phases dispersed in polymeric matrices offered attractive electrochemical, physical, mechanical and economical features compared to the classic metallic conductors [28]; especially considering that the incorporation of modifiers can significantly improve the analytical characteristics of the resulting sensors. Among those, carbon paste electrodes (CPEs) and graphite-epoxy composites (GECs) arose as two of the most widely employed electrodes when developing voltammetric ETs [29−36], using as modifiers redox mediators/electrocatalysts such as metals, conducting polymers, phthalocyanines or nanoparticles, among others.

Nowadays, screen printed electrodes (SPEs) have arisen as the most common sensing platform for the development of electrochemical sensors due to their simple, rapid and low-cost production, plus the added advantages of their disposable character, small size suited to work with micro-volumes, and portability as all working, reference and counter electrodes are printed on the same strip. For the fabrication of SPE devices, many configurations have been reported, both in terms of geometry as well as materials [37]. In regards to the former, a three electrode configuration (reference, counter and working electrodes) is the more common one, but several devices including many working electrodes (2,4,8, …,20) in the same miniaturized device have been reported. As for the sensing material, a wide variety of inks are commercially available nowadays; some of the more interesting ones include graphite and different carbon-based materials such as carbon nanotubes (CNTs), graphene or nanofibers, metals such as Au, Pt, Cu, Bi, etc, mediators such as phthalocyanines or Prussian blue, etc.

Lastly, additive manufacturing (most commonly known as 3D printing) is emerging as an alternative approach for the fabrication of customized electrochemical sensors, owing to their many unique advantages such as its low-cost (both of the material and equipment), tuneability and easy prototyping [38,39]. One of the reasons that makes 3D printing so appealing is that it combines the ease of
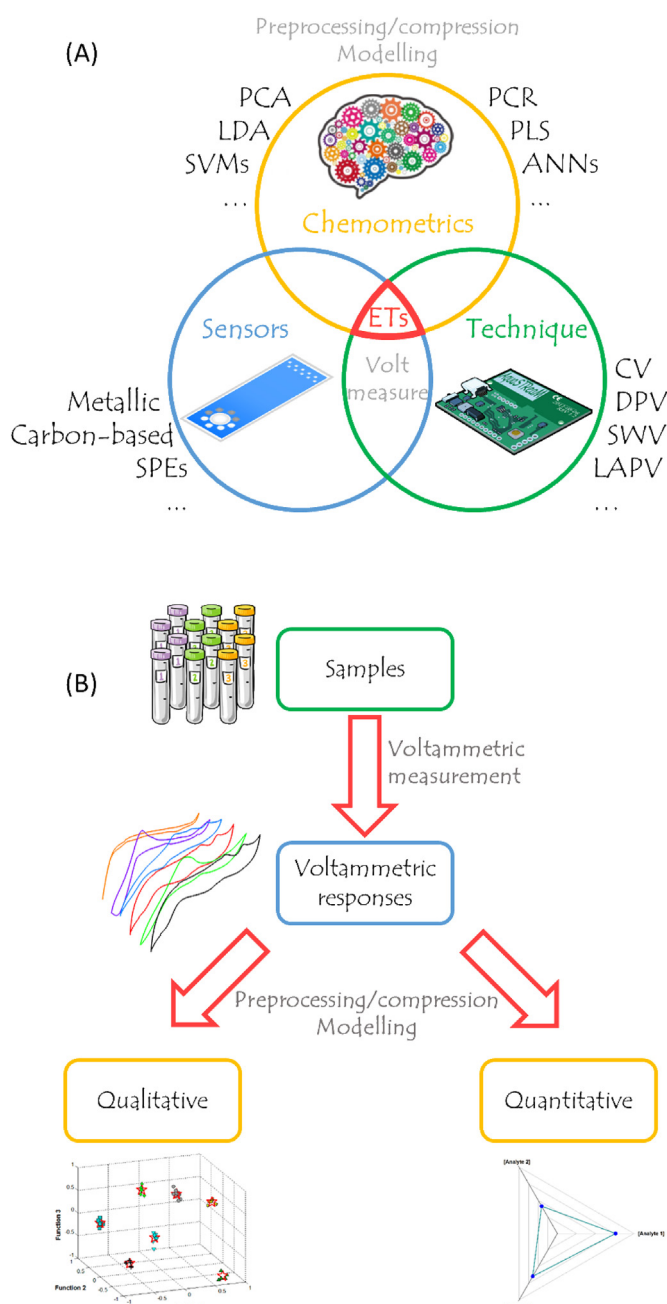

Fig. 2. Schematic illustrating (A) the main components that define an ET, and (B) block diagram of the ETs approach.
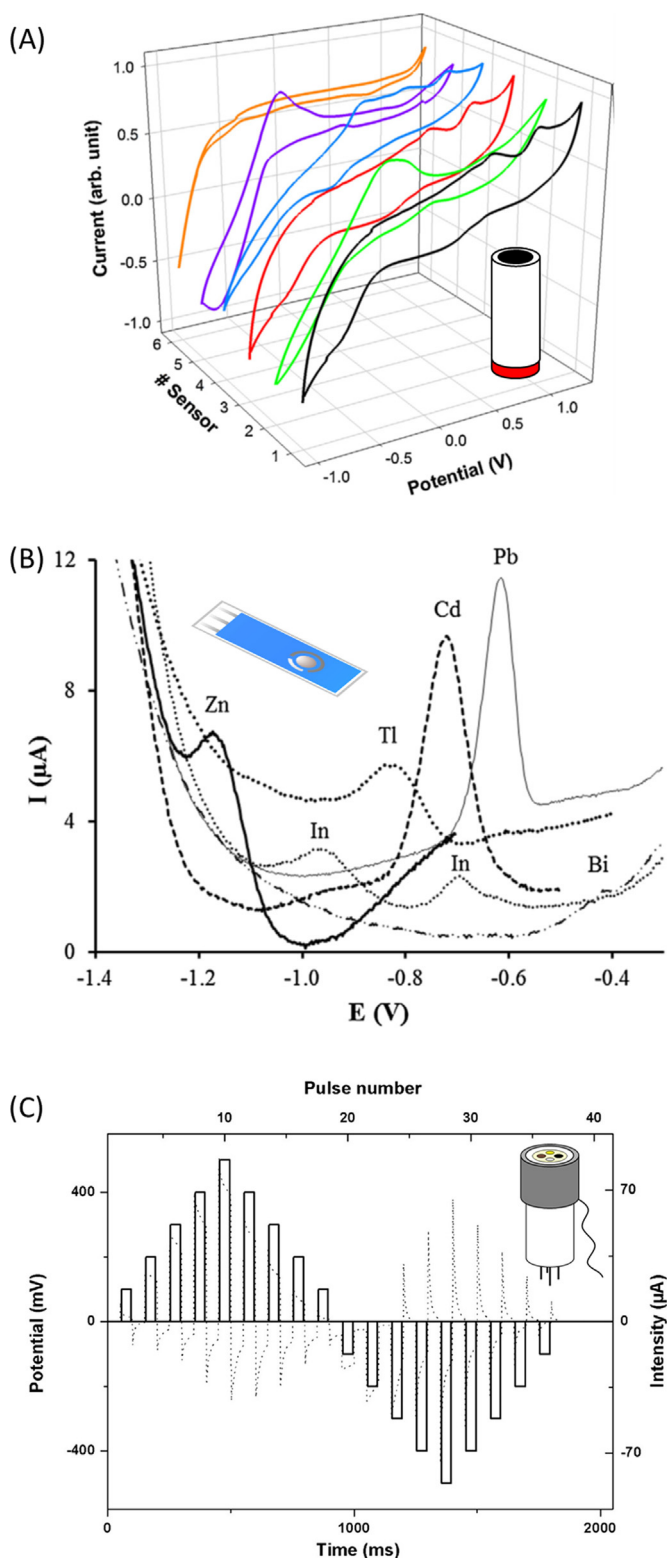
Fig. 3. Illustration of the different type of sensors used when developing voltammetric ETs, as well as the voltammetric responses obtained with those when using different voltammetric techniques. Measurement of (A) a wine sample with different composite sensors employing CV, (B) a water sample containing different metal ions with screen-printed electrodes employing DPV, and (C) a vegetable milk with metallic electrodes employing LAPV. Images reproduced with permission from Refs. [21,26,27].

fabrication of other composite materials such as CPEs and GECs with the automatized fabrication and miniaturization of SPEs. Concretely, electrodes are fabricated by fused deposition modelling (FDM) from thermoplastics such as poly-lactic acid (PLA) or acrylonitrile-butadiene-styrene (ABS), commonly doped with different carbon-based materials such as carbon black, CNTs or graphene to overcome the insulating nature of PLA and ABS. Additionally, other redox mediators/electrocatalysts, as those above mentioned, can also be incorporated by extrusion of customized filaments.

Hitherto the usage of bare materials or their bulk modifications have been discussed, but chemically modified electrodes (CMEs) have also played a key role in the development of voltammetric ETs. Modification of the electrodes is usually performed through the irreversible adsorption of substances with desired functionalities [40,41], covalent binding of components [26], or coating with polymeric or non-polymeric films [13,17,42,43]. The aim of such modifications is to improve the selectivity and the sensitivity of the sensors towards specific analytes. That is, despite is true that ETs are based on the usage of low-selective sensors showing cross-response features, certain degree of selectivity is still required.

Lastly, special mention has to be devoted to the incorporation of biosensors into ETs sensor arrays, an approach that has been referred as bioelectronic tongues (BioETs) [3]. In the same line as CMEs, and despite the higher selectivity and specificity associated with the usage of bioreceptors, it has to be taken into account that still those also show some cross-reactivity, although towards a narrower group of compounds. In this line, the coupling of bio-sensors and ETs presents huge potential as it exploits the combination of chemometrics to solve interferences issues from biosensors, and biosensors to improve the lack of selectivity sometimes attributed to ETs when applied to complex samples. Thus, the development of BioETs allows improving ETs performance and tackling new application fields. Among the different examples that can be found in the literature, two scenarios have been extensively studied: (i) the detection of pesticides through the measurement of enzymatic inhibition, mainly of cholinesterase enzymes (ChE) [44], and (ii) the detection of phenolic compounds using tyrosinase (Tyr) and laccase (Lac) enzymes as bioreceptors [10,31,45].

2.2. Voltammetric methods

In voltammetric methods, both qualitative and quantitative information of the electroactive species present in the sample is obtained from the application of a time-dependent potential (excitation signal), and the measurement of the resulting current as a function of the former [46,47]. Precisely, how the applied potential is changed and the current is measured, is what distinguishes the different voltammetric methods (Fig. 3).

In this regard, linear sweep voltammetry (LSV) or cyclic voltammetry (CV) are the most common voltammetric techniques (Table 1). This is because they are considered the most classical and simplest voltammetric methods, plus the fact that CV provides, in one step, information of the compounds present in the sample that can be either oxidized or reduced.

With the advance of electrochemistry, new methods appeared aiming to overcome some of the limitations found with LSV/CV, especially in terms of detection limits. Among them, pulse voltammetric methods, such as differential pulse voltammetry (DPV) or square wave voltammetry (SWV), have also been widely used in ETs (Table 1). The main advantage of those is their high sensitivity and the fact that non-faradaic current contributions are minimized.

To achieve the detection of minute concentrations, stripping methods such as anodic (ASV) and cathodic stripping

Table 1

Summary of some of the most relevant quantitative applications involving the use of voltammetric ETs.

Sample	Analyte/Attribute	Sensors	Technique	Data processing	Ref.
Physicochemical parameters of natural food products					
Animal feed	Amino acids: tryptophan, cysteine and tyrosine	Pt sensor	DPV	DWT + ANNs	[48]
Honey	Protein, colour, phenolic compounds, acidity, sugars	4 metallic electrodes: Pt, Au, GCE, Ag	CV	Feature extraction + PLS	[22]
Juices and water	Nitrate	GCE modified biosensor	CV	SVMs	[12]
Milk	Antibiotics: Chloramphenicol, Erythromycin, Kanamycin sulfate, Neomycin sulfate, Streptomycin sulfate and Tetracycline HCl	5 metallic electrodes: Au, Ag, Pt, Pd, Ti	MLPAV	PCR, PLS, LS-SVM	[16]
Oil	Carotenoids	7 metallic electrodes: Cu, GCE, Au, Ni, Pd, Pt, Ag	CV	Feature extraction + PLS	[17]
		3 interdigitated electrodes modified with polyelectrolytes			
Saffron	Safranal, Picrocrocin and many esters	SPEs of C, Pt, Au and PB	CV	kernels + PLS	[40]
		SPEs chemically modified with phtalocyanines			
Tea	Theaflavin and thearubigin	7 metallic electrodes: Au, Ir, Pd, Pt, Rh	LAPV	DWT + PLS/ SVMs	[18]
Wine	Total polyphenols in wine	4 graphite-epoxy modified enzymatic (bio)sensors	CV	FFT + ANNs	[45]
Wine	Anthocyanins, sugar content, titratable acidity, pH, optical density, colour, etc.	PEDOT modified Pt and sonogel carbon	DPV	PLS	[13]
Wine (cava)	Sugar	6 graphite-epoxy modified sensors	CV	FFT + ANNs	[29]
Contaminants					
Food and vegetable extracts, water	Organophosphate pesticides: dichlorvos, malaoxon, chlorpyrifos-oxon, chlorpyrifosmethyl-oxon,chlorfenvinphos and pir-imiphos-methyl-oxon	6 AChE-based enzymatic biosensors	CAmp	ANNs	[44]
Standards	Explosive compounds: RDX, TNT and PETN	SPE	CV	DWT + ANNs	[11]
Standards	Nerve Agent Mimics: diisopropyl fluorophosphates (DFP), diethyl chlorphosphate (DCP) and diethyl cyanophosphate (DCNP)	8 metallic working electrodes: Au, Pt, Ir, Rh, Cu, Co, Ni and Ag	LAPV	PLS	[19]
Standards	Phenolic compounds	Tyrosinase modified graphite-epoxy composite	LSV	ANNs	[10]
Water	Heavy metals: Cu^{2+}, Cd^{2+}, Pb^{2+}	4 peptide-modified gold electrodes	SWV	PLS, nPLS	[41]
Water	Heavy metals: Zn^{2+}, Cd^{2+}, Pb^{2+}	3 peptide-modified graphite-epoxy composite	AdSV	FFT + ANNs	[30]
Water, tap	Heavy metals: Cd^{2+}, Pb^{2+}, Tl^+ and Bi^{3+} in the presence of Zn^{2+} and In^{3+}	4 modified SPEs with peptides and Sb	DPV	PLS	[26]
Water, tap	Haloacetic acids: HAA3	Au sensor	CV/SWV	FFT + ANNs	[49]
Water, wastewater	Phenolic compounds	4 graphite-epoxy modified (bio) sensors	CV	FFT + ANNs	[31]
Medical diagnostics					
Pharmaceutical drugs	Diclofenac, paracetamol and naproxen	Multiwall carbon nanotubes CPE	DPV	DWT + ANNs	[32]
Urine, serum and milk	Antibiotics: tetracycline and cefixime	SPE modified with gold nanoparticles and cysteine	SWV	PCA + ANNs	[43]
Urine, human	Creatinine	7 metallic electrodes: GCE, Au, Pt, Ag, Ni, Pd, Cu	CV	PLS	[20]
Perception attributes					
Coffee	Adulteration	CPE	DPV	MLR, PLS	[33]
Milk	Sensorial attributes	8 metallic electrodes: Au, Pt, Rh, Ir, Cu, Co, Ag, Ni	LAPV	PLS	[21]
Oil	Bitterness	CPE modified with olive oil	CV	kernels + PLS	[34]
Oil	Adulteration	CPE modified with olive oil	SWV	kernels + PLS	[35]
Pear	Firmness and sugar	Au, Ag, Pt, Pd, W, Ti	MLAPV	PCR, PLS, SVMs	[24]
Rice	Flavour attributes: softness, stickiness, sweetness and aroma	6 metallic electrodes: Pt, Au, Pd, W, Ti, Ag	MLPAV	FFT + ANNs	[25]
Wine	Scores of a sensory panel	6 graphite-epoxy modified sensors	CV	FFT + PLS	[36]

CPE: carbon paste electrode, GCE: glassy carbon electrode, SPE: screen-printed electrode.
AdSV: differential pulse adsorptive stripping voltammetry, CAmp: chronoamperometry; CV: cyclic voltammetry, DPV: differential pulse voltammetry, LAPV: large amplitude pulsed voltammetry, LSV: linear sweep voltammetry, MLPAV: multifrequency LAPV, SWV: square wave voltammetry.
ANNs: artificial neural networks, DWT: discrete wavelet transform, FFT: fast Fourier transform, MLR: multiple linear regression, PCA: principal component analysis, PCR: principal component regression, PLS: partial least-squares regression, SVMs: support vector machines.

voltammetries (CSV), as well as adsorptive stripping voltammetry (AdSV) have been considered [47]. Stripping methods comprise three steps: accumulation, rest and measurement. The main difference between ASV/CSV and AdSV lies in the accumulation step: in the former the analyte is electroplated through the application of a negative or positive potential, whereas in the latter, the pre-concentration is achieved by direct adsorption onto the electrode surface or through incorporating chemical modifiers. Those methods are highly suitable for the detection of metal ions as well as organic molecules that, upon application of a potential, generate insoluble species adsorbed onto the electrode surface, allowing a decrease of the detection limits of ca. 2 to 3 orders of magnitude.

Finally, not only the use of small amplitude pulsed voltammetric (SAPV) methods such as DPV has been considered, but also the use

of large amplitude pulsed voltammetry (LAPV), either at constant or at different sweep frequencies (multi-frequency LAPV, MLAPV) [50]. The application of those has been mainly related to the usage of different bare metallic electrodes.

2.3. Data analysis

As already introduced, data analysis is the other key element of ETs in conjunction with the sensor array. Chemometrics is the discipline that seeks to extract information from chemical systems through the application of statistical and mathematical methods.

Despite voltammetric signals may provide richer information in comparison to other electrochemical techniques given the higher order of the obtained data (polarization potentials x sensors x sample), such dimensionality can also hinder its analysis, requiring the use of multi-way processing methods or a pre-processing step in order to reduce the dimensionality of the input signal [3,51].

This pre-processing step usually starts with the unfolding of the data into a 2D matrix, and might also be followed by a compression step devoted to reduce data complexity and redundancies, while preserving the relevant information [51]. The latter, although not being always mandatory, it has been demonstrated that it can improve the performance of the model and its generalization ability, as well as reduce the computational requirements. In this regard, more common approaches reported in the literature are: feature selection algorithms (including genetic algorithms) [17,22,36], "kernel" functions [34,35,40], fast Fourier transform (FFT) [25,29−31,36,45,49] or discrete wavelet transform (DWT) [11,18,32,48].

The next step in data analysis is the modelling itself, that is to infer the underlying relationships between the measured analytical signals and the chemical properties of the samples, both for descriptive and predictive purposes. For this purpose, principal components analysis (PCA), partial least squares regression (PLS) and artificial neural networks (ANNs) are the most commonly used methods. In quantitative analysis which is the topic covered in this review, methods can be further categorized based on the regression analysis form, distinguishing between linear and nonlinear ones. In the former, linear predictor functions are used to fit the data, usually through least-square methods (e.g. PLS), whereas in the latter, both linear and non-linear functions are combined and adjusted through an iterative process (e.g. ANNs or support vector machines (SVMs)).

Despite the unfolding of the data is the most common approach in ETs, it fails harnessing the so-called "second-order advantage" [6], which allows the prediction of the analytes/indexes of interest even in the presence of unknown interferents. In this direction, the alternative is to make use of trilinear methods such as parallel factor analysis (PARAFAC) or Tucker decomposition for qualitative approaches, or multiway PLS (nPLS) for quantitative analysis. Furthermore, new trends in chemometric analysis focus on the development of even more powerful analysis tools to better exploit the information contained in such complex data sets, and be able to cope with the advances in data generation [52]; e.g. when the responses of an array are also measured at different pH values [30]. However, despite their advantages, their usage is still very limited when developing ET applications, being rarely used.

For a more in-depth revision of the different chemometric methods and the main differences between them, readers may consult [51,9,53].

2.4. Applications

After discussing the sensors, the measuring techniques and the data processing approaches used when developing ET applications, the focus now is on the reported applications. The potential of ETs is based on the synergies between electrochemical (bio)sensors and chemometrics, taking advantage of the inherent benefits of both of them to obtain an analytical tool with huge versatility and wide applicability. Precisely, the advances in those two research fields is what allows to spawn new application areas, offering a wide spectrum of possibilities.

Although traditionally ETs have been mainly related to qualitative analysis, they have also been used for quantitative purposes, in which herein we will focus. Moreover, despite the ET definition states that a sensor array has to be used, the nature of voltammetric responses allows that the same principles can be applied when using a single sensor. Such is the case of voltammograms being of first-order and showing cross-response features. Consequently, some of those will be also reviewed here. To better illustrate the potential of voltammetric ETs in quantitative analysis, relevant applications in different fields are summarized in Table 1.

Firstly, it is important to note the variety of scenarios studied, not only in terms of samples (e.g. honey, juice, oil, milk, water, wine, drugs, urine, serum, etc.), but also of analytes (e.g. amino acids, phenolic compounds, antibiotics, pesticides, explosives, heavy metals, etc.). In this direction, it is observed that most of the applications are related to the analysis of physicochemical parameters of food products, in line with initial studies with ETs (i.e. qualitative analysis of food products), although their usage for the detection of contaminants such as heavy metals is also spreading [41,26]. Secondly, ETs success has not only been demonstrated through the determination of specific compounds, but also through the quantification of subjective indexes such as flavour attributes [25] or the scores given by a sensory panel [21,36]. Actually, the latter represent a straightforward solution to the lack of knowledge of the specific compounds (or concentration levels) responsible for certain sensations that do not allow to achieve such tasks with classical methods.

Other aspects to be taken into account are related to the operation mode of ETs. In this regard, there are three key factors that would help in making ETs more attractive: i) miniaturization, ii) automation and iii) portability. In this direction, electrochemical systems present many advantages by themselves as they offer fast and accurate information in a cost-effective manner, while their instrumentation has the potential for miniaturization and portability, minimal power requirement and cost-effectiveness.

Back on the 2010, Crew et al. actually demonstrated the portability of ETs with a portable BioET prototype for the in situ determination of organophosphate pesticides [44]. The automated system consisted of an array of six AChE-based biosensors incorporating an ANN program, and powered via the lighter socket from a car battery. Nowadays, with the significant advances that have been made since then in the development of portable compact potentiostats, in conjunction with the advance in screen printing technology, it is even possible to integrate such a system into a small hand-held device controlled through a smartphone app [12].

Automation is key for ETs, because unlike "conventional" methods (based on univariate regression), multivariate methods require the preparation and measurement of a high number of standards and/or samples to build the model. Moreover, the preparation of the stocks may become more tedious when tackling the multi-determination of several analytes. In this regard, the use of flow systems such as flow injection analysis (FIA) or sequential injection analysis (SIA) can provide many benefits as those can comprise the preparation of the stocks, their measurement and the data collection steps [10,54].

Even more interesting is the use of microfluidic devices to develop ET applications; an approach that has been already reported carrying out capacitive measurements [55], but not yet with voltammetric sensors to the best of authors knowledge.

3. Conclusions and future trends

This review provides an overview of the approaches followed when developing voltammetric ETs as well as their capabilities for quantitative analysis. The publications reviewed herein were selected to illustrate the huge versatility and wide applicability of ETs.

ETs take advantages of the synergies between (bio)sensors and chemometrics to provide comprehensive information of complex samples by simultaneously detecting a large spectrum of compounds in a rapid manner, without requiring any pre-treatment step as the data processing stage may offset potential matrix effects from the sample. This is especially significant when tackling the classification of samples or the quantification of subjective perceptions where no specific compounds (or concentration levels) can be associated with such characteristics, focusing in this way on the overall profile rather than on specific compounds. Consequently, ETs represent an attractive alternative to conventional or sophisticated methods, with many advantages over those such as their low-cost, portability, or fast-responses; or even allowing to meet new challenges in environmental monitoring, food safety and public health.

However, despite the huge capabilities of ETs, their implementation is still quite meagre and mainly limited to research purposes. One of the reasons is that despite ETs are sometimes defined as an instrument, it has to be reckoned that the number of commercial devices is still rather low, being mainly used in research laboratories working on their development. Another reason might be the mathematical background behind these methods, which were usually coded in e.g. Matlab or R, and that can be quite complex and bewildering for the non-expert. However, this could change as nowadays many software packages with user-friendly interfaces are available. Besides, the large number of samples required to build the model and the recalibration of the system might also be a disincentive. To this aim, usage of model transfer methods represents a very promising approach to tackle this problem [56].

Finally, future trends in ETs will be obviously based on the separate advances achieved both in the (bio)sensors and the chemometrics fields, and more interestingly in the new concepts that arise from their combination such as data fusion approaches, or the development of systems that lead to and actually exploit high multi-dimensional data. On the (bio)sensors side, advances in materials science and nanotechnology have underpinned the evolution of voltammetric sensors and spurred their potential. However, ETs are one step behind "conventional" research in (bio) sensors, thus the incorporation of more recently developed sensing devices will foster ETs performance. For example, sensors based on novel nanomaterials such as porous silicon (pSi) or mesoporous carbon surpass the performance of the above-mentioned electrodes. Similarly, 3D printing offers enormous potential not only for the development of novel sensing devices, but also due to its prototyping capabilities. Lastly, the incorporation of different biorecognition elements such as antibodies or aptamers is a topic that has still not been exploited, but also the usage of artificial receptors such as molecularly imprinted polymers (MIPs), which opens the door for the development of many compound-tailored quantitative applications. On the chemometrics part, one of the biggest challenges is tackling the absence of an established methodology in the field of ETs. For example, the lack of classical analytical figures of merit such as sensitivity, selectivity or limit of detection (LOD). Another aspect that has to be further investigated is the selection of the sensors that constitute the ET array. That is, while the benefits of sensor arrays have been widely demonstrated, the criteria employed for the selection of the sensors that constitute the arrays and the effect that such selection has in the overall performance have been rarely reported. Lastly, as already pointed out, the combination of different types of sensors can actually boost the performance of such biomimetic systems as it clearly maximizes the information extracted from the samples as some types of sensors might be more suitable than others depending on the analytes considered.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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