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Plasmonic Cross-Reactive Sensing Noses and Tongues

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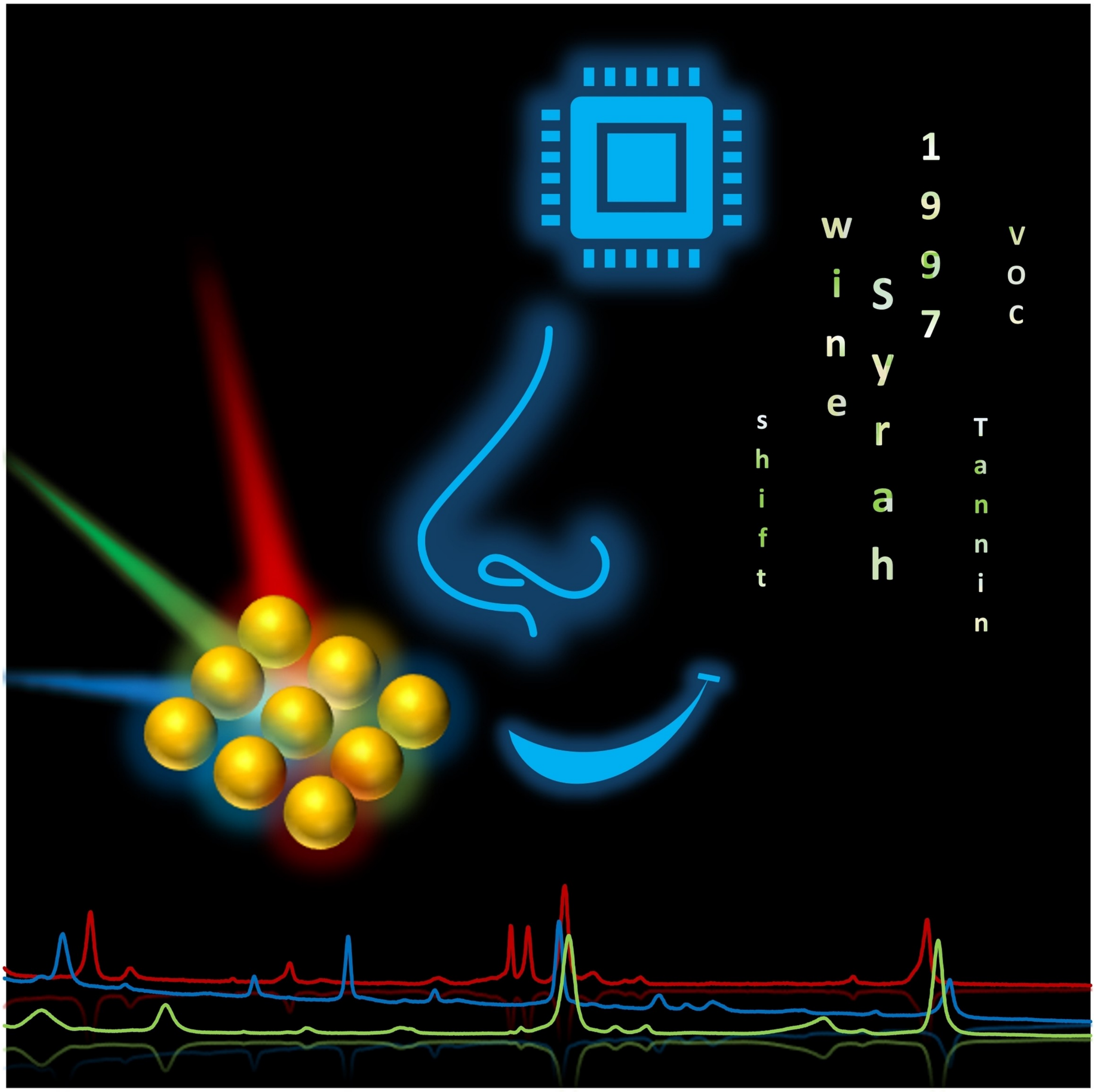

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The advancements in the capabilities of artificial sensory technologies, such as electronic/optical noses and tongues, have significantly enhanced their ability to identify complex mixtures of analytes. These improvements are rooted in the evolving manufacturing processes of cross-reactive sensor arrays (CRSAs) and the development of innovative computational methods. The potential applications in early diagnosis, food quality control, environmental monitoring, and more, position CRSAs as an exciting area of research for scientists from diverse backgrounds. Among these, plasmonic CRSAs are particularly noteworthy because they offer enhanced capabilities for remote, fast, and even real-time monitoring, in addition to better portability of instrumentation. Specifically, the synergy between the localized surface plasmon resonance (LSPR) of metallic nanoparticles (NPs) and CRSAs introduces advanced techniques such as LSPR, metal-enhanced fluorescence (MEF), surface-enhanced infrared absorption (SEIRA), surface-enhanced Raman scattering (SERS), and surface-enhanced resonance Raman scattering (SERRS) spectroscopies. This review delves into the importance and versatility of optical-CRSAs, especially those based on plasmonic materials, discussing recent applications and potential new research directions.

1. Introduction

Sensory technology has revolutionized our engagement with the environment, bridging the gap between digital quantification and physical sensations. Initially, devices such as thermometers and microphones – our technological eyes and ears – were indispensable across various sectors including industry, security, healthcare, and entertainment. Nowadays, the advent of systems that emulate mammalian smell and taste,[1,2] known as electronic/optical noses/tongues, marks a significant evolution in our capacity to analyze complex mixtures of analytes. These systems, utilizing advanced materials for chemical composition analysis, have been extensively proposed and researched to enhance food safety,[3,4] environmental monitoring,[5] and medical diagnostics.[6]

Achieving the ability to screen multiple substances simultaneously with quantitative resolution is considered a "holy grail" in sensory technology. For instance, the "Nanomedicine Vision paper" by the European Technology Platform[7,8] highlight the challenges of traditional in-vitro diagnostics, such as sample deterioration, cost, lengthy waiting times, and poor standardization of sample collection. Thus, detection methods that can perform fast detection in a highly multi-component sample, with minimal to no preparation, have been pursued extensively. For example, historical practices dating back to around 400 BC[9] and modern examples, like a dog named Frankie detecting thyroid cancer with 88% accuracy as reported by The Guardian in March 2015,[10] illustrate the potential of analyzing complex matrixes of volatile organic compounds (VOCs) that are exhaled or eliminated from the body and can be associated with certain diseases.[11,12] Many of these efforts have taken mammalian senses as inspiration models for the development of cross-reactive sensor arrays (CRSAs) for medical diagnostic and analytic devices that meet all these requirements.

CRSAs emulate the mammalian olfactory system by utilizing a variety of sensors to monitor sample interactions, generating "fingerprint" responses. This method allows for the screening of numerous substances in a single process, a stark contrast to traditional single-target analytical methods that require sample division or sequential analysis.[13–15] The effectiveness of CRSAs depends on the quality and diversity of the sensing elements (degree of cross-reactivity), the output transduction (the conversion of chemical interactions from the array into quantified data) and the pattern recognition algorithm used.[13,14,16] Notably, optical-CRSAs (noses and tongues) stand out since they offer several advantages.[17] First, optical sensors can detect target molecules at much lower concentrations and distinguish between closely related compounds more effectively than many conventional sensors. Moreover, optical sensing often provides faster results, enabling real-time monitoring and decision-making. In medical diagnostics, optical methods can detect biomarkers without the need for invasive procedures. And finally, the same optical sensing platform can be adapted to detect a wide range of substances by modifying the sensor surface or the detection mechanism. Recent advancements in optical-CRSAs underscore the potential of these technologies. This review discusses the importance and versatility of optical-CRSAs, especially those derived from plasmonic materials. We suspect that within these progresses in plasmonic-CRSAs lay the foundation for newcoming advancements in sensory technology.

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2. Optical detection in plasmonic CRSAs

In optical CRSAs, changes in the sensor's optical properties can be quantified (transduction process) through shifts in emission or absorption bands, intensity changes, or band splitting, using absorbed, reflected, or scattered light.[17] Moreover, various optical phenomena, such as colorimetry and fluorescence, can be monitored and quantified.[18] Plasmonic-CRSAs enhance these classical techniques through the near-field effects provided by the excitation of surface plasmons, known as surface plasmon resonance (SPR). Specifically, metallic nanoparticles exhibit localized surface plasmon resonance (LSPR) due to their size.

LSPRs is a phenomenon associated with the collective oscillation of electrons in metallic nanoparticles when they are excited by light. Unlike SPR which occurs at the interface between a metal and a dielectric material and requires propagation along the interface, LSPR is confined to the vicinity of the nanoparticle. This confinement is due to the interaction of light with nanoparticles of sizes smaller than the wavelength of the light itself, leading to a localized electromagnetic field enhancement around the particle. Thus, when light of a certain frequency illuminates these metallic nanoparticles, it induces a resonant oscillation of the conduction band electrons with respect to the lattice of positive ions in the metal. This resonance condition is highly sensitive to the size, shape, and material of the nanoparticles, as well as the dielectric environ-

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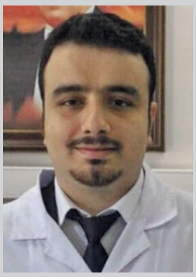

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ment around them. The specific wavelength at which this resonance occurs can thus be finely tuned by adjusting these parameters. LSPR leads to a sharp peak in the extinction (absorption and scattering) spectrum of the nanoparticle, marking the resonant frequency. The heightened electromagnetic field at this resonance enhances various optical phenomena, making LSPR a powerful tool for detecting molecular interactions at the nanoparticle surface. This sensitivity to changes in the local refractive index near the nanoparticle surface is exploited in sensors for detecting chemical and biological species, enabling the development of highly sensitive and specific biosensing platforms.

Classical methods for optical transduction in CRSAs rely on optical spectroscopy,[19] including UV-Vis,[20] fluorescence,[21] FTIR[22] or Raman.[23] Conversely, in plasmonic CRSAs, equivalent plasmonic-enhanced techniques are utilized: LSPR, metal-enhanced fluorescence (MEF), surface-enhanced infrared absorption (SEIRA), surface-enhanced Raman scattering (SERS), and surface-enhanced resonance Raman scattering (SERRS). LSPR employs the excitation of surface plasmons by light, a phenomenon highly sensitive to changes in the refractive index near the metal surface, such as when chemical species bind to the sensor surface.[24] MEF involves enhancing fluorescence signals using plasmonic nanoparticles, which can increase the fluorescence intensity of nearby fluorophores, shorten their lifetime, and improve detection sensitivity.[25,26] MEF is particularly valuable in biological assays and imaging, enhancing the visibility of fluorescent markers. SEIRA amplifies the infrared absorption signals of molecules by leveraging nanostructured metallic surfaces to increase the local electromagnetic field, thereby boosting their infrared absorption. The molecules in the intensified field absorb more infrared radiation than they would under typical conditions. This heightened absorption results from the strong interaction between molecular vibrations and the enhanced local field generated by the localized surface plasmon resonance (LSPR) of the plasmonic surfaces when illuminated with IR light.[27] SERS enhances the typically weak Raman signals associated with molecular vibrations using nanostructured plasmonic surfaces, which amplify the electromagnetic field around molecules in close proximity, facilitating the detection of molecules at trace levels and significantly improving sensitivity.[28] SERRS combines the benefits of SERS with resonance Raman scattering for even greater signal enhancement for molecules in resonance with the laser light used.

The ability of these techniques to detect minute structural or chemical changes induced in each sensor upon contact with the sample, combined with their high spatial resolution, provides a solid foundation for effective signal transduction in CRSAs. Moreover, these enhanced techniques can become ultra trace detection methods, since under ideal circumstances, plasmonic enhancements could be reached up to 10^6 for MEF[29] and 10^{12} for SERS.[30,31]

3. Nanofabrication Techniques for Plasmonic CRSAs

The fabrication of CRSAs is a sophisticated process that necessitates the creation of two-dimensional arrays of diverse plasmonic sensors. This process is crucial for achieving the desired specificity and sensitivity in detecting various components of a sample. Depending on the optical transduction technique employed for signal acquisition, it may be necessary to know the exact position of each sensor within the array. Techniques like SPR and MEF require precise knowledge of sensor placement due to their low-structure spectra characterized by few broad/overlapping bands. In contrast, spectra from vibrational techniques as SEIRA, SERS or SERRS can be easily deconvoluted due to the narrow bands in the characteristic vibrational spectra of each sensing element. For instance, using widefield SERS, the position and full spectra of each small NP's clusters, randomly placed in a hypothetical CRSA, could be determined without previous knowledge of their placement within the sensor.[32] Creating a CRSAs involves not only the strategic arrangement of sensors but also ensuring each sensor is distinct enough to selectively react with different sample components. This differentiation is typically achieved by altering the plasmonic sensing elements' composition or surface functionalization. The fabrication process generally includes two main steps: depositing the plasmonic materials and then functionalizing each sensor with a specific sensing interlayer. Alternatively, some approaches, such as inkjet printing,[33] allow for the simultaneous deposition and functionalization of the sensor, streamlining the fabrication process.

Fabrication methods can be broadly categorized into lithographic and non-lithographic techniques, each with its own set of advantages and challenges. Nanoimprint lithography (NIL, Figure 1A), for instance, is a high-throughput, cost-effective method ideal for creating large-scale sensor arrays with uniform nanoscale of colloidal particles. In the first step, the appropriate micro-structured template is prepared directly on topographically patterned silicon masters,[34] through laser or e-beam lithography,[35] or prepared *via* replica molding[36] through microcontact imprinting. Then a concentrated solution of plasmonic NPs is cast on the template, allowed to dry, and then transferred to the surface to yield a periodic array of sensors. While NIL offers high resolution and low cost, it does require the initial creation of a mold, which can be expensive and time-consuming. Also, as the different sensing elements are deposited in a single step, the plasmonic materials cannot be functionalized with different chemical interfaces previously to the casting and thus they are usually deposited unfunctionalized, requiring further processing with high-resolution printing techniques.

Dip-pen nanolithography (DPN) is a scanning probe lithography technique where an atomic force microscope (AFM) tip is used to create patterns directly on a range of substances with a variety of inks, including those formulated with plasmonic nanoparticles (Figure 1B).[37–39] DPN stands out for its high spatial resolution and material versatility, allowing for the direct

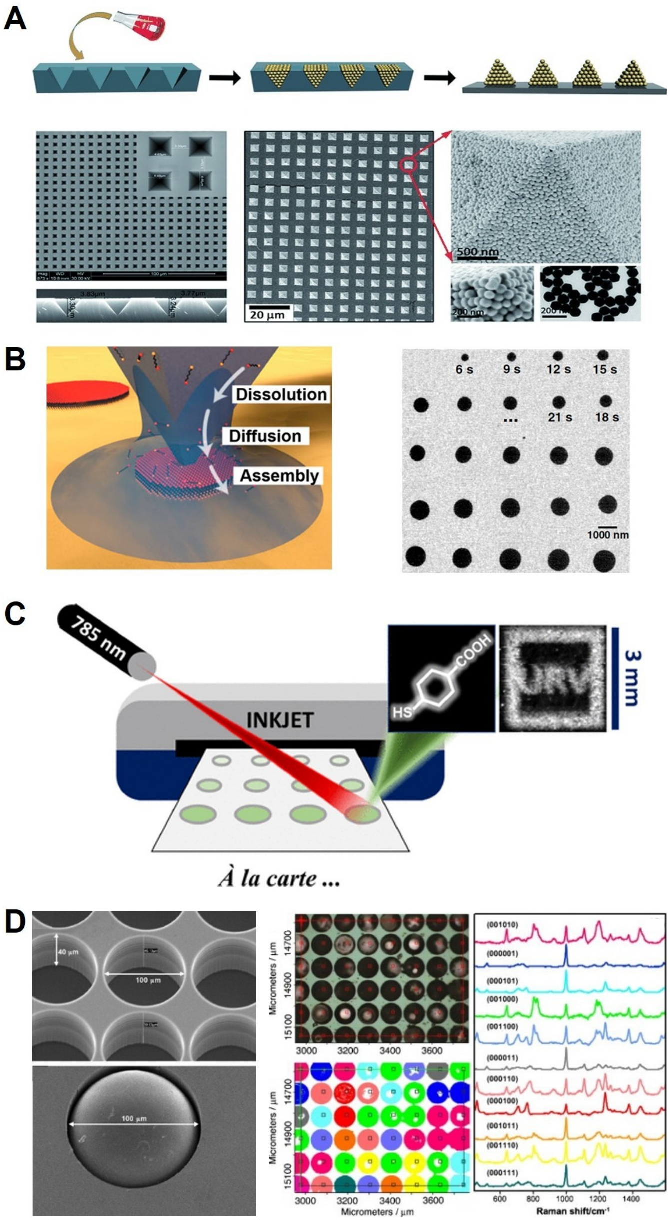

Figure 1. (A) Nanoimprint lithography schematizing the fabrication process and showing the final array of nanoparticles sensing elements. (B) Ink transport mechanisms in dip-pen nanolithography (DPN) illustrating the deposition of the ink through the AFM tip and the sensing array obtained. (C) Nanoparticle inkjet printing of functionalized silver nanoparticles to generate the plasmonic sensing elements. (D) Microwell loading showing the micro well, the fitted sensors and the self-deconvolution of the array by the Raman scattering of each sensor. (A) Adapted with permission from ref.[34] Copyright 2013, Wiley-VCH. (B) Adapted with permission from ref. [38] Copyright 2013, Higher Education Press and Springer-Verlag Berlin Heidelberg; and ref. [39] Copyright 2002 The American Physical Society. (C) Adapted with permission from ref. [33] Copyright 2022 The Authors. Published by American Chemical Society. (D) Adapted with permission from ref. [40] Copyright 2007, Elsevier.

writing of nanoscale patterns. Despite its precision, DPN is limited by its low throughput and the complexity of operating atomic force microscopes. Also, as in NIL, DPN cannot print different sensing elements and thus requires further functionalization after preparation of the plasmonic array of sensors.

Inkjet printing offers a non-contact method for patterning functional inks, supporting rapid prototyping of sensor arrays with a wide range of materials (Figure 1C).[41] This technique allows the deposition, simultaneously of different plasmonic inks, already functionalized in many substrates including common paper.[42] However, its resolution is typically constrained by the droplet size, and the ink's viscosity and surface tension require careful adjustment. Further the number of different sensors that can be integrated into the array is limited by the number of channels of the printer. Microwell loading is based in the fabrication of microwells with defined geometries and the filling of the wells with the appropriated beads functionalized with the desired chemical interface (Figure 1D).[43] In these cases, polymer and silica microbeads may be functionalized with nanoparticles and the chemical interface, one by one, mixed and deposited. In such a case, the resulting arrays contain a mixture of nonlocalized sensors. While this is by far the most powerful method to build up CRSAs, it can only be used when transduction methods are SEIRA or SERS/SERRS as the measurement requires the auto-deconvolution of the sensing element.[40]

Each fabrication technique contributes uniquely to the development of CRSAs, with the choice of method dependent on specific sensor application requirements, such as resolution, throughput, material compatibility, and overall cost. Remarkably, paper has been re-discovered as a supporting material for environmentally friendly, low-cost and mass-scale sensing platforms.[44–46]

4. Sensing Elements

As previously described, each sensing element in a plasmonic CRSA is composed by a plasmonic core, responsible of the generation of the strong electromagnetic field upon illumination with light and a chemical interface deposited on the surface. The plasmonic nanoparticles, their synthesis, functionalization and optical properties had been extensively described in many reviews.[47–49] Most common plasmonic metals include gold and silver, although other plasmonic materials such as aluminum can be found.[50] The chemical interface of each sensing element plays a pivotal role in CRSAs. This functionalized outer layer crucially determines the reactivity and affinity of each sensor in the array towards the diverse species present in a complex sample. To effectively contribute to the CRSAs functionality, this layer must meet several criteria. Ideally, it should enable the generation of a combinatorial library where the sensing materials, while similar, exhibit sufficient differences to be discernible from each other. This variance enhances the resolution of the entire CRSA. Additionally, the layer should be easily functionalizable onto the plasmonic material and capable of promoting geometrical or chemical changes detectable by the chosen transduction technique. A straightforward approach to create this gradient of reactivity/affinity within the CRSAs sensing elements involves modifying the composition of the plasmonic nanoparticles (mainly gold and silver) by introducing other metals such as Co, Cu, Ni, Fe, etc. These additional metals promote an stronger interaction with elements such as O. For optimal functionality, these doping metals should predominantly decorate the nanoparticle surface, as their presence in the bulk may alter the nanoparticle's optical response rather than its surface chemistry. However, conventional fabrication methods, which typically rely on chemical reduction, struggle to control dopant distribution within the nanoparticles. If pursued, this strategy necessitates separate nanoparticle deposition via techniques like inkjet printing or microwell filling.

The most prevalent sensing interfaces in plasmonic CRSAs are aliphatic thiols, which include various functional groups and chain lengths.[51] These materials are commonly deposited as self-assembled monolayers (SAMs), allowing each sensor within the CRSA to uniquely interact with the sample components, thereby aiding in the classification of complex fluids (Figure 2A). The density of the SAM can also be adjusted to modify sensor reactivity; high-density SAMs limit interactions to the surface, whereas lower-density SAMs permit some analyte intercalation.[52] However, aliphatic SAMs exhibit a low SERS cross-section and do not fluoresce, making them more suitable for transduction methods like SPR or SEIRA. This limitation can be addressed by substituting aliphatic SAMs with aromatic ones.

Recent advancements in the synthesis and functionalization of organic materials have expanded the options for refined interfaces. For instance, interfaces based on host-guest interactions, such as cyclodextrins,[53,54] calixarenes,[55,56] or cucurbiturils,[57] leverage a variety of weak interactions determined by the cavity's chemical nature, size, and functionalization of the outer ring. These molecular systems, when functionalized with thiols on the inner ring, can be employed across all CRSA fabrication methods, offering versatile and sophisticated sensing interfaces.

Films of nanoporous materials, such as metal-organic frameworks (MOFs), seem perfectly suited for sensing applications in CRSAs. In addition to their record specific surface area and homogeneous porosity, a striking advantage of MOFs is their huge variety with several thousand of published structures.[58] These structures allow fine tuning of their porosity, in size and geometry, by just changing their coordination metal and/or the length of the organic ligand.[59] Further, the substituent of the organic ligand can also be tuned to generate the desired chemical environment within the pore (Figure 2B).[60] When coating the plasmonic materials, MOF can form solid, complex or Yolk shells in single particles or in controlled aggregates (Figure 2C).[61,62] As the MOF coating only acts as a barrier, the plasmonic surface can be also functionalized with SAMs adding an unprecedent diversity and allowing for almost infinite combinations. However, as a drawback, the requirements for the preparation of these materials makes them only suitable for inkjet printing or microwell coating.

Another approach for the fabrication of sensing elements for optical CRSAs is the use of a single chemical interface for the individual sensing elements.[63] Tuning the pH and ionic strength of the surrounding media, of the single components, enable the interaction with the target analytes through different binding modes (e.g. charged or uncharged analytes).[64] Thus, this surrounding media modification provides the required cross-reactivity for multiplex detection and removes the possible laborious and time-consuming development of the different individual sensing elements of the CRSA. However, their current application in colloidal sensors, makes them non-attractive for long shelf-life systems. While this approach breaks the similarities between CRSAs and the mammals olfactory/taste senses, where all the receptors are embedded in the same media, it emphasizes the role of the chemical interface in the reactivity and affinity of the analytes present in a complex sample.

5. Signal Processing

The incorporation of plasmonic noses and tongues into chemical sensing represents a significant advancement in our capability to detect and analyze various substances. These innovations enable us to detect, recognize, and quantify mixtures of chemical species with enhanced precision and sensitivity.[46] These devices mimic mammalian sensory capabilities but with a level of precision and objectivity unattainable by humans. For instance, electronic tongues have the capability to detect and categorize odors, extending their utility beyond traditional chemical sensing applications. In the realm of food and beverage, they prove invaluable for classifying items based on their perceived "deliciousness".[65] Plasmonic noses and tongues encompass a range of technologies, including nanostructured sensors, array-based sensors, and colorimetric sensors, each contributing to the advancement of chemical sensing methodologies.[66]

The fusion of traditional signal processing techniques with cutting-edge artificial intelligence (AI) methodologies has greatly enhanced the functionality and applicability of these devices. In the realm of plasmonic sensor array applications, we can find several unique hurdles: (i) Noise Interference: external disturbances can obscure the signals generated by the sensors, leading to inaccuracies in detection and analysis; (ii) Data Dimensionality: plasmonic sensor arrays generate multidimensional datasets and managing and analyzing high-dimensional data pose significant challenges; (iii) Signal Complexity: plasmonic sensor arrays exhibit complex signal patterns influenced by various factors, including analyte concentration, surface properties, and sensor morphology.

Classical signal processing techniques, such as wavelet transforms and feature extraction methods, constitute foundational tools in the analysis of sensor data from optical noses and tongues. These methods offer a robust framework for extracting relevant information from complex sensor signals, facilitating meaningful interpretation and decision-making in various applications.

Wavelet transforms[67] are powerful mathematical tools used to decompose signals into different frequency components, enabling the identification of both localized and global features within the data. By representing signals in terms of wavelet coefficients, wavelet transforms offer a flexible approach to signal analysis, allowing for efficient denoising, compression,

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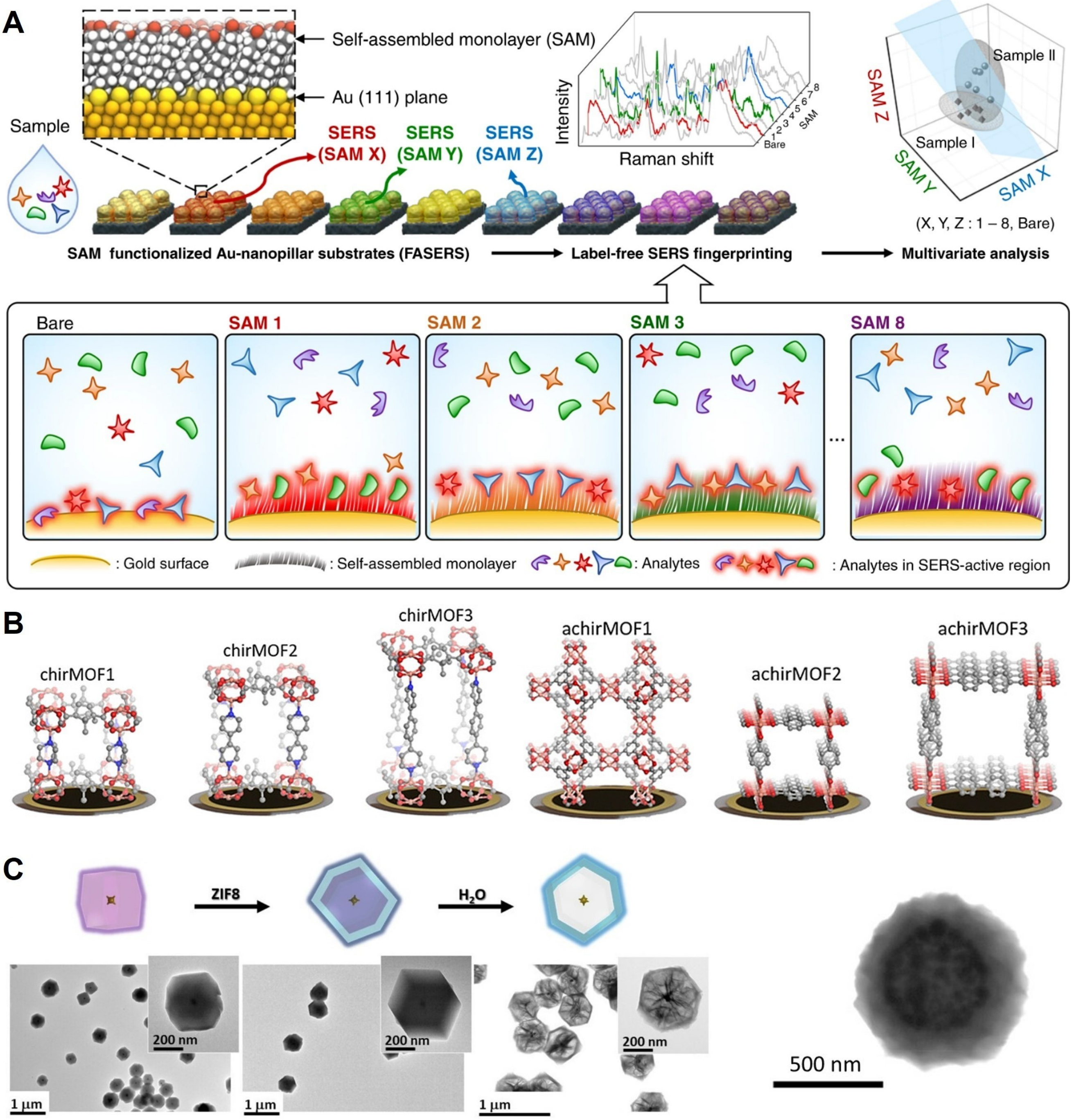

Figure 2. (A) Example of CRSA for SERS sensing elements composed of gold nanoparticles each functionalized with a different self-assembled monolayer of aliphatic thiols. A range of molecular interactions takes place within complex biological media at each unit sensor where mildly selective SERS enhancement of the constituents gives multiplexed spectral datasets. The increased data dimensionality obtained enables facile identification of closely related samples through multivariate analysis. (B) Example of CRSA using sensing elements by tuning cavities MOFs size, shape, and ligand functionalization (i.e., different chemical environment within the pore (C) Examples of single and aggregated plasmonic nanoparticles coated with MOF from solid, complex, and Yolk shells. (A) Adapted with permission from ref. [51] Copyright 2020 The Authors. Published by Springer Nature. (B) Adapted with permission from ref. [60] Copyright 2020 The Authors, published by Wiley-VCH GmbH. (C) Adapted with permission from ref. [61] Copyright 2023 The Authors, published by Wiley-VCH GmbH.; and ref. [62] Copyright 2023 The Authors. Published by American Chemical Society.

and feature extraction. Wavelet transforms have become a cornerstone in the processing of signals from optical noses and tongues. The ability of wavelet transforms to localize in both time and frequency domains makes them particularly useful for analyzing transient, non-stationary signals that are common in chemical detection. However, the selection of appropriate wavelet functions and scales can be challenging and may require domain expertise to ensure optimal signal processing.

Feature extraction methods[68] involve the identification and extraction of relevant features or characteristics from sensor signals that are informative for a particular task or application. These features may include statistical measures, frequency-domain representations, or time-domain descriptors, among others. Feature extraction facilitates dimensionality reduction and enhances the discriminative power of the data. Feature extraction techniques such as principal component analysis (PCA) and linear discriminant analysis (LDA) are pivotal in reducing the dimensionality of sensor data, thereby highlighting relevant features that distinguish between different chemical compounds. PCA identifies the directions (principal components) that maximize the variance in the data, which helps in reducing the complexity of the data while retaining essential information. LDA, on the other hand, aims to find a feature space that maximizes the separation between multiple classes.

However, these methods may struggle with highly complex or non-linear data, potentially limiting their effectiveness in certain chemical sensing tasks.

In turn, AI-based methods, particularly deep learning models like CNNs and RNNs, provide powerful tools for identifying patterns and predicting outcomes from complex sensor data. These models can automatically learn and adapt to new data, improving their performance over time. However, their need for extensive datasets, computational resources, and expertise in model tuning can be prohibitive for some applications.

The choice between these approaches depends on the specific application requirements, including the complexity of the sensor data, computational resources available, and the need for real-time processing. Combining these methods can leverage the strengths of each, offering a balanced approach to the development of advanced chemical sensing systems.

Convolutional neural networks[69] represent a breakthrough in the pattern recognition capabilities of optical noses and tongues. By automatically learning spatial hierarchies of features from sensor data, CNNs can identify complex patterns associated with specific chemicals or chemical mixtures. This is particularly useful in applications where the sensor signals are influenced by a variety of factors, including concentration, temperature, and humidity.[70] CNNs provide a robust framework for analyzing sensor data, leading to improved accuracy in chemical detection. However, they require large datasets for training and can be computationally intensive, which might limit their deployment in resource-constrained environments.[71] Recurrent neural networks are adept at analyzing temporal patterns in chemical sensing data, making them ideal for applications where the sensor response evolves over time.[72] RNNs can process sequences of data, allowing for the prediction of future sensor responses based on past and present observations. This capability is invaluable for monitoring dynamic chemical processes or for detecting changes in the concentration of a substance over time. However, RNNs can be prone to issues like vanishing or exploding gradients, making them challenging to train. Moreover, their performance can be significantly affected by the sequence length and the complexity of the temporal patterns.[73]

Deploying AI algorithms holds immense promise for advancing the capabilities of optical noses and tongues.[74,75] However, integrating these algorithms effectively requires careful consideration of various aspects: (i) Data preprocessing: For plasmonic sensor arrays, preprocessing may involve noise reduction techniques, normalization to account for variations in sensor responses, and feature extraction to extract relevant information from raw signals.[76] Recent advancements in data preprocessing techniques, such as adaptive filtering methods and data augmentation strategies, can further optimize the quality and diversity of training datasets, enhancing the robustness and generalization capabilities of AI models. (ii) Model training: Training CNNs and RNNs for chemical sensing applications necessitates the availability of large and diverse datasets encompassing a wide range of chemical species, concentrations, and environmental conditions. Collecting and curating such datasets pose significant challenges but are essential for ensuring the effectiveness and reliability of the trained models. Transfer learning techniques, leveraging pre-trained models on related tasks or domains, can expedite the training process and improve the performance of AI algorithms, especially in scenarios with limited labeled data or computational resources.

6. Applications of Optical Noses and Tongues

The applications of optical noses and tongues span a diverse array of fields, from environmental monitoring and food safety to healthcare and industrial processes. These innovative sensing technologies, characterized by their ability to detect and analyze chemical compounds with high sensitivity and selectivity, offer significant advantages over traditional sensing methods. This section delves into specific applications, showcasing case studies, experimental results, and comparisons to traditional sensing technologies.

6.1. Environmental Monitoring

Optical noses and tongues may be pivotal in detecting pollutants and hazardous substances in air and water. A notable case study involves the detection of volatile organic compounds (VOCs) in industrial emissions using surface-enhanced Raman Scattering (SERS)-based optical noses. The SERS technique, with its enhanced signal sensitivity, was able to detect VOC concentrations at parts-per-billion levels, surpassing the capabilities of conventional gas chromatography methods. This application not only demonstrates the sensitivity of optical noses but also their potential for real-time environmental surveillance, offering a more efficient and cost-effective approach to maintaining air quality standards. Moreover, improvements could be achieved using MOF-enabled molecular preconcentration effect on the plasmonic array.[81] Other applications for plasmonic-noses is the measure of other VOCs (gaseous ethylene, methanol, ammonia) as plant health indicators.[77] As a result of the continuous monitoring is possible to speculate a more thoroughly study to Increase the quality and quantity of food production.

The presence identification of acidic and oxidizing gases and other air pollutants not only has impacts on the human health, but it can also be detrimental to the conservation of historical materials such as exhibitions in museums including ancient manuscripts and books.[82] Thus, the non-invasive methods of plasmonic noses for the detection of reactive gases offers an excellent application for the monitoring of trace airborne pollutants.[83]

For water it's crucial to assess its quality, especially at the household level, to ensure it's safe for consumption. For instance, a plasmonic-tongue based on microfluidics and nano-patterned surfaces modified with SAM of functional thiols allows the real-time water monitoring between treated and non-treated water with a 95% accuracy (Figure 3). This allows the integration of this device into water treatment and distribution facilities to obtain an early warning about water quality.[84] Related monitoring works include the identification of toxic metal ions.[80] In water, the detection of antidepressants has also been achieved.[63]

6.2. Food Safety and Quality Control

In the food industry, optical tongues/noses have been employed to assess the quality of products and/or classify a variety of products. Highly multicomponent system, such as beers and coffees, has been studied using a low-cost, sensitive colorimetric sensor array to detect and identify coffee aromas. The sensor array's color changes were digitized and analyzed using statistical methods, such as principal component analysis (PCA) and hierarchical clustering analysis (HCA). This method shows excellent potential for analyzing complex systems and discriminating among similar mixtures.[85,86]

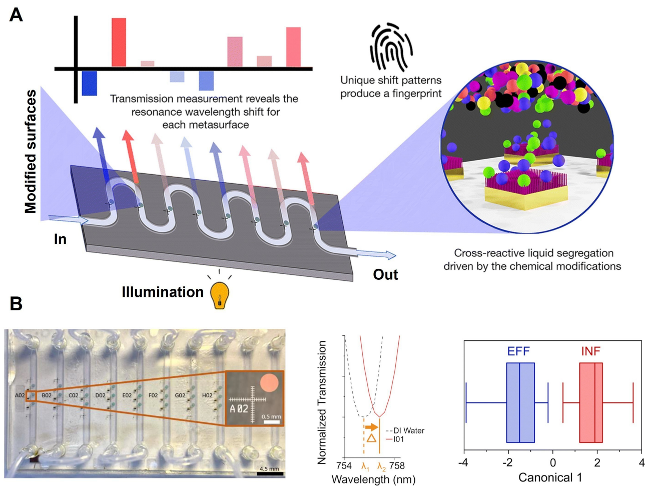

Figure 3. (A) Example of plasmonic-CRSA for drinking water assessment. (B) At the left is the representation of the microfluidic device and at the right the shift in the transmission spectra they detected and the PCA and LDA in which treated and non-treated water can be classified. Adapted from ref. [84] Copyright 2023 The Royal Society of Chemistry.

During food spoilage, pathogenic and spoilage microorganisms act on food substrates, emitting specific VOCs.[4] These odor-active molecules are produced as a result of the breakdown of food.[4] The monitoring of such VOCs using plasmonic-noses allows to detect food spoilage[87] by, for example, integrating scalable plasmonic arrays and multi-dimensional chemometrics for simultaneous detection of multiple food-borne VOCs using SERS (Figure 4).[88] This innovative approach, combining direct and indirect SERS strategies, as well as optical concentrators, enhances sensitivity and accuracy, offering a reliable platform for real-time food smell evaluation and quality assessment, which in turn demonstrates the broad and versatile application of plasmonic-CRSAs.

Within beverages, an important set of works have been published regarding the classification of spirits, particularly Baiju, using plasmonic-CRSAs.[89–93] These results hold immense significance not only due to their ability to discern subtle differences in the chemical composition but also because showcase the variability of capabilities of the recognition pattern algorithm to even recognize the geographical region of origin.[78] While this results can be of special interest for organizations that hold origin denominations, the final consumer also can be a beneficiary since plasmonic-CRSAs could offer a new tool in mitigating the risks associated with methanol and other harmful substances in adulterated or low quality alcoholic beverages.[94] Another proof of concept for wines was presented with the successful integration of machine learning algorithms in a SERS plasmonic-tongue taster that enables multiplex profiling of five representative molecules for various wine flavors with 100% accuracy at the parts-per-million level.[95] Besides Baiju, other plasmonic-CRSAs have been utilized for

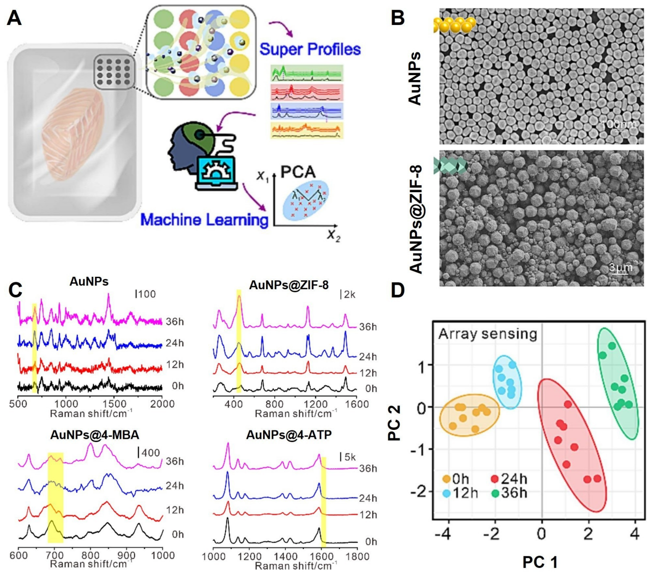

Figure 4. Example of plasmonic-CRSAs using SERS to identify the freshness of the food. (A) Scheme of the array gas sensor for detecting VOCs released from the food. (B) SEM images of the AuNPs and AuNPs@ZIF-8 that conform the sensing elements. (C) SERS spectra of individual sensing elements for 4-time intervals of food without refrigeration. (D) PCA score plot of the array sensing platform for the previous time intervals. Adapted from ref. [88] Copyright 2024, Elsevier.

classification of whiskies[50] and tea.[96] As well as Identification of aminoglycoside antibiotics in milk.[97]

6.3. Healthcare Diagnostics

The healthcare sector has witnessed the application of optical noses and tongues in non-invasive diagnostics. A breakthrough study involved the use of a plasmonic nanoparticle-based optical nose for the detection of disease biomarkers in breath samples. This technology was able to identify markers associated with lung cancer at early stages, offering a promising alternative to conventional diagnostic methods like biopsies, which are invasive and stressful for patients. Another interesting study was the use of systems that couples plasmonic CRSAs with an smartphone as a cost-effective sensor platform for detection of gastric cancer (Figure 5).[79] Gastric cancer is one of the most common cancer and the second leading cause of cancer-related death worldwide.[98] The prognosis for gastric cancer patients is generally poor, with more than 80 % of cases being diagnosed at an advanced stage.[99] Because this colorimetric sensor array detects a broad spectrum of VOCs, it was able to distinguishes between VOC profiles of gastric cancer patients and healthy subjects with 90 % accuracy. It is worth notice that it also includes a wide range of NPs including AgNWs and AgNRs.

Diagnosis of neurodegenerative disorders is challenging due to the unavailability of tools for detecting preclinical biomarkers. Thus, the detection occurs in a period around 10 years after the beginning of the neuropathy and better outcomes can be expected from preventive therapy.[100] An initial advance was made by using AuNPs with distinct surface properties to detect and discriminate Alzheimer's disease and multiple sclerosis based on disease-specific protein coronas.[101] The unique protein compositions, including Alzheimer's disease and multiple sclerosis biomarkers, was used for disease differentiation and detection. Building upon, an interesting proposal is the monitoring of misfolded proteins, such as alpha-synuclein, into oligomeric and fibrillar aggregates. Using SEIRA signals coupled with an artificial neural network, is possible to obtain quantitative predictions of protein aggregates, offering a promising avenue for clinical diagnosis, disease monitoring, and therapeutic evaluation of neurodegenerative disorders including Parkinson's disease and Alzheimer's disease.[102] Other catecholamine neurotransmitters (dopamine, epinephrine and norepinephrine) known as substantial indicators of various neurological diseases have been detected based on their reducing ability to deposit silver on the surface of AuNRs.[103]

The fast and accurate detection and discrimination of pathogenic microorganisms is highly desirable in medicine to diagnose infections, guide appropriate antibiotic treatments, and prevent the spread of infectious diseases. The long culturing time, and the requirement of specialized/expensive equipment are among the most common problems with the identification process. The plasmonic-CRSAs have successfully demonstrate the possibility of faster detection and identification microorganism as bacteria[104] and fungi.[105]

The detection of opioids can aid in preventing overprescription and abuse where their use is essential for managing pain. The use of unmodified AuNPs with different sizes in the analysis of real samples, exemplifies the potential application of plasmonic tongues on the detection an discrimination of controlled substances.[106]

The optical nose's sensitivity to trace amounts of biomarkers presents a non-invasive, early detection tool that could revolutionize cancer and neurodegenerative disorders diagnosis, as well as detection of pathogenic microorganisms and therefore, improve treatment outcomes. Moreover, the broad

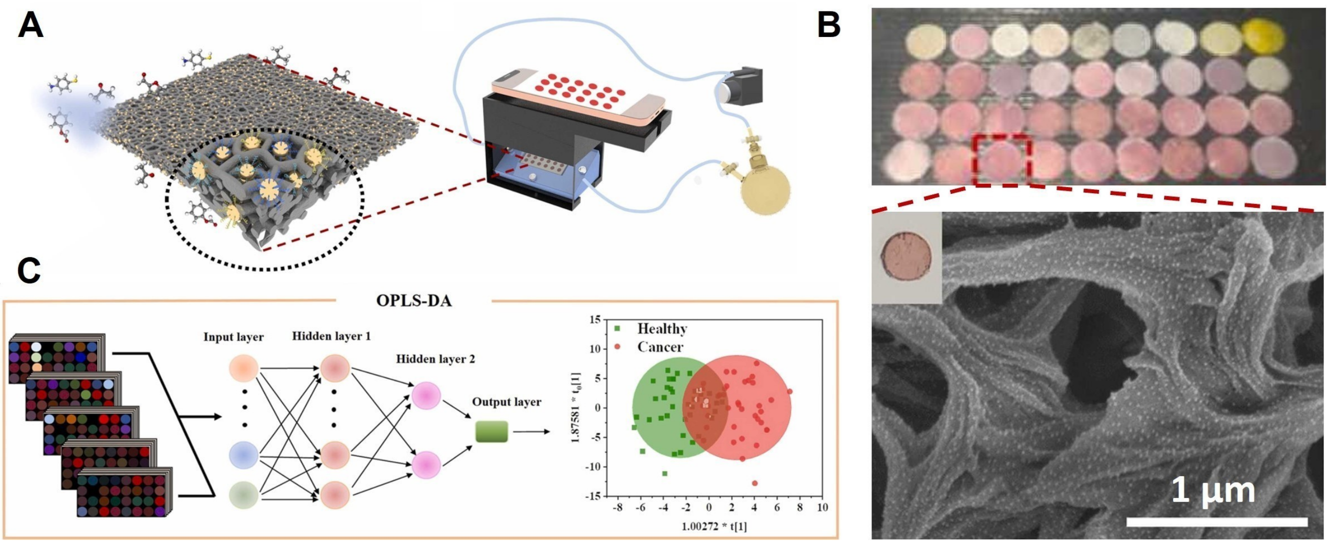

Figure 5. Example of plasmonic-CRSAs using SPR for the detection of gastric cancer. (A) Schematic diagrams of the filter paper (Nylon66 membrane) smartphone system. (B) (Top) Optical image of the full CRSA prior measurements. (Bottom) SEM image of filter paper with 11-mercaptoundecanol modified AuNPs. (C) Scheme of the orthogonal partial least squares discriminant analysis used to obtain a plot of the sensor response to 40 healthy people and 40 gastric cancer patients; Adapted from ref. [79] Copyright 2023 Elsevier B.V.

spectrum of available biomarkers, makes also possible the simultaneous screening of different diseases,[64] including male infertility diagnosis.[107]

7. Comparison to Traditional Sensing Technologies

Challenges associated with optical sensing technologies, include the need for calibration against known standards, potential interference from other substances in complex mixtures, and the initial cost of setting up the sensing system. Despite these challenges, the continuous improvement in sensor design, along with advances in material science and AI, is steadily overcoming these hurdles, broadening the scope and effectiveness of optical noses and tongues across various applications.

In conclusion, optical noses and tongues represent a significant advancement in sensing technology, with the potential to impact numerous fields positively. Through case studies and comparisons with traditional technologies, it's evident that these optical sensors offer superior sensitivity, speed, and versatility, promising to revolutionize environmental monitoring, food safety, and healthcare diagnostics. As research and development in this area continue, we can expect even broader applications and improvements in sensor performance, further cementing the role of optical noses and tongues in future sensing applications.

8. Conclusions and Outlook

Optical noses and tongues represent a significant leap forward in the field of sensory technologies, offering unparalleled sensitivity, selectivity, and versatility across a wide range of applications. Despite their impressive capabilities, these technologies face challenges that must be addressed to fully realize their potential. Moreover, the future of optical sensory technologies holds promise for even more groundbreaking advancements, which come with their own set of ethical and societal considerations.

One of the primary challenges facing optical noses and tongues is sensor drift, where the sensitivity and selectivity of the sensors may degrade over time. Cross-sensitivity, where sensors respond to multiple substances, making it difficult to identify specific target molecules, and the extensive calibration needed to maintain accuracy are also significant concerns. Ongoing research is tackling these issues head-on, focusing on the development of more robust sensor materials that are less prone to environmental variations and degradation. Furthermore, novel calibration algorithms and machine learning techniques are being explored to compensate for sensor drift and cross-sensitivity, enhancing the reliability and usability of these devices over extended periods.

The next generation of optical noses and tongues is likely to see breakthroughs in several key areas. Innovations in materials science, such as the development of self-healing and adaptive materials, could significantly reduce sensor drift and extend the lifespan of sensors. AI and machine learning algorithms will become increasingly sophisticated, improving the accuracy of chemical detection and enabling the sensors to learn and adapt to new substances and environments autonomously. Combining optical noses and tongues with other types of sensors, such as acoustic or electronic sensors, could lead to the creation of multi-modal sensory systems. These systems would provide a more comprehensive analysis of samples by capturing a broader range of chemical and physical properties.

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Conflict of Interests

The authors declare no conflict of interest.

Keywords: Plasmonic cross-reactive sensor arrays · optical nose/tongue · signal processing · plasmon-enhanced spectroscopies

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