A March to Shape Optical Artificial Olfactory System toward Ultrasensitive Detection of Improvised Explosives

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Improvised explosives (IEs) have been frequently used in explosion-based terrorist attacks, and have aroused widespread concerns from governments to academic societies. Due to the fact that IEs mostly exist as solids, there is a pressing demand for sensors to adapt to acquire the information from the solid state. Chemical sensors usually comprise with probes designed based on the chemical properties of the analytes, and generate signals through specific chemical interactions, which would not be affected by the state of the target substance. Colorimetry and fluorescence, known for their intuitionistic (recognizable by human eyes), portable (independent of large-scale analytical equipment), highly specific, sensitive, and environmental interference-free characteristics, are commonly adopted optical chemical detection methods in materials analysis and environmental monitoring. Based on this, the exploration of optical artificial olfactory system, which mimics the working principle of natural olfactory system and acquires sensing signal by optical methods, has emerged to be a promising tool for IEs detection. Here, the basic working principle and the necessary components of optical artificial olfactory system are recommended, including probe molecule, array composition, pattern recognition and device construction. The potential development direction employing molecular recognition of IEs, generation, and acquisition methodology of optical signals are also prospected.

1. Introduction

Since 1990s, terrorist attacks spread rapidly all over the world, and explosion attack is a common form.\textsuperscript{[1,2]} Explosive can burn violently in a very short time and release a lot of heat energy accompanied by releasing high-temperature and high-pressure gas. Since Nobel stabilized nitroglycerin with diatomite, nitrated compounds have been widely used as military explosives. These nitro explosives have electron-rich structures and usually volatilize in the atmosphere. To address the threats, various detection technologies for explosives have been developed, such as mass spectrometry,\textsuperscript{[3]} ion mobility spectrometry,\textsuperscript{[4]} Raman spectrometry,\textsuperscript{[5,6]} semiconductor gas sensor,\textsuperscript{[7,8]} and fluorescence sensor.\textsuperscript{[9]} Due to the strict control of military explosives in most countries, improvised explosives (IEs), usually known as oxidant-fuel explosives, have become the main tools for terrorists to conduct explosive attacks due to the easily accessible materials and simple preparation process. IEs are usually mixed with several substances in which oxidant components (such as nitrate, nitrite, chloride, perchlorate peroxide, permanganate, and chromate) release a lot of energy through redox reaction and fuel (such as sugar, diesel, nitrocellulose, and so on) generates a lot of gas in a short time (classified by improved explosive thread card of the Federal Bureau of Investigation).\textsuperscript{[10]} For example, ammonium nitrate, which is widely used in agricultural fertilizer, can be used as an explosive once it is mixed with diesel oil or kerosene. Similarly, potassium chlorate only needs to be mixed with paraffin or vaseline and then added with aluminum powder to make explosives. However, IEs, except peroxides, are mainly inorganic salts existing as solid and they cannot be recognized in air like the common volatile nitro explosives, bringing unique analytical challenges for explosive detection.\textsuperscript{[11]} At present, preadsorption sampling is needed for the detection of nonvolatile chemicals which will undoubtedly put the tester in danger. From the investigation of the spatial distribution of solid particles in air,\textsuperscript{[12]} it could be confirmed that for nonvolatile IEs, the solid particles will also be distributed in atmosphere due to dispersion. Thus, for the sake of safety, it is necessary to detect IEs by developing the detection instrument with the capability to sense the IEs themselves directly, possibly, by their suspended particles in air with non-contact sensing technology.
Optical chemical detection transmits chemical information of substances through optical signals, such as infrared spectrum and Raman spectrum, in which the surface-enhanced Raman spectroscopy has unique vibration fingerprint and high signal enhancement characteristics, which has many applications in the field of chemical detection and environmental monitoring. The highly sensitive detection of trinitrotoluene (TNT) by using SERS technology has been realized through the Raman signal generated by the reaction of the enolate ion of 3-mercapto-2-butanol complex with nitroaromatic with the limit of detection (LOD) as low as 6.81 ng mL\(^{-1}\). These methods have strong specificity and sensitivity, and have the potential to be developed to be portable and fast analysis methods to face the multiple components detection of IEs. Visualized chemical probes based on a “lock-and-key” strategy have been applied in the early stage, and systematic research work has been carried out since 1860s (Figure 1). Changing the optical properties of the probe through chemical interactions between the probe and the object can recognize substances with high specificity based on the color or fluorescence changes caused by intermolecular interactions. With the diversification of the form of the analyte and the real-time response of the detection, the detection is immobilized from solution reaction itself and expanded to the paper- and hydrogel-based detection chip for even sampling steps. As more specific optical chemical probes have been designed and the ability of pattern recognition was improved, the optical chemical sensor array was developed since 2000s and showed superior selectivity and sensitivity on different kinds of analytes. Furthermore, by combining logic and brain-computer design, the optical chemical sensors have the function to analyze complex systems, leading to the building of intellectual artificial olfactory for IEs detection.

To simulate the olfactory neurons, the chemical information of gases is converted into electrical signal transmission and there have been a series of work to explore rapid, sensitive, and recognizable electronic nose applying for explosive detection. The optical artificial olfactory system is also based on bionic principle, which uses the substrate to simulate the mucosa, the optical chemical probe to simulate the recipient units, the sensor array to simulate the neuron group, and the pattern recognition to simulate the signal integration of the silk sphere. Herein, we discussed the principle of the optical artificial olfactory system for the detection of IEs, as well as the latest progresses in this field, including the chemical probes, formation of sensor array, pattern recognition, and optical artificial olfactory system. We also speculated the development trends and challenges to improve the detection performance.

2. From Optical Chemical Sensor to Artificial Olfactory System

Biological olfactory system’s resolution of matter comes from its discrimination of molecules or particles in the atmosphere,
which is usually a mode of chemical combination—signal transmission. Police dogs are considered to be the most effective assistant for explosive detection and they can be trained to have a higher level of olfactory recognition ability for military explosives and many IEs (Figure 2). However, dogs’ training is expensive and they are easily affected by the surrounding environment and their live mood. Moreover, behavioral characteristics of dogs corresponding detection of explosives are not well understood. By simulating the olfactory system, many detectors have been developed to detect military explosives and IEs, for example, MetOne (QS-H150 based on the principle of ion mobility spectroscopy) and Fido (based on fluorescent polymer materials) have realized the detection of most military explosives and peroxide IEs. Besides, by constructing a colorimetric array (Prof. Suslick’s group) and functionalizing fluorescent polymers (Prof. Fang’s group and Prof. Cheng’s group), the detection of oxchloride and oxynitride IEs was additionally realized. For the realization of detecting more IEs, our group explored and integrated a series of colorimetric principles for the detection of potassium permanganate, S, urea, sugar, and other components of IEs.

From the research on optical detection of IEs from 2010 to 2021 (Figure 3), it can be found that the detection limits of hypochlorite, perchlorate, peroxide, nitrate, and nitrite based on solution reaction are mostly between $10^{-5}$ and $10^{-9}$ M, and it is difficult to achieve higher sensitivity detection by merely optical probes designing. By combining the sensing probes with paper-based and hydrogel-based substrate and optical microscope device, the detection sensitivity has been greatly improved in 2020 and 2021 reaching a level of $10^{-15}$ M. To better improve the detecting sensitivity, optical artificial olfactory system takes chemical sensor array as the detection modules of different IEs, as well as considering the automatic analyte collection with airflow and the ultrasensitive recognition of optical signals has been explored from the design of different components.

![Figure 2. Explosive detection dog](image1)

![Figure 2. Explosive detection instrument based on artificial olfactory](image2)

![Figure 2. H2O2, TATP, HMTD, BP](image3)

![Figure 2. ClO4-, ClO3-, NO3-](image4)

![Figure 2. MnO4-, NO2-, Sugar, Sulphur, Urea](image5)
2.1. Basis of Detection—Optical Chemical Probes

In the optical artificial olfactory system, the most important part to realize the function of detection is the recognition unit, which is composed of optical chemical probes. Due to the noncolorimetric and nonfluorescent characteristics of explosives, the optical chemical detection of IEs is an indirect method that utilizes the optical changes that occur when chromophores and fluorophores interact with explosives.\[107\] In theory, any phenomenon that changes the state (turn on or turn off), intensity (increase or decrease), or wavelength of the optical signal can be used to detect explosives. The structure of the probe molecular generally consists of three parts: 1) the recognition group of the substance to be measured; 2) the signal group which converts the recognition information into optical signal; 3) the linker between the recognition group and the signal group. According to the change of absorption spectrum or emission spectrum of the signal group, the optical probes can be divided into colorimetric probe and fluorescent probe.

2.1.1. Colorimetric Probes for IEs

Colorimetric detection can realize qualitative analysis by observing color changes with the naked eye, without relying on analysis equipment and power supply. It is not interfered by sample purity, environmental humidity, dust, etc., and is very suitable for the detection of IEs.\[108\] From 19th century, the color reaction of substances was used to perform qualitative analysis. Many commonly used colorimetric method have been invented, such as the Griess reaction for nitrite detection, the Berthelot reaction for ammonium detection, and so on.\[109,110\] These methods are empirical, and the principle is not easy to refer to. Thus, it is necessary to clarify the principle of color reaction and design colorimetric probes with higher sensitivity and specificity. The design of colorimetric probe is mainly based on the electron transfer caused by light excitation when electron donating and electron withdrawing groups are connected to chromophore. Analyte is partially bonded to electron donor or acceptor, and then the degree of intramolecular charge transfer will change accordingly, resulting in color change to achieve the purpose of recognition.

One possible design idea of color reaction is to extend or break the conjugated chain of colorimetric probe molecules by chemical reaction with IEs. In organic conjugated molecules, the energy of the ground state and the excited state molecular orbitals is affected by the length of conjugated chain.\[111\] Changing the length of conjugated chain can adjust the energy level of frontier orbital, thus affecting its spectral properties, resulting in color change, such as the formation of Schiff bases, azo dyes, and α,β-unsaturated carbonyl compounds. Kim et al. used the oxidation of ammonium salt to imine and condensate with salicylic acid to form indophenol blue, and successfully obtained a stable colorimetric test paper and realized the colorimetric detection of ammonium by modifying the reagent on the filter paper with a detection limit of 10 mg L\(^{-1}\) for naked eye (Figure 4a).\[112\] Shoronia et al. used 4-dimethyl-aminocinnamaldehyde to react with nitrourea in neutral environment to form a red protonated Schiff base structure, which is the condensation reaction product between amino group and carbonyl group, and thus realized the detection of residue on fingers (Figure 4b).\[113\]
mechanism was characterized in detail, and it was proved that the reaction process was the condensation reaction of amino group and carbonyl group, and the red protonated Schiff base structure dye was finally produced.

Another design method of probe molecule could be a strategy of indirect detection. Some IEs, such as sugar and perchlorate, which are difficult to react with probe molecules to produce conjugated chain changes, can be endowed with rich optical properties through hydrogen bond, coordination bond, and other physical actions, which can affect the photophysical process of the system and produce color change. Mashazi et al. decorated nanomagnet-silica shell (Fe₃O₄@SiO₂) decorated with Au@Pd nanoparticles based on effectively catalyzing the oxidation of 3,3',5,5'-tetramethylbenzidine (TMB) in the presence of H₂O₂ (Figure 4c). The UV–vis absorption spectra change from 652 to 370 nm and the absorbance is linear in the range of 0.01–60 μM with a LOD of 60 nM. Correa et al. synthesized silver nanoparticles with cellulose nanowhiskers and they would catalyze decomposition in the presence of H₂O₂, weakening the absorption peak at 410 nm with a linear range of 0.01–30 μM and LOD of 14 nM (Figure 4d).[115]

2.1.2. Fluorescent Probes for IEs

The fluorescent probe combines with IEs through physical or chemical interaction, which affects the energy or electron transfer state in the system and changes the excitation and emission processes of fluorophore, resulting in fluorescence changes. Through different fluorescence detection mechanisms, such as photoinduced electron transfer (PET), Förster resonance energy transfer (FRET), and electron exchange (ET), a large number of fluorescent dyes with turn-on or turn-off signals are synthesized based on different fluorescent groups (Figure 5a).[116] However, devices composed of IEs often coexist with fuel and it can make the reaction results of the sample and reagent be covered, or directly produce physical quenching effect on the fluorescent probe, which will seriously affect the observation or recognition of fluorescence quenching phenomenon. Therefore, it is appropriate to design fluorescent turn-on molecules to better realize the analysis of IEs.

The most common fluorophores are multielectron conjugated organic compounds, for which the fluorescence is regulated by π–π conjugation with the electronic structure changing when
reacting with IEs. We precisely modulated the binding sites of benzothiazole and realized the specific detection of nitrites with an ultrasensitive detection limit (2.2 fg) and a rapid detection time (<5 s) on paper substrate (Figure 5b). However, some organic fluorescent molecules may interact with each other to produce nonradiation deactivation, and the change of solubility before and after the reaction may accelerate this process. One solution is to use the traditional fluorescent molecules combined with nanoparticles, for which the existing state is controlled by nanoparticles and the interference generated by the reaction is

Figure 5. a) Molecular orbital schematic illustration for different fluorescence detection mechanisms. Reproduced with permission.[116] Copyright 2015, Royal Society of Chemistry. b) Optical images of the test strips used to detect a nitrate solution (0–800 μM) and nitrite solid (0–1 mg). Reproduced with permission.[103] Copyright 2020, Wiley-VCH. c) Structure of nJG and detection of H₂O₂ and TATP. Reproduced with permission.[70] Copyright 2016, Royal Society of Chemistry. d) Optical changes and stacking modes in fluorescence emission of nitrate detection probe. Reproduced with permission.[81] Copyright 2018, Royal Society of Chemistry. e) Constructing detection arrays on paper-based analysis equipment. Reproduced with permission.[117] Copyright 2013, Royal Society of Chemistry. f) Colorimetric detection of perchlorate by platinum complex in different sampling situation. Reproduced with permission.[106] Copyright 2021, Elsevier.
reduced. Joseph et al. synthesized fluorogenic silicon nanomaterials with silica and perylenemonoides modified by substituted pyridine group.\(^\text{[79]}\) By adjusting the electronic donor–acceptor effect on the fluorescent core, strong fluorescent response in a vacuum flow of triacetone triperoxide (TATP) can be generated at 665 nm, and the fluorescence turn-on detection of TATP is realized (Figure 5c). Considering the light stability, fluorescence quantum yield, maximum emission wavelength, and Stokes shift, the fluorescent probes can be endowed with excellent photophysical properties and improved detection sensitivity for IEs.

Aggregation-induced emission (AIE), which generally causes molecular structure of luminescent compounds to produce special molecular stacking, can greatly reduce the intermolecular interaction and limit the intramolecular rotation in the aggregation state, thus effectively inhibiting the nonradiation deactivation process of single molecule. By controlling the dispersion of AIE molecule, the detection of IEs can be achieved by combining with a variety of substrate materials. Chen et al. activated the divinylanthracene core by phenylevinylene peryridinium cation motif and prepared a fluorescent turn-on molecule based on ionic interaction-induced aggregation, and thus realized the detection for NO\(_2^-\) in acidic, neutral, and basic aqueous solutions (Figure 5d).\(^\text{[81]}\) As this method usually does not require severe reaction conditions, it can form sensing materials through simple device processing, such as constructing detection arrays on paper-based analysis equipment (Figure 5e).\(^\text{[117]}\) We employed Br\(^+\) salt of platinum complex to form anion exchange with perchorlate, which resulted in the shortening of Pt-Pt spacing between complex molecules and a luminescent color change from yellow to red, with a LOD of 25 nM in solution and a minimum of 1.12 ng detected perchorlate in the detection for firecrackers, soil, and fingerprints with hydrogel substrate (Figure 5f).\(^\text{[106]}\)

In general, the optical chemical probe is based on the design concept of “one on one,” which converts the chemical properties of IEs into visual optical signals through specific chemical reactions or physical bonding. In practice, some IEs even if detected cannot be considered as contraband, such as sugar and some ammonium salts. Only when they are detected simultaneously with oxidizing IEs, they can be considered as potential threats. Therefore, it is necessary to design methods that can comprehensively analyze the substance to be tested instead of a single substance.

2.2. Formation of Optical Chemical Sensor Array

The optical chemical sensor array can make a variety of analytes to get results in one test, and the combination of optical signals of the array can complete a single substance identification. However, chemical probes usually correspond to the reaction of the solution phase and it is usually necessary to conduct additional collection and processing for analytes which may put operators in danger. It is necessary to reduce the processing steps and sampling times by designing the formation of sensor array.

2.2.1. Application of Liquid and Solid Sensor Arrays for IEs Detection

The detection method based on chemical reaction needs to provide reaction medium. For most IEs, the detection needs to be dissolved first and then react with the probe in the liquid phase, and the liquid array provides the substrate for both dissolution and reaction. Swager et al. prepared an ionic liquid–carbon nanotube sensor array, which can distinguish volatile organic compounds (VOCs) relevant to human disease with five units (Figure 6a).\(^\text{[118]}\) Liquid–liquid segmented microfluidic technology is a mature droplet-based platform, which uses monodisperse droplets to immerse in a second immiscible continuous phase in a closed microfluidic channel, with a very small amount of reagent is used in the physically isolated droplet.\(^\text{[119]}\) In order to prevent the droplets from coalescing rapidly in the device, proper surfactants are usually added into the continuous phase to stabilize the liquid–liquid interface of the droplets.\(^\text{[120]}\) A droplet microarray is printed on the surface of complementary metal oxide semiconductor (CMOS) imager with colorimetric droplets composed of nonvolatile solvent that provides a permanent liquid environment (Figure 6b).\(^\text{[121]}\) Through these nonvolatile droplets to assist in sampling and transfer the object to be measured to the surface of the CMOS, the sensor array which can realize chemical method and good optical imaging is fabricated.

The protection and storage capacity of liquid array for detection reagents needs to be improved, and it is necessary to develop the application of stationary array. Solid arrays are mainly loaded with the optical probe onto the paper- or polymer-based substrate, and then used for detection of the gas emitted by the target analyte or dissolving it by predissolution. Mostly, paper is used as the substrate for qualitative detection of substances based on optical chemical methods. It was not until the concept of μPad was introduced by Whiteside using photographically patterned filter paper that the concept of paper-based sensor was explored and applied.\(^\text{[122]}\) The feasibility of paper as sensor substrate depends on three points: the surface will not interfere with the optical signal; the hydrophilic and hydrophobic regions can be regulated by modifying the surface groups to change the contact angle to the liquid; the fiber stack structure enables it to load solid reagents. Bruce et al. prepared a IEs colorimetric detection array by paper-based microfluid (Figure 6c)\(^\text{[123]}\), where paraffin was used to make five hydrophobic channels on the chromatographic paper, and then solid colorimetric reagent was loaded into each channel. After the detected substances were dissolved, it can provide colorimetric detection of common IEs (chlorate, nitrate, ammonium, nitrite, perchorlate, nitrourea, and hydrogen peroxide) by capillary action. Paixão et al. comprised a disposable paper array fabricated with printer and three reagents producing a unique color pattern arrangement for five kinds of explosives according to the chemical interaction between them and the reagents.\(^\text{[124]}\) It realized the colorimetric detection of many kinds of IEs including H\(_2\)O\(_2\), hexamethylene trioxide diamine (HMTD), TATP, ammonium nitrate, petroleum, nitro, chloride, and sulfur. 3D printing technology provides a simpler preparation method for paper-based sensor. Printing a substrate with open microchannels on its surface can not only control the channel depth and control the capillary flow rate, but also serve as a template for the synthesis of sensing materials (Figure 6e).\(^\text{[125]}\)

Generally, there is a pumping system to transfer the floating IEs gas or solid particles in the target area to the detection array surface. A turbulent area is designed in the acquisition chamber, which can keep the airflow containing the object to be measured in the detection chamber for a longer time, ensuring the full
contact between the micro detection array and the atmosphere to be measured. For devices that are not directly in contact with gas, the controlled injection system is usually made to ensure the uniformity of the input sample through the motor and the injection system.\(^\text{[126]}\)

However, there is still a great challenge for paper-based materials in optical chemical detection. The signal of the optical chemical sensor is not transmitted unidirectionally and the absorption of the signal by the substrate material in other dimensions will reduce its sensitivity. Paper is usually regarded as a 2D material, but in fact, its thickness cannot be ignored in optical chemical detection. The penetration of optical signals (colorimetric or fluorescent dyes) in the vertical direction will lead to the reduction of signal sources in recognition. This is reflected in the fact that many paper-based optical sensors have a small linear recognition range of concentration. After reaching the concentration threshold in microdevices, the accumulation of signal molecules inside the material is faster than that on the surface. It is also necessary for paper-based materials with good wetting ability for sampling which will lead to the diffusion of chemical products along the fiber in optical chemical detection. However, from the

Figure 6. a) Color and fluorescence change diagram of liquid array composed of eight sensing units. Reproduced with permission.\(^\text{[118]}\) Copyright 2018, American Chemical Society. b) Microarray formed by droplets with different volumes on CMOS and images before and after detection of ammonia. Reproduced with permission.\(^\text{[121]}\) Copyright 2020, American Chemical Society. c) Comparison of the inorganic explosives and high/organic explosives μPAD device before and after contacted with explosive mixtures. Reproduced with permission.\(^\text{[123]}\) Copyright 2015, Royal Society of Chemistry. d) Disposable paper array fabricated with printer. Reproduced with permission.\(^\text{[124]}\) Copyright 2014, Royal Society of Chemistry. e) 3D printing substrate with open microchannels. Reproduced with permission.\(^\text{[125]}\) Copyright 2016, MDPI. f) Structure of PVA network paper and color changed regions for chlorate detection. Reproduced with permission.\(^\text{[19]}\) Copyright 2020, Wiley-VCH.
perspective of optical signal recognition, the rapid diffusion will reduce the signal concentration within the range, and will also bring greater marginal effect, resulting in the reduction of signal recognition accuracy. Therefore, new requirements are put forward for the optimization of paper-based materials. We prepared a layered polyvinylalcohol (PVA) network paper and investigated the sensitivity of the paper substrate in terms of physical geometry and chemical composition, such as the Steiner network, layered and pore structures. The detection performance was compared by spraying potassium chlorate solution and the signals on PVA–methylene blue (MB) paper were more intense than those on the filter–MB paper substrate (Figure 6f). These sensor arrays provide reaction sites for IEs and can be used for multitarget analysis. However, the unity of sampling and reaction is not simple enough and it is necessary to design a kind of substrate material which can not only complete the sampling but also fix the probe molecules.

2.2.2. Hydrogel Used in Optical Chemical Sensor Array for Probe Anchoring, Liquid Phase Medium, and Adsorption Sampling

Considering the real-time monitoring of IEs in crowded places and environmental detection in the areas polluted, in situ detection and identification is very important. Due to the fact that IEs generally exist in a nonvolatile solid state, paper cannot be treated as “mucosa” to adsorb particles in air and provide reaction substrate. Soft materials have good flexibility, and can be endowed with adsorption properties of solid particles by modifying surface groups. The typical soft material hydrogel can bear the function of sampling and chemical reaction substrate simultaneously, and because of its good transparency, it is a potential substrate material for optical chemical detection. Zhang et al. utilized indole-based (4-HINF) hydrogel as a platform for colorimetric detection of urea in aqueous solution (Figure 7a) and exhibited linear response in the range of 0–10 mM with a LOD of 10 mM. It can directly contact the nitrite solid by hydrogel and complete the sampling and reaction simultaneously. Guo et al. loaded the probe that could detect nitrite by using the modified amino group on the carbon quantum dot and the principle of fluorescence quenching of nitrite into agar hydrogel to prepare the nitrite detection sensor (Figure 7b). It not only realizes the detection of nitrate, but also distinguishes the optical signal of the hydrogel sensor from the nitrate concentration, showing a semiquantitative nature. We proposed a hydrogel colorimetric sensor with an interpenetrating P-F127-B-hydrogel with alternating hydrophilic and hydrophobic structure constructed by micelles and rigid chains. The remarkably restricted color diffusion of the reaction product resulting from the probe with urea is realized through the strong water anchoring ability (Figure 7c). The application of hydrogel provides a new idea for the substrate of optical chemical detection. However, in practical application, two
problems should be considered: due to its dispersive medium, hydrogel is susceptible to environmental interference, such as slow volatilization of solvents and freezing at low temperature; hydrogel provides the ability of sampling while causing the problem of signal diffusion in vertical direction.\textsuperscript{[131,132]} The study of the influence of the structure of hydrogels on the internal environment and the diffusion mechanism of the surface signals of hydrogels may be helpful to the application for optical chemical sensors.

2.3. Pattern Recognition—From Discrimination to Processing

The optical artificial olfactory system can respond to gases and particles in air through the units in the sensor array. However, further analysis and recognition depend on the color model of the optical signals given by the sensors. The color model reflects the different expression of different light, which comes from the recognition of light by human eyes. In most human retinas, there are three types of cone cells, L (long), M (medium), and S (short) types,\textsuperscript{[133]} which are sensitive to different wavelengths of light (Figure 8a).\textsuperscript{[134]} The colors in human eyes become a linear superposition of three cone signals, according to Grassmann’s law.\textsuperscript{[135]} John Guild led some experiments and obtained the matching function of human eyes for different colors of light through matching with three kinds of light sources.\textsuperscript{[136]}

Therefore, defining color space according to color matching function has become the main method to express color in color model. In the optical artificial olfactory system, the colorimetric signal or the spectral signal of fluorescence can be transformed into the color space by color matching function (CMF): red, green, and blue (RGB) and hue, saturation, and value (HSV). Based on the human visual system, RGB expresses all colors by additive mixing of three primary colors. Commission Internationale de l’Eclairage (CIE) established a new chromaticity system based on RGB system in 1931 by using three imaginary primary colors X, Y, and Z. It is named “CIE 1931 XYZ” by matching the tristimulus value of the isoenergetic spectrum. In order to facilitate the display and calculation, the projection of the system on the “x + y + z = 1” plane is generally used in image processing, that is, chromaticity diagram.\textsuperscript{[137]} HSV is a kind of color space created according to the intuitive characteristics of color. HSV color space can be described by a cone space model,\textsuperscript{[138]} and because people are more sensitive to brightness than to color, in order to facilitate color processing and recognition, a large number of algorithms in image processing and computer vision are used in HSV color space.

By representing the optical signal of the detection reaction in the chromaticity space, the optical artificial olfactory systems contain multiple color data from different sensors. High-dimensional data need multivariate pattern analysis techniques.
to present the results in 2D or 3D space. The analysis of multivariate patterns is a process of dimensionality reduction. For example, 3D coordinates can be defined as a Cartesian product of three sets of real number—$R^3$. As $R^n$ and $R$ is equipotential ($R_1$), there is a bijection between $R^n$ and $R^2$ (any natural number $p$, $q$). Therefore, for 3D coordinates, any two coordinates can be selected to form a new $R^2$ set, and the original three coordinates can be simplified into $R$ and $R^2$ coordinates, realizing the transformation from 3D coordinates to 2D coordinates.

Pattern analysis methods include Euclidean distance, linear analysis, such as principal component analysis (PCA) and linear discriminant analysis (LDA); nonlinear analysis, such as hierarchical cluster analysis (HCA) and intelligent analysis. In response to the change of color value, displaying color in RGB 3D space is an intuitive processing method,[28] but the representation of 3D coordinates will be difficult to handle in comparison. Therefore, it is a simplified way to calculate the Euclidean distance of the color values before and after the reaction in RGB space (Figure 8b).[139] However, the Euclidean distance cannot be made use of all of the information in the data set due to dimensionality reduction,[140] and it is difficult to separate different data settlements like the distribution in RGB space (Figure 8c).[28] PCA uses an orthogonal transformation to create a new set of dimensions called principal components using linear combinations of the initial dimensions. By eliminating variables with similar variance, large variance (mutual uncorrelated) variables were established and preserved to achieve linear dimensionality reduction. Paixão et al. used PCA to analyze the colorimetric sensor combined with a disposable paper array, and realized the distinction of five kinds of explosives according to the unique color pattern (Figure 8d).[124] LDA is another linear processing method.[141] Different from PCA removing redundant dimensions in the original data set and making entropy as large as possible, LDA is to find the discriminative dimension by reducing the dimension, and thus the projection of the original data on these dimensions can distinguish different categories as much as possible. Minmoy et al. used LDA to process the data of nitric compounds (Figure 8e), and through sequential addition of queuing and masking agents, the sensitivity and classification accuracy were improved.[142] The basic idea of HCA is to calculate the similarity between nodes by some similarity distance metric, and then sort them from high to low, and gradually reconnect each node. Suslick et al. produced a colorimetric sensor array for the identification of nine separately synthesized samples of TATP and three HMTD, and discriminable ability was shown against each species through HCA (Figure 8f).[24] The advantage of this method is that clustering can stop at any subnode, and IEs can be grouped according to chemical properties. The above several statistical approaches are based on the assumption that the array signal distribution can be described by probability density function. Its mathematical structure is clear and easy to implement. However, due to the nonlinearity of signal nature and the limitation of sample model, it lacks robustness in artificial olfactory information processing. Intelligent analysis, mainly from the application of artificial neural network (ANN), can make up for these shortcomings.[143] It can automatically establish the nonlinear mapping between input and output through training, and solve the problem of cross sensitivity of sensors.

2.4. Optical Artificial Olfactory System—In Situ Detection

Arranging receptor molecules on the body surface to contact and recognize gas molecules is just like looking for a needle in a haystack, and mucosa acts as a medium for receptor molecules to react with the gas or particles in air. It provides a substrate for different olfactory receptor arrangements, while it relies on its adsorption to contact with the atmosphere and allows the substance to contact with the receptor. The probes in biological olfactory system are olfactory neurons expressing receptor genes.[144] Each odor receptor specifically recognizes a single odor molecule, and olfactory neurons with different odor receptors are randomly distributed to improve the olfactory sensitivity.[32] By mimicking the working principles of these elements, the artificial olfactory system could be constructed to realize the conventional human smelling for gases and particles in the air.[145] Since Persaud created the electronic nose in 1982,[146] many studies have realized the detection of gaseous substances or other analytes by simulating biological olfactory activity and signal transmission mode, such as electrical sensors and bioelectric sensors, and realized high selectivity and sensitivity detection through biological system strategy.[147,148]

Based on the bionic idea and optical signal recognition, an optical artificial olfactory system can be constructed for in situ detection for IEs (Figure 9a). Its core is a chemical sensor array derived from olfactory nerve and mucous. The instrument simulates human breathing through a gas collection system, and inhales the atmosphere into a chamber containing a chemical sensor array. The chemical sensing array is based on the hydrogel as a substrate to simulate the adsorption of solid particles in the air by olfactory mucosa. After the reaction, the optical signal given by the sensor array is transformed into electrical signal through the image acquisition system, and the mode analysis is carried out following with the output of the results. We proposed an artificial olfactory system based on colorimetric hydrogel sensor arrays for the detection and identification of airborne explosive microparticles.[28] Figure 9b shows the schematic diagram of the artificial olfactory system using colorimetric method to detect explosive particles and the capture process of solid particles by sensor array. First, solid particles adsorb near the hydrogel substrate through airstream guidance or random movement and similar to olfaction, there is a brief diffusion contact reaction process (Figure 9c). When an effective collision occurs, the color probe will change color, and then the optical signal penetrates the transparent hydrogel, which is recorded by a signal recognition system. It is also a fundamental part to recognize the optical signal made by chemical sensor. With the gradual enrichment of smart phone functions, such as powerful CPU, touch screen display, high resolution camera, embedded sensors, and the ability to connect to the Internet, more and more portable devices are developed based on smart phone platform. In order to improve the ability of smart phones to collect optical signals, additional accessories need to be developed.[149] For the optical chemical sensor array, a significant way to improve the sensitivity is to improve the resolution. The microdevice can remove the
limitation of camera lens resolution on optical signal acquisition. Figure 9d shows a smart phone-based contact microscopy platform, termed contact scope, which can image highly dense or contact samples in transmission mode. This kind of microscope usually has a discontinuous light source, but for the optical chemical sensor array, if the recognition molecule is based on fluorescent signal, it may put forward higher requirements for the light source. This is also a challenge for microcamera/spectrum miniaturization.

### 3. Potential Strategies and Technologies to Improve Optical Artificial Olfactory System

In general, the optical artificial olfactory system for IEs detection is the integration of molecular design, substrate synthesis, sensor array, and pattern recognition. Based on the existing technologies or feasible design schemes in these different fields, the detection and recognition of IEs can be realized, but obviously, the sensitivity and diversity of detection are not comparable to biological olfactory. Besides, the development of optical artificial olfactory system for IEs detection is still in a very initial stage. Thus, in this section, we will discuss some advanced methods related to chemical recognition and optical detection, and hope to put forward the future development ideas of optical artificial olfactory system for IEs detection.

#### 3.1. Single Molecule Recognition from the Perspective of Conformation Dynamics

Trained detector dogs can distinguish micrograms of explosives wrapped in multilayer boxes, which indicates they are sensitive to single molecules or small solid clusters. The improvement of the sensitivity needs the optimization of each unit in the artificial olfactory system. The first one is the design of optical chemical probes. Among the existing recognition molecules, the most common one is the use of chemical reactions (such as oxidation and condensation). Inevitably, this will cause a decrease in the recognition sensitivity because these reactions require the effective collision between the IEs molecules and the recognition molecules. On the other hand, although multiunit recognition can improve the specificity, the sensors need more units to cross-react because molecules with similar redox ability and molecules with the same group will interfere with one unit. In biology, olfactory recognition of molecules is based on the specific binding of receptor proteins which can recognize specific structural molecules through multiple site bonding (hydrogen bonding, hydrophobic interaction, and van der Waals force). This suggests that nonreactive recognition may be more specific in screening molecular structures. In addition, the recognition group synthesized under the guidance of receptor protein binding mode may have higher binding energy. In this way, the affinity between IEs and the recognition probe could be improved.
from the recognition principle, and the improvement of the sensitivity of optical artificial olfactory system could be expected.

The common feature of nonreactive molecular structure recognition is designing the binding groups and spatial structures for the groups at different positions of the analyte molecules to form a molecular “cage” rather than using the chemical reaction. Molecularly imprinted polymers mimic the behavior of antibodies and can effectively identify the target (Figure 10a).\cite{154,155} and due to their unique binding sites, they are expected to selectively recognize the analytes. These binding sites are usually produced by copolymerization of functional monomers and cross-linkers in the presence of template molecules, which are then removed to complement the target analytes in shape, size, and functional groups.\cite{156} In addition, molecularly imprinted polymers can withstand more severe environments than protein receptors, including high temperature, high pressure, acid, base, and organic solvents.

Another strategy is a “bottom-up” biomimetic receptor synthesis. Through the analysis of the space structure and group, the hydrophilic part was designed by hydrogen bonding, and the counterpart was designed by hydrophobic association. Small molecules containing different hydrophilic/hydrophobic groups are used to synthesize cyclic molecules with certain spatial structure, and filling groups are used to supplement the position with insufficient space distance.\cite{157} Through molecular design and optimization, biomimetic receptor can have binding energy as large as that of biological protein, which improves the binding ability and recognition characteristics of probe molecules (Figure 10b).\cite{157} These two methods are generally suitable for organic molecules with complex spatial structure.

For the other part of IEs in the form of ions, electrostatic interactions, anion-p binding effects applied in supramolecular systems provide a new idea for the design of probe molecules. Lehn\cite{158} proposed “anionic coordination chemistry” in supramolecular system, which shows that anions have two chemical valence: charge and coordination number, and the ligands are arranged in polyhedra centered on anions to coordinate with them.\cite{159,160} Figure 10c shows the forms of an anionic coordination in supramolecular chemistry by ditriflate-functionalizing pillar[5]arene and a 1,1,2,2-tetrakis(4-ethynylphenyl)ethylene (TPE) linker through a Sonogashira–Hagihara cross-coupling reaction.\cite{161} Based on the different properties of the ions to be tested, supramolecules with different binding modes can be designed to realize the recognition of IEs. In addition, for solid

![Figure 10](image-url)
microcrystalline clusters in the air, supramolecules can be combined with repeating units in a simpler way to realize the detection of ion clusters (Figure 10d).\textsuperscript{162} The above molecular design based on the structure of the substance can make the analyte and the recognition group have stronger binding effect, and emphasize the specificity between the target substance and the probe.

### 3.2. Design of Optical Absorption and Luminescence Signal Group

The design of the recognition group determines the binding ability of the probe molecule to IEs, while the optical group (fluorophore and chromophore) in the recognition molecule determines the intensity of the reaction signal. Higher fluorescence quantum yield or stronger absorption spectrum transfer can enhance the sensitivity of the probe molecules from the signal strength. The common optical groups are fluorescent groups or chromophores based on conjugated organic molecules. Many different kinds of groups have been used in the field of detection probes, such as xanthene, coumarin, BODIPY, etc., and some atypical chromophores have also been used in the design of optical probes with AIE effects.\textsuperscript{163–165} These optical groups are widely used in the design of probe molecules, but the enhancement of optical signals needs to be considered from another aspect. Conjugated polymers generally have large delocalized electronic structures.\textsuperscript{166} The combination of conjugated polymers as “molecular wires” with optical groups will lead to energy transfer and amplification within the fluorescent molecules, forming antenna effect and improving the optical signal intensity. For instance, the fluorescence signal is enhanced by 100 times by using the coumarin residues induced by fluorescence in the polyacetylene chain as the “bandgap trap” of exciton motion.\textsuperscript{167} Hua et al. connected rigid skeleton and flexible iodine binding site through Sonogashira–Hagihara coupling reaction to construct fluorescent conjugated mesoporous polymer, which can detect iodine with high sensitivity at 4 °C and low vapor pressure of 16.8 Pa due to the fluorescence quenching amplification of conjugated skeleton (Figure 11a).\textsuperscript{168}

**Figure 11.** a) Conjugated and atypical chromophores in organic luminescent materials. Reproduced with permission.\textsuperscript{179} Copyright 2020, Royal Society of Chemistry. b) Schematic of controlling the photoluminescence properties of nanoclusters. Reproduced with permission.\textsuperscript{167} Copyright 2020, Elsevier. c) Lanthanide-doped upconversion nanoparticles for tyrosinase detection. Reproduced with permission.\textsuperscript{178} Copyright 2019, Wiley-VCH. d) Modification strategy of quantum dots. Reproduced with permission.\textsuperscript{178} Copyright 2019, Wiley-VCH. e) Synthesis of carbon dots. Reproduced with permission.\textsuperscript{179} Copyright 2014, Tsinghua University Press and Springer-Verlag Berlin Heidelberg.
Due to its size close to the Fermi wavelength of electrons, nanomaterials have quantum confinement effect and cause energy-level splitting. This makes them have better optical properties and can be used as optical groups in probe molecules. Metal nanoclusters are aggregates composed of several to hundreds of metal atoms. When the particle size is in phase with the average free path of electrons, electrons will concentrate on the surface of nanoparticles, causing the surface plasmon resonance effect reflected in the spectral changes (Figure 11b), and it has been used as a signal conversion unit in sensing detection, medical imaging, and other fields. Lanthanide-doped upconversion nanoparticles absorb low-energy photons and emit fluorescence in the visible band. They have the advantages of strong light stability and easy surface modification, and can shield most of the background fluorescence interference. It is hoped to achieve highly sensitive and anti-interference IEs detection by modifying its surface ligand to act as an energy donor or electron donor and combining with specific recognition groups (Figure 11c). Quantum dots have the properties of stable luminescence and easy surface modification, which can be easily connected with recognition groups to realize optical chemical detection. The recognition molecules of IEs were modified on quantum dots and the energy levels were regulated by functional ligands. By establishing the energy matching transfer between the recognition reaction and quantum dots, it is expected to develop a general method to synthesize optical chemical probes for IEs (Figure 11d). Carbon dots are a kind of carbon nanomaterial synthesized by cutting carbon material or organic carbon source. The optical properties of carbon quantum dots are derived from the sp^2 and sp^3 hybrid carbon atoms (Figure 11e). Because of their abundant surface groups, they have some optical properties, such as controllable color, high quantum yield, and can also be used as signal group of probes to realize the detection of IEs.

3.3. Construction of Antidrying and Antifreezing Hydrogels

The substrate in the optical artificial olfactory system has two main functions: fixing the probe molecules and maintaining the stable external structure and providing the liquid phase site for chemical reactions. Therefore, when using the hydrogel substrate, its environmental self-adaptability needs to be guaranteed. The hydrogel network contains more than 90% of water, thus the evaporation of water at high temperature or longtime storage or the freezing of water at low temperature will affect the stability of the structure of the hydrogel and the containment of the chemical reaction in the liquid environment. The antidrying and antifreezing properties of hydrogel can be improved from two

Figure 12. a) Schematic of the solvent displacing to fabricate organohydrogels. Reproduced with permission.[184] Copyright 2018, Wiley-VCH. b) Hydrogel behavior in subzero environment illustrated for containing CaCl_2. Reproduced with permission.[185] Copyright 2018, Wiley-VCH. c) Schematic of the EG-waPUA/PAM hydrogel and twisting behavior compared with PAM hydrogel. Reproduced with permission.[186] Copyright 2019, Royal Society of Chemistry. d) Interpenetrating structures of organohydrogel and mechanical properties at different temperatures. Reproduced under the CC BY license.[147] Copyright 2017, The Authors. Published by Springer Nature.
aspects: the nature of dispersion medium and the enhancement of polymer skeleton. Commonly, evaporation and condensation can be explained by vapor pressure of liquid. The vapor pressure is related to the number of molecules evaporated from the liquid surface in unit time and the freezing point of a liquid is the temperature when the vapor pressure of the solid is equal to the vapor pressure of the liquid.\cite{183}

The addition of nonvolatile solutes reduces the number of volatile solvent molecules contained in the unit volume of solution, and the surface of the solution will be occupied by some nonvolatile solutes, thus reducing the vapor pressure. On one hand, the number of solvent molecules escaping from the liquid surface per unit time decreases correspondingly. On the other hand, the vapor pressure of the solution decreases, which makes the vapor pressure of ice higher than that of the solution, leading to nonfreezing properties. Nonvolatile polyols can combine with water through a large number of hydrogen bonds, which can further inhibit the evaporation and crystallization of water. Zhou et al. used solvent displacement method to replace the medium in hydrogels by using glycol, glycerol, and other solvents to form a water—alcohol solvent system organohydrogel (Figure 12a).\cite{184} The hydrogel can remain flexible at almost −70 °C, and it is weightless after storing in air for 8 days. Inorganic salts can also play a similar role as additives because of its ion–dipole interaction with water, such as the use of snow removers and lithium chloride solutions to maintain low humidity environments. Vlassak et al. added CaCl\textsubscript{2} to the polyacrylamide sodium alginate double network hydrogel, which significantly reduced the freezing point of the prepared salt ionic hydrogel (Figure 12b).\cite{185} The hydrogel can also maintain good tensile properties, high toughness, and excellent electrical conductivity at a low temperature of up to −57 °C.

The addition of volatile solvents and inorganic salts can improve the dry and frost resistance of hydrogels, but the change of solvent properties may affect the chemical reaction in optical artificial olfactory system. Therefore, it may be a better method to optimize the polymer skeleton with eminent water holding capacity than to change the solvent composition. Zhi et al. cooperated with ethylene glycol onto polymer chains and synthesized EG-waPUA/PAM-based cross-linked hydrogels by radical polymerization (Figure 12c). The structure gave hydrogel a large number of hydrogen bonding interactions to lock water in the network, which still has \( \approx \)100% Coulombic efficiency and good flexibility in −20 °C environment.\cite{186} There are many kinds of fat in plants and animals at high latitudes whose cell membranes inhibit the growth of ice and maintain its stability. Based on the bionic strategy, Jiang et al. used N,N-dimethylacrylamide hydrophilic network and laurylmethacrylate-co-n-butyl methacrylate hydrophobic network to form the interpenetrating heteronets.\cite{187} This structure made the modulus of the hydrogel almost constant in the temperature range of −78 to 80 °C, and has better flexibility and stability than that of ordinary hydrogel or organogel (Figure 12d). Except these methods, the formation of nano-coating on the surface of hydrogel by using surfactants or elastomers can also maintain its liquid phase. In optical artificial olfactory system, the dissolution and reaction of IEs depend on the surface properties of hydrogel, thus the principle and design of more antidrying and antifreezing hydrogels are still to be developed.

4. Conclusions and Perspectives

In this article, we put forward the overall structure and assumption of the optical artificial olfactory system, and the performance optimization strategy is proposed for IEs detection. In the domain of environmental monitoring, public security and anti-terrorism, the detection technology of IEs is indispensable. Unlike military explosives, the special nature, multisource, and multipurpose of IEs make it difficult to be completely banned in society. Therefore, high sensitivity, high specificity, portable, simple response, and identification of IEs sensors are in urgent need. Optical artificial olfactory system may be a good strategy to identify IEs and determine whether there is danger through the comprehensive analysis of array. With the development of sensing technology, optical artificial olfactory system will be well constructed to realize the rapid, sensitive, and specific detection of a variety of IEs. The design and synthesis of probe molecules and sensor substrates provide “neurons” and “mucosa” for the formation of optical artificial olfactory system. The sensor array can achieve pattern recognition of the IEs, and detect it through the discrimination and processing of artificial olfactory system. Through the integration of probe molecular design, sensor substrate material, sensor array logic, and optical signal pattern recognition, an optical artificial olfactory system can be formed and the detection of IEs can be realized.

However, the binding ability and optical signal intensity of probe molecules, the environmental adaptability of sensor substrate, and the sensitivity of signal acquisition system still need to be improved to achieve high sensitivity and adapt to various occasions for IEs detection instrument. For the detection of volatile and insoluble IEs (carbon, sulfur, and metal powder), the long-term stability of sensors in the environment and the interference of other background substances in explosive devices on optical signals remain to be solved. More efforts should also be made on the gap between research and application, such as the general design method of optical chemical probes, the 2D limitation of sensor signals, and the design of in situ sensors integrated with injection and reaction. The development of other fields, such as the upgrading of imaging system and the invention of substrate materials, will provide a wide design space for optical artificial olfactory system. As the optical chemical sensors for IEs detection become simpler and cheaper, the widespread application of optical artificial olfactory system will significantly contribute to the intelligent monitoring of various scenarios.

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Conflict of Interest

The authors declare no conflict of interest.
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[66] M. Chen, L. Sun, Y. Ding, Z. Shi, Q. Liu, *New J. Chem.*, 2017, 41, 5853.

[67] H. Y. Chen, A. J. Fang, L. He, Y. Y. Zhang, S. Z. Yao, *Talanta* 2017, 164, 580.

[68] Y. Zhang, Z. Jiao, W. Xu, Y. Fu, D. Zhu, J. Xu, Q. He, H. Cao, J. Cheng, *New J. Chem.* 2017, 41, 3790.

[69] X. Zhu, W. Chen, K. Wu, H. Li, M. Fu, Q. Liu, X. Zhang, *New J. Chem.* 2018, 42, 1501.

[70] J. Garcia-Calvo, P. Calvo-Gredilla, M. Ibáñez-Llorente, D. C. Romero, J. V. Cuevas, G. García-Herbosa, M. Avella, T. Torroba, J. Mater. Chem. A 2018, 6, 4416.

[71] Y. Shen, X. Zhang, Y. Zhang, Y. Wu, C. Zhang, Y. Chen, J. Jin, H. Li, *Sens. Actuators B-Chem* 2018, 255, 42.

[72] B. Goldere, A. Uzer, S. Durmazel, E. Erçag, R. Apak, *Talanta* 2019, 202, 402.

[73] W. F. Deng, Y. Peng, H. Yang, Y. M. Tan, M. Ma, Q. J. Xie, S. W. Chen, *ACS Appl. Mater. Interfaces* 2019, 11, 29072.

[74] Z. Zhou, Y. Li, W. Su, B. Gu, H. Xu, C. Wu, P. Yin, H. Li, Y. Zhang, *Sens. Actuators B-Chem* 2019, 280, 120.

[75] W. Li, Z. Liu, B. Zhao, J. Liu, *Langmuir* 2020, 36, 4194.

[76] T. Liu, S. Zhang, W. Liu, S. Zhao, Z. Lu, Y. Wang, G. Wang, P. Zou, X. Wang, Q. Zhao, H. Rao, *Sens. Actuators B-Chem* 2020, 305, 127524.

[77] Z. Xu, W. Shi, C. Zhang, Y. Yang, Z. Li, J. Liu, *Sens. Actuators B-Chem* 2021, 336, 129728.

[78] Y. X. Ma, S. G. Wang, L. Y. Wang, *Tract-Trends Anal. Chem.* 2015, 65, 13.

[79] M. Xu, B. R. Bunes, L. Zang, *ACS Appl. Mater. Interfaces* 2011, 3, 642.

[80] P. Griess, *Chem. Ber.* 1879, 12, 426.

[81] M. P. E. Berthelot, *Rep. Chimie Appl.* 1859, 1, 284.

[82] K. R. J. Thomas, J. T. Lin, M. Velusamy, Y. T. Tao, C. H. Chuen, *Adv. Funct. Mater.* 2004, 14, 83.

[83] Y. B. Cho, S. H. Jeong, H. Chun, Y. S. Kim, *Sens. Actuators B-Chem.* 2018, 256, 167.

[84] S. N. Cross, E. Quinteros, M. Roberts, *J. Forensic Sci.* 2015, 60, 193.

[85] O. Adeniyi, S. Sicwetsa, P. Mashazi, *ACS Appl. Mater. Interfaces* 2020, 12, 1973.

[86] K. B. R. Teodoro, F. L. Migliorini, W. A. Christini, D. S. Correa, *Carbohydr. Polym.* 2019, 212, 235.

[87] X. C. Sun, Y. Wang, Y. Lei, *Chem. Soc. Rev.* 2015, 44, 8019.

[88] R. V. Tautde, A. Beavis, L. Wilson-Wilde, C. Roux, P. Doble, L. Blanes, *Lab Chip* 2013, 13, 4164.

[89] M. Lyon, M. V. Wilson, K. A. Rouhier, D. J. Symonsberg, K. Bastola, I. Thapa, A. E. Holmes, S. M. Sikich, A. Jackson, *Signal Image Process.* 2012, 3, 51.

[90] W. Q. Feng, E. Ueda, P. A. Levkin, *Adv. Mater.* 2018, 30, 1706111.

[91] E. Ueda, F. L. Geyer, V. Nedashkovska, P. A. Levkin, *Lab Chip* 2012, 12, 5218.

[92] K. R. Mallires, D. Wang, P. Wiktor, N. J. Tao, *Anal. Chem.* 2020, 92, 9362.

[93] A. W. Martinez, S. T. Phillips, G. M. Whitesides, E. Carrillo, *Anal. Chem.* 2010, 82, 3.

[94] K. L. Peters, I. Corbin, L. M. Kaufman, K. Zreibe, L. Blanes, *Biosens. Bioelectron.* 2014, 58, 1252.

[95] J. Guild, *Langmuir* 2006, 22, 7042.

[96] J. Guild, *Adv. Sci.* 2018, 5, 109383.

[97] J. Guild, *Proc. Phys. Soc. London* 1917, 29, 354.
[137] M. J. Weber, K. Creath, H. Kogelnik, T. G. Brown, M. Kriss, J. Schmit, Wiley-VCH, Hoboken, NJ 2004.

[138] K. Erdogan, N. Yilmaz, presented at the Second Intl. Conf. on Advances in Computing, Electronics and Electrical Technology-CEET, Kuala Lumpur, December, 2014.

[139] Y. Liu, J. G. Li, G. F. Wang, B. Y. Zu, X. C. Dou, Anal. Chem. 2020, 92, 13980.

[140] S. H. Qian, Y. M. Leng, H. W. Lin, RSC Adv. 2016, 6, 7902.

[141] R. C. Graham, Data Analysis for the Chemical Sciences, VCH, Weinheim, Germany 1993.

[142] P. Behera, A. Mohanty, M. De, ACS Appl. Nano Mater. 2020, 3, 2846.

[143] J. E. Haugen, K. Kvaal, Meat Sci. 1998, 49, S273.

[144] K. Touhara, presented at the Second Intl. Conf. on Advances in Computing, Electronics and Electrical Technology-CEET, Kuala Lumpur, December, 2014.

[145] S. Giannoukos, B. Brikic, S. Taylor, A. Marshall, G. F. Verbeck, Chem. Rev. 2016, 116, 8146.

[146] K. Persaud, G. Dodd, Nature 1982, 299, 352.

[147] L. J. Zhuang, T. T. Guo, D. X. Cao, L. Q. Ling, K. Q. Su, N. Hu, P. Wang, Biosens. Bioelectron. 2015, 67, 694.

[148] T. Wasilewski, J. Gebicki, W. Kamysz, Trac. Trends Anal. Chem. 2021, 142, 116330.

[149] S. Amloy, P. Preechaburana, IEEE Photonics Technol. Lett. 2019, 31, 307.

[150] I. Navruz, A. F. Coskun, J. Wong, S. Mohammad, D. Tseng, R. Nagi, S. Phillips, A. Ozcan, Lab Chip 2013, 13, 4015.

[151] L. E. DeGreeff, B. Weakley-jones, K. G. Furton, Forensic Sci. Int. 2012, 217, 32.

[152] K. Kristiansen, Pharmacol. Ther. 2004, 103, 21.

[153] H. Q. He, R. D. Ye, Molecules 2017, 22, 455.

[154] Q. Yang, J. H. Li, X. Y. Wang, H. L. Peng, H. Xiong, L. X. Chen, Biosens. Bioelectron. 2018, 112, 54.

[155] J. Qi, B. W. Li, N. Zhou, X. Y. Wang, D. M. Deng, L. Q. Luo, L. X. Chen, Biosens. Bioelectron. 2019, 142, 111533.

[156] K. Haupt, K. Mosbach, Chem. Rev. 2000, 100, 2495.

[157] R. A. Tromans, T. S. Carter, L. Chabanne, M. P. Crump, H. Y. Li, J. V. Matlock, M. G. Orchard, A. P. Davis, Nat. Chem. 2019, 11, 52.

[158] J. M. Lehn, Acc. Chem. Res. 1978, 11, 49.

[159] K. Bowman-James, Acc. Chem. Res. 2005, 38, 671.

[160] H. J. Schneider, Angew. Chem. Int. Ed. 2009, 48, 3924.

[161] X. Li, Z. Li, Y. W. Yang, Adv. Mater. 2018, 30, 1800177.

[162] Q. He, P. Y. Tu, J. L. Sessler, Chem 2018, 4, 46.

[163] K. Ino, Y. Kanno, T. Arai, K. Y. Inoue, Y. Takahashi, H. Shiku, T. Matsue, Anal. Chem. 2012, 84, 7593.

[164] Y. Tan, L. Zhang, K. H. Man, R. Peltier, G. C. Chen, H. T. Zhang, L. Y. Zhou, F. Wang, D. Ho, S. Q. Yao, Y. Hu, H. Y. Sun, ACS Appl. Mater. Interfaces 2017, 9, 6796.

[165] N. N. Wang, M. Chen, J. H. Gao, X. Ji, J. L. He, J. Zhang, W. L. Zhao, Talanta 2019, 195, 281.

[166] S. W. Thomas, G. D. Joly, T. M. Swager, Chem. Rev. 2007, 107, 1339.

[167] T. H. Kim, T. M. Swager, Angew. Chem. Int. Ed. 2003, 42, 4803.

[168] M. Y. Xu, T. Wang, L. Zhou, D. B. Hua, J. Mater. Chem. A 2020, 8, 1966.

[169] R. Poo, Science 1990, 248, 1186.

[170] H. Q. Wang, L. G. Da, L. Yang, S. Y. Chu, F. Yang, S. M. Yu, C. L. Jiang, J. Hazard. Mater. 2020, 392, 122506.

[171] X. Kang, M. Z. Zhu, Chem. Soc. Rev. 2019, 48, 2422.

[172] M. L. Cui, Y. Zhao, Q. J. Song, Trac. Trends Anal. Chem. 2014, 57, 73.

[173] Y. Li, D. L. Jia, W. Ren, F. Shi, C. H. Liu, Adv. Funct. Mater. 2019, 1902191.

[174] P. Wu, X. D. Hou, J. J. Xu, H. Y. Chen, Nanoscale 2016, 8, 8427.

[175] I. L. Medintz, M. H. Stewart, S. A. Trammell, K. Susumu, J. B. Delehanty, B. C. Mei, J. S. Melinger, J. B. Blanco-Canosa, P. E. Dawson, H. Mattoussi, Nat. Mater. 2010, 9, 676.

[176] D. R. Baker, P. V. Kamat, Langmuir 2010, 26, 11272.

[177] E. Petryayeva, W. R. Algar, I. L. Medintz, Appl. Spectrosc. 2013, 67, 215.

[178] S. M. Tawfik, M. Sharipov, S. Kakkhvorov, M. R. Elmasry, Y. I. Lee, Adv. Sci. 2019, 6, 1801467.

[179] S. J. Zhu, Y. B. Song, X. H. Zhao, J. R. Shao, J. H. Zhang, B. Yang, Nano Res. 2015, 8, 355.

[180] Q. L. Zhao, Z. L. Zhang, B. H. Huang, J. Peng, M. Zhang, D. W. Pang, Chem. Commun. 2008, 5116.

[181] B. H. Chen, Y. Y. Bai, F. Xiang, J. Y. Sun, Y. M. Chen, H. Wang, J. X. Zhou, Z. G. Suo, J. Polym. Sci. Part B: Polym. Phys. 2014, 52, 1055.

[182] H. Yu, N. Rouelle, A. Qiu, J.-A. Oh, D. M. Kempaiah, J. D. Whittle, M. Aakii, W. Xing, J. Ma, ACS Appl. Mater. Interfaces 2020, 12, 37977.

[183] J. Tellinghuisen, J. Chem. Educ. 2010, 87, 619.

[184] F. Chen, D. Zhou, J. H. Wang, T. Z. Li, X. H. Zhou, T. S. Gan, S. Handschuh-Wang, X. C. Zhou, Angew. Chem. Int. Ed. 2018, 57, 6568.

[185] X. P. Morelle, W. R. Illeperuma, K. Tian, R. B. Bai, Z. G. Suo, J. J. Vlassak, Adv. Mater. 2018, 30, 1801541.

[186] F. N. Mo, C. J. Liang, Q. Q. Meng, Z. X. Liu, H. F. Li, J. Fan, C. Y. Zhi, Energy Environ. Sci. 2019, 12, 706.

[187] H. N. Gao, Z. G. Zhao, Y. D. Cai, J. J. Zhou, W. D. Hua, L. Chen, L. Wang, J. Q. Zhang, D. Han, M. J. Liu, L. Jiang, Nat. Commun. 2017, 8, 15911.

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