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Current Opinion in Electrochemistry

Emerging trends in miniaturized and microfluidic electrochemical sensing platforms

Jaligam Murali Mohan[1,3], Khairunnisa Amreen[2,3], Arshad Javed[1,3], Satish Kumar Dubey[1,3] and Sanket Goel[2,3]

Abstract

Electrochemical sensing has established a strong presence in diverse areas. The conventional electrochemical sensing approach consumes large sample volumes and reagents and requires bulky potentiostat, macro-electrodes, and other equipment. The synergistic integration of electrochemical sensing systems with miniaturized or microfluidic electrochemical devices and microelectrodes in a single platform provides rapid analysis with a disposable, reusable, and cost-effective platform for multiplexed point-of-care detections. Such microdevices have created scope for using several materials as electrodes and sensing platforms by using appropriate fabrication techniques. One of the most recent advancements in miniaturized devices includes the integration of automation and Internet of Things to realize fully automated and robust electrochemical microdevices. The review summarizes the emerging trends in fabrication methods of miniaturized and microfluidic devices, their multiple applications in real-time, integration of Internet of Things, automation, identifying research gaps with strategies for bridging these gaps, future outlook, and recent approaches to intelligent electrochemical sensing.

Addresses

[1] Department of Mechanical Engineering, Birla Institute of Technology and Science, Hyderabad 500078, India

[2] Department of Electrical and Electronics Engineering, Birla Institute of Technology and Science, Hyderabad 500078, India

[3] MEMS, Microfluidics and Nanoelectronics Laboratory, Birla Institute of Technology and Science, Hyderabad 500078, India

Corresponding author: Goel, Sanket (sgoel@hyderabad.bits-pilani.ac.in)

Current Opinion in Electrochemistry 2022, **33**:100930

This review comes from a themed issue on **Sensors and Biosensors 2022**

Edited by **Luís Moreira Gonçalves**

For complete overview about the section, refer Sensors and Biosensors 2022

Available online 28 December 2021

https://doi.org/10.1016/j.coelec.2021.100930

Keywords

Miniaturized devices, Microfluidic devices, Electrochemical sensing, Microfabrication, Nanotechnology.

Introduction

The amalgamation of electrochemistry and microfluidics has allowed seamless integration of sensing and detection systems with automation, miniaturization, and simplification. These integrated systems, owing to their inherent advantages, are amenable to be used as point-of-care devices in fields such as biomedical diagnostics and environmental sensing. The evolution of newer technologies and upgradation of well-established methods of microfabrication has paved way toward the utilization of various substrates such as paper, glass, elastomer polymers, and so on for fabrication of these devices [1]. Depending on the substrates used, various fabrication techniques can be adopted. Generally, fabrication methods such as (a) screen printing, (b) three-dimensional printing, (c) laser-induced or laser-engraved, (d) photolithography, (e) cutting shaping, and (f) wax printing are used.

Significance of miniaturized and microfluidic devices

Most present-day analytical methods primarily rely on laboratory-based analytical techniques that can be costly, cumbersome to use, have low sensitivity, and incur substantial testing expenses. Because point-of-care detection is crucial for several on-field applications, the focus has been shifted toward realizing smaller analytical instruments. Various miniaturized and microfluidic electrochemical (MMEC) sensors, with novel and smart materials, have gathered great demand in the domain of analytical science owing to their high sensitivity, mobility, operation, and rapid analysis [2]. The surface enhancement plays a vital role for detection of trace analytes by measuring electrochemical changes, such as voltage, current, and impedance potential, owing to the redox reaction (oxidation or reduction) signals of biological/chemical molecules with the use of electrodes and electrochemical units [3,4]. The ability of the sensor to detect various targets, such as tiny organic molecules, metal ions, and biomolecules, gives them enormous potential and advantages over conventional testing methodologies [5,6]. There have been numerous applications of MMEC sensors, particularly in the health-care industry, environmental monitoring, food safety, forensic analysis, military, defense, artificial intelligence, and so on. [7,8]. The present review focuses on the recent advancements in the fabrication of these

devices and their applicability. It also discusses the research gaps, scalability prospects, recent literature updates, and future outlook.

Fabrication methods

A variety of fabrication techniques are generally selected depending on the specific requirements of a product. Although comparing the fabrication methods, diverse characteristics, such as the material, deposition thickness, uniformity of deposition, space, cost, size, and tolerance of the unit are considered. The established fabrication methods provide precise control over device dimensions, surface modification, and other related parameters and provide scope for the usage of diverse materials. The surface modification methods used in the production of MMEC devices include evaporation, sputtering, photolithography, and chemical vapor deposition. However, because the underlying expertise and experience required for traditional electrode manufacturing methods are enormous, the costs to use these techniques can be incredibly steep. Moreover, the associated equipment is costly and requires special facilities, such as cleanrooms for their proper working. In addition, a large amount of floor space is needed for many of these specialized equipment.

Several other manufacturing approaches such as ink-jet printing, screen printing, and microwire placement have emerged as alternative methods to overcome the aforementioned challenges. Numerous scientific research groups have demonstrated the use of electrode fabrication on different substrates including flexible and paper-based materials. Techniques such as photolithography, ink-jet, plasma treatment, wax printing, and screen printing have significantly contributed toward increasing the ease of fabrication. In addition, screen printing and ink-jet printing are two prominent methods for patterning of electrodes and incorporating hydrophobic barriers. Figure 1 represents the classification of general fabrication methods based on the type of substrate used.

Paper-based fabrication methods

Paper has been used in analytical chemistry for decades, but it was recently rediscovered as a valuable and affordable substrate to work as a sensor. Advantages such as biodegradability, biocompatibility, easy availability, facile fabrication method, simple surface modification, and flexibility make them a suitable candidate to work as a substrate for electrochemical sensing [6].

The commonly used paper is Whatman chromatography paper, which has a smooth surface uniformity on both sides, an average flow rate, and 0.18 mm thickness compatible with commercial office printers. These papers consist of 98% α-cellulose, without any additives for strengthening or whitening agents, limiting the likelihood of any intervention. In addition, proper tuning and property adjustment are required for paper-based electrodes based on the intended electrochemical experiment. Few fabrication methods that incorporate electrodes over the paper substrate are (a) screen printing, (b) ink-jetting, (c) pencil drawing, and (d) laser-induced printing. These methods are discussed in the next section.

Screen printing

Screen printed electrodes (SPEs) are the first type of electrodes to be integrated into paper analytical devices and become the most common electrodes [9–11]. Screen printing equipment is relatively low-priced, and several devices are reported so far [12–14]. This is popular in analytical instruments, making the manufacturing process more streamlined [15–17].

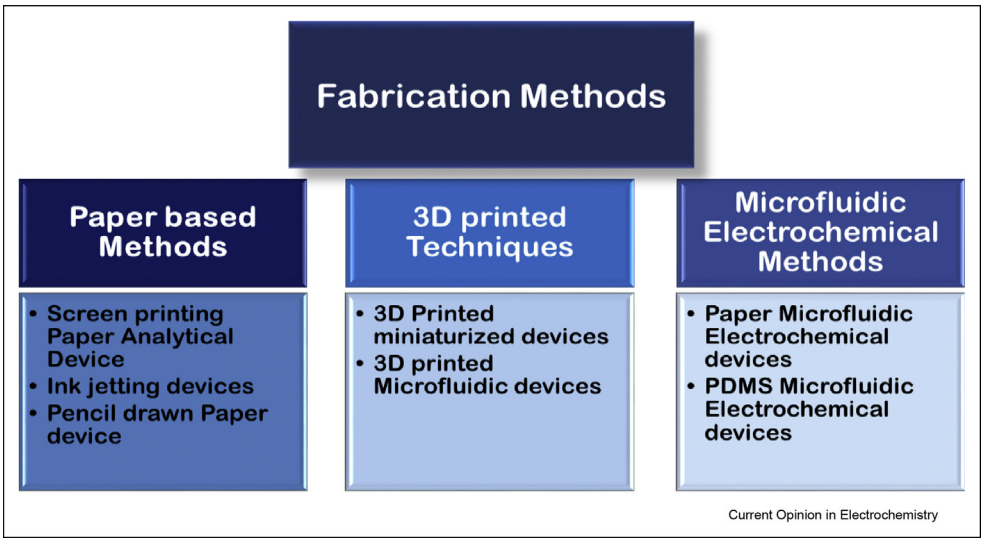
In a recent work where office paper was explored to develop screen printed paper strip for sensing of organophosphate pesticides as shown in Figure 2a. The strip was developed by both the wax printing and screen printing technologies. In the first step, a circular wax pattern was created to avoid solution diffusion toward the connector, and it might affect the readout of signal. In the second step, graphite ink and silver chloride ink were used to screen print the reference, counter, and working electrode. In the third step, the working electrode was modified with mixture of carbon black, Prussian blue, and butyrylthiocholine by drop-casting method. The developed portable strip can detect a lower limit of 1.3 ng/mL of organophosphate. To check its applicability, organophosphate was checked in the fruits, vegetables, and soil with the impressive recovery percentages in the range of 110%–90% [14].

Recently, Mohan et al. [18]reported a paper-based miniaturized screen-printed device for sensitive recognition of hydrazine on a paper substrate of dimensions 50 mm × 50 mm. As shown in Figure 2b, both reference and counter electrodes with dimensions of 40 mm × 5 mm were screen-printed on this substrate using carbon conductive ink and the Ag/AgCl ink. Furthermore, as a working electrode, a paper-based graphite sheet coated with the copper oxide nanoparticles was used. The working electrode was placed in between the counter and the reference electrode using double-sided tape. The wax barrier was produced to limit the 20 μL of the sample volume in the vicinity of all three electrodes. Finally, the platform was examined with 20 μM hydrazine. The actual sample analysis was also performed using tap and lake water for the device applicability, showing the appreciable recovery values.

Ink-jetting

Herein, ink-jet printing is used to deposit materials on the different substrates [19]. This technique aims to minimize the fixed costs of production while increasing

Figure 1



General classification of fabrication methods.

the number of materials used. The ink-jet printing technique overcomes disadvantages, wastage of the materials, lower production rate, and the nonuniformity of the conductive ink layer coatings [20]. The expensive materials can also be ink-jetted using ink-jet printing precisely with efficient resources [21].

A high level of accuracy and precision of required geometrical features of the electrodes is possible with ink-jet technology that satisfies specific industrial requirements [22]. The major ink-jet printing applications include light-emitting diodes and printed circuit board [23]. The ink properties, such as flow rate and viscosity values, must be adjusted as per the nozzle head for efficient application of this method. Various accessories and tools are required for the ink-jetting process, such as conductors, cartridges, paper, glass, or any flexible substrates and probe. Figure 4 gives a detailed representation of the ink-jet printing method. The process starts with filling the required conductive ink of specific viscosity in the cartridges using a fixed conductor. The substrates are fixed on the base plate of the ink-jet printing machine using substrate clamps. The final design is fed into the device with the compatible file format, as shown in Figure 3a. The distance between the substrate and nozzle is calibrated using the probe tool. The ink viscosity can be optimized with other parameters such as Z-axis distance, nozzle height, and line spacing [22].

Among various printing techniques, the ink-jet printing technique has a greater degree of flexibility and higher patterning capability and eliminates the need for predepositions or template/mask [24]. Multiple ink cartridges may be used to print various materials at the same time. Several substrates such as paper, glass, and polyimide with high reproducibility can be used [25].

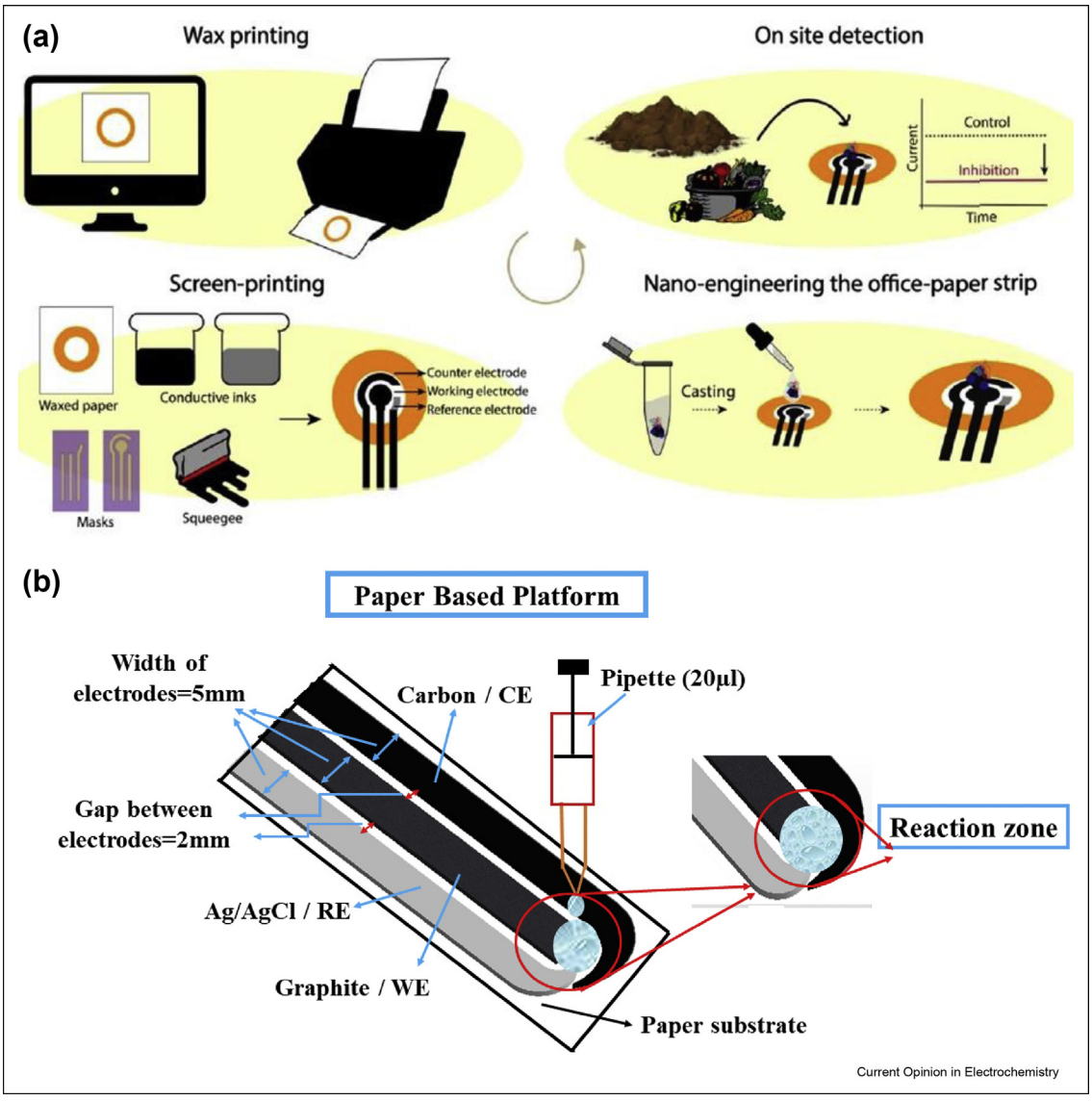
Bai et al. developed a biosensor system using ink-jetted printing technology as shown in Figure 3b. The developed biosensor system can able to detect phosphate in the saliva samples. From the fabrication point of view, a screen-printed electrode (SPE) was used to test the saliva samples. A bare SPE was cleaned with DI water and ethanol of 1:1 ratio. The cleaned SPE device was dried using nitrogen gas. Three different kinds of inks (Nafion, enzyme, and glutaraldehyde) were used to modify and to enhance the working electrode by ink-jet printing technology. These layers were formed layer by layer. The optimized parameters used for ink-jet printing were 6 kHz, 28 V [19].

Srikanth et al. [26] reported a three-electrode device using the same ink-jet printer on the glass substrate, and one electrode at the tip is modified with Ag/AgCl paste using a microneedle. Then, the electrodes were kept in an oven to dry for 2 hours. The cured polydimethylsiloxane (PDMS) microchannel was prepared with a DLW system integrated on the glass ink-jetted electrodes using plasma bonding. Finally, the integrated device is tested with the three different concentrations of ascorbic acid. The oxidation peaks were observed at a flow rate of 1 μL/min. Figure 3c is the reprint of the device with copyright permission.

Pencil drawing

Pencils can be used for fabrication of electrochemical devices as they are economic, available easily, and

Figure 2



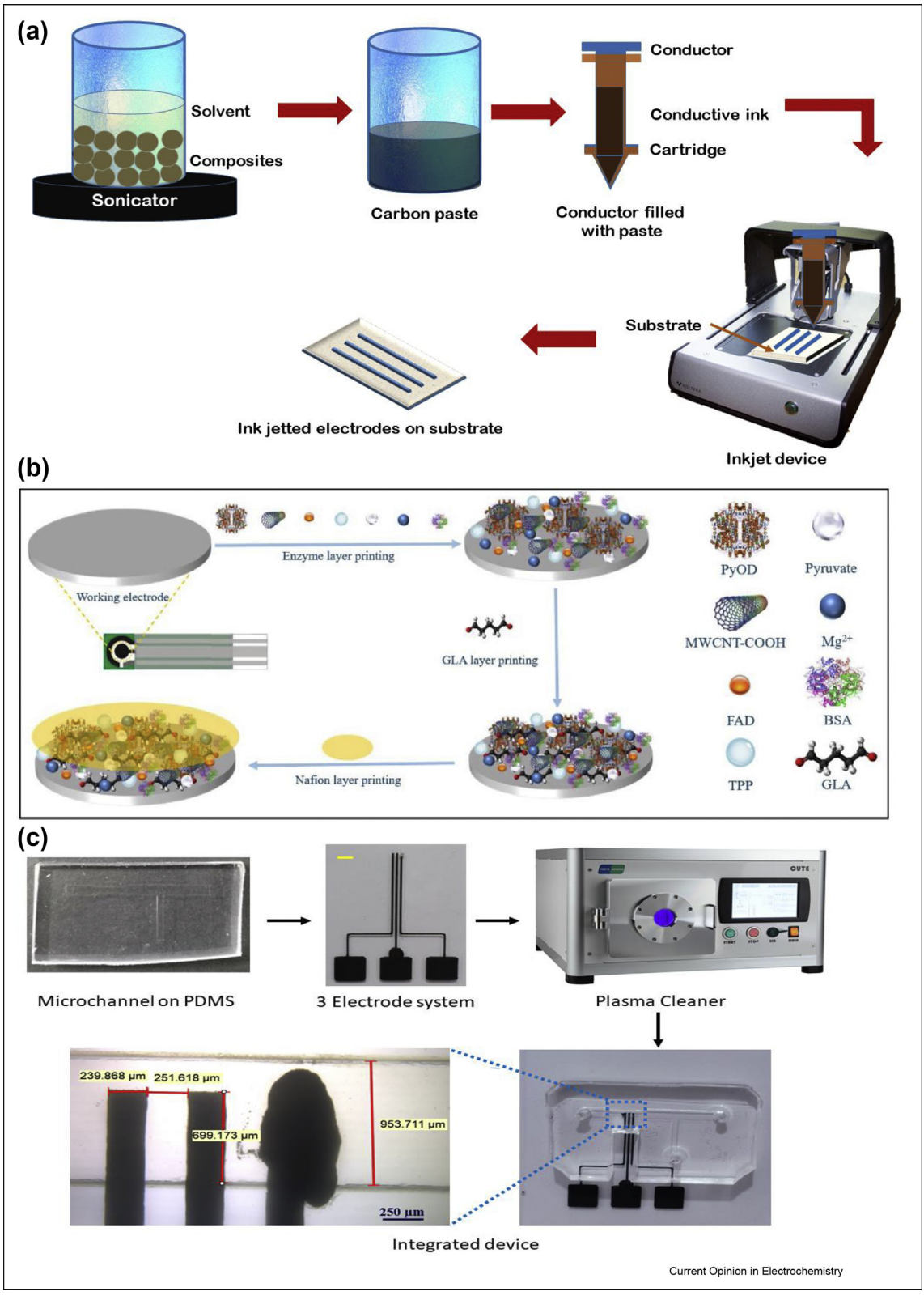
(**a**): Representation of development of office paper strip for pesticide detection. Reprint with the copyright permission from [14]. (**b**): A paper-based screen-printed electrochemical device for hydrazine sensing. Reprinted with copyright permission from Mohan et al. [18].

disposable. Some of the scientific reported works where pencil electrodes used are.

Franca et al. presented a simple and easily available inexpensive disposable electrochemical platform as shown in Figure 4a. In the fabrication, first, the tracing paper substrate was laminated with the laminating film using an office laminator. After that, the three electrodes were manually drawn on the tracing paper using a 6B-graded pencil. To draw the accurate shape and dimension of the electrodes, a layout of the design was produced on polyester film using the cutter and plotter. Later, the polyester film mold was placed over the tracing paper, and electrodes were drawn. Finally, to delimit the sensing area, 14 mm diameter of adhesive tape was covered on the outside of three electrodes. Finally, the working electrode was modified with quantum dots to improve the sensitivity toward the dopamine. A lower limit of 96 nM/L was obtained on the developed platform [27].

Rocha et al. fabricated a pencil graphite on sand paper by friction process. Initially, the three-electrode layout was drawn using Corel draw software. Later, the layout design was printed on the sand paper using the ink-jet printing. Then, the working and counter electrodes were painted manually with a graphite pencil. The reference electrode was modified with Ag/AgCl ink. To

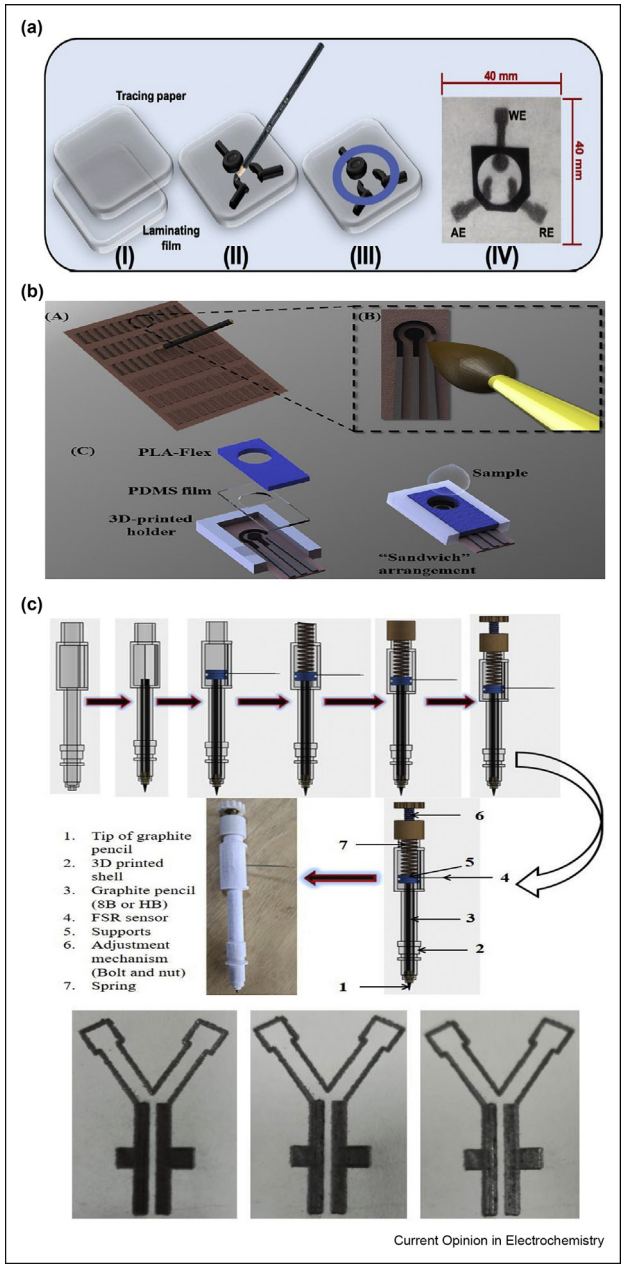
Figure 3



(**a**): Fabrication steps of ink-jet printing on substrates. (**b**): The functionalized procedure of the screen-printed electrodes is depicted in this diagram. Reprinted copyright permission from [19]. (**c**): An ink-jetted fabricated microfluidic electrochemical device for ascorbic acid detection. Reprinted with copyright permission from [26].

limit the geometric area, a three-dimensional (3D)-printed polylactic acid (PLA) was printed as shown in Figure 4b. To place the sand paper device, a 3D-printed holder was printed, in between the PLA and 3D-printed device holder, a PDMS film was sandwiched to avoid any leakages. The developed device was successfully tested with midazolam maleate which is also called as rape drug. To check the feasibility of the device, the device was also treated with vodka, beer, and liquor [28].

Figure 4



(**a**): Fabrication steps for pencil-drawn electrodes for dopamine detection. Reprint copyright permission from [27]. (**b**): Step-wise fabrication with a pencil on sand paper substrate. Reprint copyright permission from [28]. (**c**): Different parts and an assembled automatic pencil stroke device for stroking. Reprinted with copyright permission from Srikanth et al. [29].

In another similar work, Rao et al., an automated graphite pencil stroke device, was developed to overcome human interaction at the manual electrode fabrication time, as shown in Figure 4c. The designed automatic pencil stroke device was used for paper-based microfluidic applications. This inexpensive automated pencil-based device is used in the fuel cell applications. Sulfuric acid is used as an electrolyte with formic acid, oxygen as fuel, and oxidizing agent. In this application, a power density, current density measured to be around 135.5 μWcm^{-2} and 1305.5 μAcm^{-2}. Further fine-tuning with different pencil grades and various paper substrates, the fabricated devices can also be helpful in the electrochemical application for the various biological and chemical analyses [29].

Laser-induced and cut printing

Laser ablation over paper substrates is also versatile and low-cost in the manufacturing process [30]. This technique is often used for the production of paper electronics. Some reported works show platforms that were made using laser-induced on the different conductive polymers and mediator inks to produce conductive electrodes for electrochemical sensing applications [31–33].

Kothuru et al. had developed a graphene using CO_2 laser ablation process on the polyimide sheet for various electronic applications as in Figure S1.a. One of application the laser engraved polyimide sheet was used for electrochemical sensing of H_2O_2. In the reported work, a rectangular-shaped laser-induced graphene (LIG) was used as the working electrode with 50 mm × 3 mm dimensions, platinum as the counter, and Ag/AgCl as the reference electrode. The bare LIG electrode was tested with the 500 μM of H_2O_2 in phosphate buffer solution. The bare LIG electrode was able to sense the H_2O_2 up to a lower concentration of 0.3 μM [34].

In recent work, Behrent et al. performed an excellent parametric study on the Kapton foil by CO_2 laser engraving. To delimit the area of sensing, nail polish was used. To check the electron transfer rate using the laser engraving, various parameters were optimized as shown in figure S1.b. The electron transfer on the LIG electrode will depend on various inputs such as laser pulse density, laser scribing speed, and laser power. These parameters were varied with a laser power from 60% to 1% and the laser speed from 100% to 10%. The standard mediator, that is, 5 mM $K_3Fe(CN)_6$ and 0.1 M KCl, was used to check the proper electron transfer rate. Finally, it was found that lower levels of speed and power combined with high laser pulse density show the best electroanalytical performance. This optimized value was

used to detect the various biochemical analyses such as dopamine, uric acid, ascorbic acid, and paracetamol [35].

Zhu, Bicheng et al. fabricated a three-electrode system by laser scribing process using CO_2 laser on the polyimide substrate. The optimized parameters for the scribing graphene electrode were a laser speed of 0.45 cm/s, a laser power of 2.7 W, and 1000 pulse per inch. Furthermore, one of the electrodes was modified with a silver paste that acts as a reference electrode. The working electrode was modified with gold nanoparticles by electrodeposition process, as shown in Figure S1.c. The fabricated device was analyzed and tested with glucose wherein, it showed good sensitivity toward glucose sensing. The lower limit of detection (LOD) was found to be 6.3 μM. The device also offered good sensitivity toward the other interferants such as dopamine, uric acid, and ascorbic acid [36].

Three-dimensional-printed electroanalytical devices

Three-dimensional printing technology permits to making of three-dimensional solid objects from a designed file. The availability of 3D printing gives the ability to make complex shapes using less material than conventional manufacturing methods. Rapid fabrication, portability, and repeatability are unique features offered by 3D printing microfabrication. Although numerous 3D printing methods exist, only a handful have found mainstream use in production. They include stereo-lithography, fused deposition modeling, selective laser sintering, selective laser melting, and electronic beam melting. Among the aforementioned processes, fused deposition modeling, also mentioned as the fused filament fabrication technique, is the most widely used for desktop printers containing two standard filaments. This process extrudes filaments layer by layer onto a surface [37]. A nozzle-operated system uses filaments that melt and extrude filaments in a motion cycle. Then objects formed create 3D structures by extrusion layer by layer. Using fused deposition modeling technology, printable conductive filaments can be used in various sensors, antennas, metamaterials, filters, and various other applications [38]. The accessories which are used in the 3D printing fabrication are filaments and scrapers. Initially, the 3D model is designed using design software. The design is converted into the standard triangle language (STL), wavefront object (OBJ) file using the computer aided design (CAD) exchanger, Spin 3D software, and other related software. After the conversion of .STL file then again, the model is sliced into hundreds and thousands of layers by using the slicing software [39]. Finally, when the file is cut, it is ready for printing. Then the file is loaded on the 3D printer using USB, SD, or Wi-Fi. Then the sliced file is prepared to print the model layer by layer. Figure S2.a is the schematic representation of the 3D printing procedure [40].

An impressive number of improvements over conventional manufacturing techniques have been reported.

Katselli et al. reported that a dual extruder nozzle was used with filaments of nonconductive polylactic acid and conductive carbon-based filament to fabricate a three-electrode system, as shown in Figure S2.b. The.STL file format was created using Tinkercard software printing conditions mentioned for 3D printing: PLA 200 °C, acrylonitrile butadlene styrene (ABS) 220 °C printing speed of 40 mm/s. The printed miniaturized electrochemical cell was used to test caffeine and paracetamol by using pulse voltammetry. The printed cell was susceptible toward both the analytes [41].

Katseli et al. fabricated a miniaturized 3D-printed electrochemical device. The device was printed using carbon conductive filament. The working electrode in the printed device was modified with gold particles by electroplating technique. The sensitivity of the integrated miniaturized cell was enhanced by gold film. The modified filament was successfully tested for the detection of Hg (II). The 3D-printed device was also successfully used to detect the Hg levels in fish oil and water. Anodic stripping voltammetry technique was used to detect Hg(II), as in Figure S2.c [42].

Rocha et al. had also used the similar electrodes and fabrication approach as shown in Figure S2.d, PLA/carbon black composite was used as the working electrode for cadmium and lead determination. To increase the sensitivity of this, the composite electrode was chemically treated with 0.5M NaOH solution. The pretreated electrode shows better results toward the cadmium and lead in saliva and urine samples. The three electrodes, platinum (counter), Ag/AgCl (reference), and carbon black electrode (working), were assembled outer chamber. The outer chamber was printed with nonconductive ABS filament [43]. To limit the working electrode area and to drop the sample, O-ring was used to limit the working electrode area.

For instance, Katseli et al. [44] proposed a work where a file was saved in .STL format and transferred to the printer. The carbon-loaded PLA filament was used to print all three electrodes. One electrode was treated as the reference electrode. The other two electrodes serve as the working and the counter electrode. The 3D printer with the printed electrode is shown in Figure S2.e. The printed electrodes do not require any posttreatment with solvents, unlike other 3D-printed carbon-based electrodes. For the proof of concept, the device was characterized in ammonia and acetate buffer solutions by scanning potential from 2.5 V to −2.5 V. The 3D-printed electrodes exhibited clear peaks for caffeine by using differential pulse voltammetry (DPV)

in the range of 0—90 mg/L^{-1}. Later, the device was tested with Hg(II) different concentrations. The calculated LOD on this device was 1.9 μg/L^{-1} with square wave voltammetry. The device was also tested for glucose by amperometric technique within the concentration ranges of 2—28 mML^{-1}.

Pal et al. designed and fabricated a single-step 3D-printed device for nitrite sensing. The three electrodes were printed with carbon conductive filament, and after that, the electrodes were treated with dimethylformamide as in Figure S2.f. Finally, the device was tested with 600 μL working volume of nitrite and oxidation peak observed at 0.82 V. Furthermore, the developed 3D printed device tested with other electrochemical studies such as scan rate and concentration analysis. The LOD found in this device was 1.96 μM [45].

Maskless lithography

One of the processes used in the microfabrication of electrochemical devices is photolithography. In conventional photolithography, the mask pattern is transferred using light, and a geometric pattern is projected on the surface of the mask. Conventional photolithography is a relatively complex, sluggish, and inefficient approach to microdimensions and nanodimensions. For this reason, an improved process of the direct laser writer (DLW) approach is developed. DLW uses a precise ultraviolet radiation beam to form the desired geometric features on a substrate layered with photosensitive polymer. DLW technique is ideal for creating dimensions from the nanometer scale to micron dimensions [46]. DLW can be used for liquid photoresists and dry film photoresists of different thicknesses on the various substrates [47].

Microfluidic electrochemical devices

Microfluidic devices provide the mixing of different reagents, regulate the flow of analytes, increase the flow rate of the analytes, reduce the volume of the analytes (microliter to nanoliter), increase the sensitivity of detection of the samples, and use a similar platform for sample preparation as well as for detection. Combining microfluidics and electrochemical technologies presents the ability to merge chemical and biological components into a single platform, which deals with new opportunities for future sensing applications, including real-time detection, portability, disposability, unparalleled accuracy, and simultaneous investigation of different analytes in a single device. The fabrication of these microfluidic devices is primarily achieved through the conventional soft lithography and laser writing process. The most common substrates that were used in the evolution and the fabrication of these microfluidic electrochemical devices are paper, PDMS, poly (methyl methacrylate), glass, and plastic, thread. Some of the reported articles where they had fabricated paper and PDMS-based microfluidic electrochemical chemical devices are as follows.

Similarly, Silva et al. [48]reported a simple method to fabricate the linear microchannels in the PDMS substrates, replacing the soft lithography, which requires expensive materials and sophisticated instruments that require photoresists and clean room laboratory facilities. First, silicon mold was used to create microchannels. Then, the PDMS monomer was mixed with the curing agent at the ratio of 9:1. Then, this PDMS mixture was poured on the mold and cured at 70 °C for around 3 hours and then peeled off of PDMS to get microchannel. Furthermore, holes for the reservoirs were drilled using the biopsy punches. Later, a glass slide was cleaned with isopropyl alcohol and dried. Thereon, the pencil graphite was coated with epoxy glue and placed on the glass to cover the microchannel, and then the boundaries of the glass were sealed with the hot glue. Then, the pencil graphite was removed, carbon paste was added to the channel, and the glass slide was placed again cured. Finally, the developed device using electrochemical techniques successfully detected the iodide and ascorbate. Figure S3.a is the reprint of the procedure with copyright permission [48].

Regiart et al. has developed a portable microfluidic-based electrochemical sensor for the detection of sry box transcription factor 2 (SOX-2) cancer biomarker detection. The microfluidic channel geometry was prepared using CAD software. The mold was prepared using negative photoresist (SU-8) conventional lithography technique. The PDMS (elastomer and curing agent of 10:1 ratio) was poured on the SU-8 mold. Then the PDMS was peeled off and bonded on the glass substrate which was sputtered with the three-electrode system. All the three electrodes were prepared with gold using sputtering process. Later on, the PDMS microchannel and the gold-sputtered glass substrate were bonded using the plasma treatment as shown in Figure S3.b. For the detection of SOX-2 detection, the channels were treated with chemical to increase the hydrophilic nature. The SOX-2 antibodies and horseradish peroxidase were sandwiched in the channel. Finally, the quinone and the catechol solution along with H_2O_2 were reduced on gold electrodes at +0.1 V [49].

Senel et al. fabricated a 3D-printed microfluidic chamber of a diameter of 10 mm and z height of 6 mm. The center of the chamber was manually drilled with a hole of 0.8 mm diameter. The pencil graphite electrodes were inserted into special cavities of the microfluidic chamber as shown in Figure S3.c. A tubing of an outside diameter of 0.762 mm was push-fit in the center of the 3D-printed chamber. Then, the electrochemical activation was performed by cyclic voltammetry for 50

cycles at 100 mVs^{-1}. Finally, the device was tested with clozapine and gave the oxidation peak at +0.2 V. The fabricated device can able to detect very lower limits and up to 24 nM [50].

Future outlook — Internet of Things

With the growing demand for the personal and integrated health-care system, there is a huge potential for Internet of Things (IoT) enabled point-of-care devices. IoT provides considerable ease for device interconnectivity, data analysis, and transmission. Miniaturized electrochemical devices, which are very sensitive, are promising for future IoT-enabled wearable biosensors and allied biomedical devices. Some reported works where the miniaturized electrochemical device integrated with a smartphone for various biological sample monitoring.

Alahi et al. developed an interdigitated electrode for nitrate sensing on the flame retardant (FR4) capacitance sensor. A smart IoT system was proposed as shown in Figure S4.a. Here, the nitrate sensor was connected to the impedance analyzer analog device (AD5933). The impedance analyzer was used to get the data from the sensor. The impedance analyzer collects the phase shift and impedance data. Later, the analyzed data were sent to IoT cloud server. The impedance analyzer was connected to the Aurdino Uno wireles fidelity (WiFi) which acts as a microcontroller. Furthermore, a microcontroller unit was connected to the voltage regulator and power supply [51].

Nagabhooshanam et al. developed a micro electrochemical device for the detection of chlorpyrifos. Gold microelectrodes used a three-electrode system where the working electrode was modified with zinc metal-organic framework. The LOD found in the device was around 6 ng/L. To transfer data collected from the sensor, it is connected with k-stat (portable potentiostat) [52] as shown in Figure S4.b.

Summary and conclusion

This review presents a wide range of fundamental aspects of electrode fabrications of miniaturized and microfluidic electrochemical devices, wherein many viable solutions to real-life applications were summarized. It is observed that researchers have attempted different fabrication techniques such as screen printing, ink-jet, 3D printing, laser engraving, and lithography for the development of the miniaturized electrochemical device. The screen printing technique is quite an old technique which is used for a long back in electrochemistry. However, its customized editions for digital printing are yet to come. However, ink-jet printing has emerged as a mature technology for digital and uniform printing of the miniaturized electrodes. Three-dimensional printing and laser engravings are the other promising and emerging technologies that pave the way for cheaper and higher-quality electrochemical devices. Lithography technique can be used to cater to the need of empathetic submicron range electrode development. To summarize, miniaturized and microfluidics fabrication methods are an emerging multidisciplinary research subject with a wide range of biochemical sensing applications. These platforms are ideal for applications including wearable biosensors, point-of-care devices, forensic testing, drug delivery and screening platforms, and microreactors for *in situ* productions of different chemicals owing to their low cost, portability, and disposable nature. It is possible to meet a vast majority of market needs by mixing and adapting these surface modification materials with the appropriate production procedures.

Furthermore, MMEC devices can attain industrial-scale production through a sequence of improvements in interrelated research domains. MMEC has received a lot of attention from researchers worldwide, even though it is still in its infancy. As a result, this field is expected to rapidly extend its understanding and utility to diverse applications and thereby address some of current most serious issues. Integration of MMEC devices with IoT can also aid in transmitting analytical data to different users and stakeholders. The further integration of MMEC devices with smartphone technology may improve specificity and sensitivity in the detection system's performance. These MMEC platforms coupled with electrochemical detectors and IoT will be critical in growing scientific knowledge in bio/chemical sensing in the near future.

Declaration of competing interest

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.coelec.2021.100930.

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* of special interest
** of outstanding interest

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