# Advances in nanomaterials integration in CMOS-based electrochemical sensors: a review

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Abstract— **The monolithic integration of electrochemical sensors with instrumentation electronics on semiconductor technology is a promising approach to achieve sensor scalability, miniaturization and increased signal to noise ratio. Such an integration requires post-process modification of microchips (or wafers) fabricated in standard semiconductor technology (e.g. CMOS) to develop sensitive and selective sensing electrodes. This review focuses on the post-process fabrication techniques for addition of nanomaterials to the electrode surface, a key component in the construction of electrochemical sensors that has been widely used to achieve surface reactivity and sensitivity. Several CMOS-compatible techniques are summarized and discussed in this review for the deposition of nanomaterials such as gold, platinum, carbon nanotubes, polymers and metal oxide/nitride nanoparticles. These techniques include electroless deposition, electro-chemical deposition, lift-off, micro-spotting, dip-pen lithography, physical adsorption, self-assembly and hydrothermal methods. Finally, the review is concluded and summarized by stating the advantages and disadvantages of these deposition methods.**
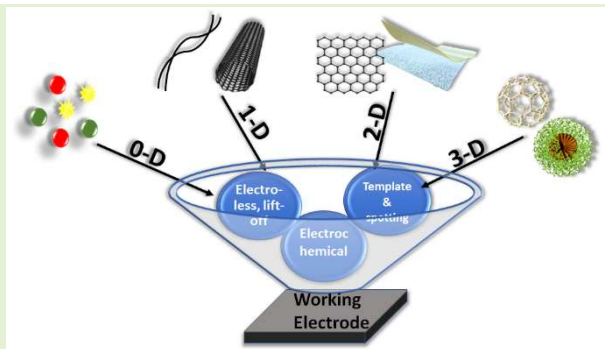
Index Terms— **CMOS microchips, electrochemical sensors, fabrication, nanomaterial, semiconductor technology,**

INTRODUCTION

Electrochemistry is the science that studies the chemical reactions occurring when electrical current or potential is applied across two or more electrodes in presence of an electrolyte. The reactions typically occur at the electrodes and have been widely used to carry out qualitative and quantitative analysis of the gaseous or liquid environment. The change in the current or potential values during the chemical reaction are a proxy measure of the concentration of target molecule [1]. Compared to alternative optical and magnetic sensors, the electrochemical sensing systems provide rapid detection and low-cost as well as the possibility for miniaturization by decreasing the required sample size [2], [3].

The electrochemical sensors and the instrumentation electronics are conventionally fabricated on two separate substrates and electrically interconnected. The long interconnects limit the scalability of the sensor array as well as signal to noise ratio of the measurement (due to electrical noise picked up at the interconnects). The monolithic integration of electrochemical sensors with instrumentation electronics provides sensor scalability and unlocks otherwise high-cost features such as sensor redundancy. The integration also improves the overall sensing performance by reducing the interconnect length leading to reduced interference, and reduced parasitic capacitances that typically improve the signal to noise ratio. Here a large array of sensors can be developed directly on top of the electronics circuit microchip.

Complementary metal-oxide-semi-conductor (CMOS) technology – the so far predominant VLSI manufacturing technology. A typical physical structure at the cross section of a CMOS integrated circuit is shown in Fig.1, where pad openings (exposed metal layers) are typically used for making electrical contacts with the microchip. These sites also where the sensing electrode of the sensor can be developed.

Aluminum has been commonly used in CMOS technology for metallization. A typical stack of Al layer may also have small quantities of copper (0.5% to 4% by weight) to prevent electromigration [5], [6]. CMOS processes continue to use aluminum as the top metallization layer due to its low resistance, low cost, and suitability for consequent wire bonding. However, aluminum is an electro-active material and thus cannot be used directly as a transducer to carry out electrochemical detection. To overcome this issue, it is required to coat the electrode with an inert metal such as gold (Au), platinum (Pt), or iridium (Ir). However, this is not a typical process offered by CMOS manufacturers and often the user arranges this step after the completion of the CMOS chip fabrication, hence the term "post-processing".
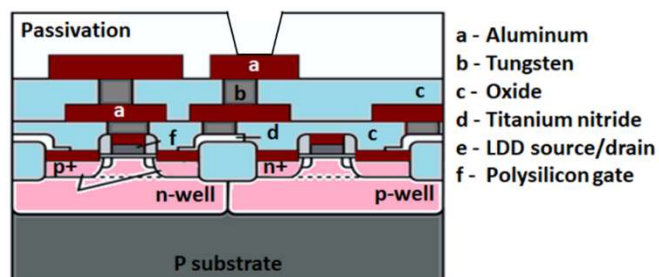

Fig. 1. The cross-section of a microchip fabricated in a typical sub-µm CMOS technology with top aluminum metallization and TiN local interconnects showing a pad opening. Adapted from [4].

Following the initial aluminum covering step, one or more extra layers are required to develop an electrode that is sensitive and selective towards the target analyte. This can be either a bio-recognition layer (e.g. enzyme, antibodies) or a nanomaterial layer or both. Nanomaterials are materials with at least one of their dimensions (x-scale, y-scale, z-scale) in the nano-range i.e. 1-100 nm. At these dimensions the materials exhibit properties such as high surface to volume ratio, high electro-active surface area, and higher sensitivity compared to their bulk counterparts. It has been shown that some nanomaterials can achieve selectivity towards specific analytes[7], [8] without the need for conventional bio-recognition layers. This review summarizes the techniques presented in literature for surface modification of on-chip sensing electrodes with various nanomaterials.

The review is organized as follows. Section II provides a short tutorial and introductory information on nanomaterials based on their dimension. Here their properties are highlighted along with general methods employed to incorporate them onto the structure of sensing electrodes. The inclusion criteria methods to shortlist articles for inclusion in this review are presented in Section III. In section IV we summaries the methods used to coat the microchip electrodes with inert metal layers Au and Pt, a step typically needed prior to the deposition of nanomaterials. This section is included for the sake of completeness. Section V presents the CMOS-compatible methods found in the shortlisted articles for the deposition of nanomaterials. The techniques are classified based on the material: Au, CNTs, Pt, polymers, and metal oxide/nitride nanoparticles. Finally, Section VI concludes the review.

NANOMATERIALS: CATEGORIES AND APPLICATION

Nanomaterials as mentioned above are a class of materials which have at least one of their dimensions in nanoscale (1-100 nm). They present various advantages as compared to their bulk counterparts, such as, higher surface to volume ratio, high porosity and higher electro-conductivity. Their application spans out in healthcare ranging from improving diagnostic systems, anti-bacterial coatings, food packaging to targeted drug delivery systems [9]. For example, metal oxide nanoparticles and nanowires such as zinc oxide (ZnO) have been employed for fabrication of electrochemical biosensing systems to enhance the detection limits [10]. Owing to their small size, nanomaterials based sensors have achieved single molecule detection for fabrication of point-of-care diagnostic systems [11], [12].
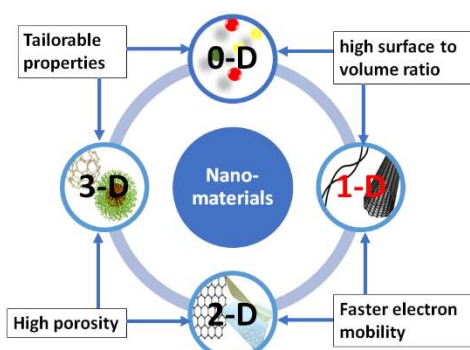
Fig. 2. Types of nanomaterials and general properties that make them better than their bulk counterparts.

These nanomaterials can be divided into four categories based on their dimensions: zero-dimensional (0-D), one-dimensional (1-D), two dimensional (2-D) and three dimensional (3-D) as conceptually shown in Fig. 2. In this section, we give a brief introduction to these categories in more details along with their key properties and applications.

Zero-dimensional (0-D) nanomaterials: These have all three dimensions (x-scale, y-scale and z-scale) in nanometer scale. These nanomaterials consist of spherical nanoparticles or nanoclusters which include quantum dots (organic and inorganic), metal nanoparticles, metal oxide nanoparticles and polymer dots [13]. 0-D nanomaterials exhibit properties such as biocompatible, wavelength-dependent photoluminescence and cellular permeability which makes them a promising candidate for biomedical applications such as biosensors, and bio-electronics [14], [15].

The incorporation of 0-D nanomaterials in the form of the sensing element or a part of the sensing element on the working electrode has shown to increase conductivity and sensitivity of the sensing system [16], [17]. Such nanomaterials can be introduced to surfaces through techniques such as electrochemical deposition, seed-mediated growth, and introduction of small amounts of 0-D nanomaterials while synthesizing the bulk layer.

One-dimensional (1-D) nanomaterials: These have their two dimensions in the nanoscale and the third in bulk range. These types of nanomaterials generally consist of nanowires, nanofibers and nanotubes [18], [19].
The 1-D nanomaterials in electrochemical sensing systems are commonly used to modify the working electrodes in electrochemical sensors due to their high conductivity leading to highly sensitive electroactive surface for detection of target analyte. The fabrication/growth of 1-D nanomaterials is carried out using various advanced nanolithography techniques, such as electron beam writing, focused ion beam writing, and proximal probe pattering and extreme-UV lithography [20].

Two-dimensional (2-D) nanomaterials: These have only one of their dimension in the nanoscale levels and the other two in the higher range. They include thin films of metals, organic, nanosheets such as graphene, boron nitride and other structures such as nano-polymeric coatings like self-assembled monolayers (SAMs) and electropolymerized layers [21],[22]. Molybdenum disulfide is another upcoming 2-D nanomaterial that is increasingly being applied for biosensing applications and is acting as a substitute for graphene and silicon dixoide due to its biocompatibility [23]. 2-D nanomaterials are covalently bonded film in a single plane with atomic level thickness which results in outstanding mechanical strength, high optical transparency, fast electron mobility and flexibility [24]-[27].

The application of 2-D nanomaterials in electrochemical sensing systems is almost similar to that of 1-D nanomaterials. Here, 2-D nanomaterials films are used to modify substrates like plastics to provide a conducting layer for fabricating the

sensor or direct modification of the working electrode with the nano-films. These thin films possess high number of reactive sites which promotes ease of surface modification, functionalization, doping and phase/defect engineering [28], [29]. These properties make 2-D nanomaterials a better candidate for immobilization of biological entities like antibodies, enzymes, aptamers as compared to the other 0-D and 1-D nanomaterials. The 2-D nanomaterials can be deposited on the substrate or electrode using techniques such as spray coating, spin coating, chemical vapor deposition and atomic layer deposition [30], [31].

Three-dimensional (3-D) nanomaterials: These nanomaterials are not bound in the nanoscale dimension but they consist of a combination of one or more nanomaterials that create a bulk structure. For example, they may contain multiple random arrangement of nano-crystalline structures, or they may include a variety of nanoparticles forming a cluster, or bundles of nanotubes, nanoribbons and nanotubes, or also stacks of 2-D nanomaterials. These can also be constituted of all three types on nanomaterials (0-D, 1-D and 2-D) stacked together to form a complex or nano porous structure. 3-D nanomaterials also include polymeric structures with nano-porous structure such as hydrogels. They provide porous structure, high specific surface area and large number of active sites, and hold a high potential for tailor-ability. 3-D nanomaterials provide possibility of storage of enzymes, antibodies and DNA in the pores which has been shown to increase the lifetime of the sensor [32]. The development and application of 3-D nanomaterials is an ever evolving area of research [33],[34]. 3-D nanomaterials such as hydrogels have been immobilized over CMOS electrodes using physical adsorption for glucose sensing [72].

METHODS: LITERATURE SELECTION

A search of literature was conducted in IEEE explorer, google scholar, google and sci-finder in February 2022 leading to 198 results published between 1985 and 2022. The articles were then shortlisted for inclusion in this review only if they satisfied all the following inclusion criteria.

(1) All steps in the electrode development process are compatible with the CMOS technology. That is, we define, as requiring temperatures that are not above 200 °C.
(2) The underlying conductive electrode material is either Al, Au or Pt.
(3) The (micro-)electrode size is up to 500 μm X 500 μm.
(4) The developed working electrode has been used for an electrochemical sensing of an analyte.

It should be noted that the term CMOS compatibility although used in literature, is not clearly defined as there are no clear set of parameters which would collectively summarize the criteria for CMOS compatibility. One such parameter involves the required temperature for post-processing of the CMOS chips. Researchers have stated temperature variations from 450 °C up to 600 °C as the compatible temperature for their chips [35-39]. However, increasing the temperature of microchip to above 200 °C has shown to cause irreversible damage to Al alloy [40] (a material that is used extensively in such microchips) in the form of decreased alloy strength and deformation. Therefore, the

maximum safe temperature in post-processing of CMOS chips in this review is considered to be 200°C as stated in the first criteria listed above.

The underlying electrode materials considered in this review are Au and Pt in addition to Al. Au and Pt are selected because there are well-established methods to deposit them onto CMOS electrodes. On the other side, they are vastly used in the structure of electrochemical sensors due to their inert and non-corroding nature, biocompatibility, and ease of conjugation with various biological recognition elements [41], [42].

Thirdly, the electrode size was chosen in the micro range to match the typical electrode sizes available on CMOS microchips. Methods to fabricate macro electrodes may not be transferrable to microscale levels. Finally, only articles with that employed the modified electrodes for electrochemical sensing applications were shortlisted thus papers reporting sensors based on for example optical transduction were excluded from the review.

DEPOSITION OF INERT LAYERS OVER ON-CHIP ELECTRODES

The typical first step in post-processing the on-chip electrodes for electrochemical sensing is to coat the Al electrode with an inert material that is suitable for electrochemical sensing. In this section, a review of the main techniques that have been employed to achieve a successful coating of Au or Pt films on Al electrode is given.

A. Electroless Au deposition on Al electrodes

The electroless deposition technique is a method used to deposit a metal layer on top of another metal without applying any electrical stimulation. This is achieved by placing the substrate in an electrolytic bath of the electroless plating solution. The bath consists of a metal complex maintained at a particular pH to preserve the complex from decomposing [44]. To achieve electroless plating, the temperature of the bath is increased to temperatures higher than room temperature (up to 90° C) to break the complex and deposit the metal ions on the target surface. The concentration of the metal in the bath changes after each use which may negatively affect the quality of the film, and frequent replenishing of the bath is needed in order to achieve a consistent quality of metal coating for multiple uses. An example for the components for electroless Au coating solutions contain potassium dicyanoaurate as the metal ion source, ethylene-diamine-tetra-acetic acid tetrasodium salt tetra-hydrate as the chelating agent to form a complex with the metal ion in a pH optimized solution.

The electroless Au plating cannot be carried out directly over the Al electrodes. This requires other metal layers in between which provides better adhesion of the Au film. On this basis the electroless route uses two different adhesive layers; the zinc/nickel and palladium.

The zinc/nickel route typically include the following steps as shown in the flow chart in Fig. 3 [45], [46]. Initially, the chip (or wafer) is treated with sodium hydroxide to remove the Al oxide layer from the surface of Al pads. Then it is dipped in de-ionized water to clean and remove any remaining sodium hydroxide. This is followed by de-smutting to remove any remains of alloys on the surface of Al pads and electrodes. After obtaining a clean Al surface, the chip is treated with a zincate

solution for 45 seconds at 45° C to allow electroless deposition of zinc on to the Al electrode. Zinc deposition is normally carried out twice to get a smooth layer of zinc as it acts as a base layer for nickel deposition. This is followed by nickel deposition and Au deposition using their respective electroless solutions as described below at 90° C.

The second, less explored adhesive layer combination for electroless Au film deposition on Al involves deposition of palladium on Al pads by lift-off, followed by electroless deposition of Au after palladium activation [47]. The palladium layer is then activated. The activation is the process of reducing palladium to zero oxidation state which helps in the subsequent electroless deposition of Au on it. Palladium activation solution is prepared by using palladium salt, hydrochloric acid, poly(ethylene glycol) and methyl gallate. After the activation, the substrate is cleaned, dried and then ready for Au coating. Another alternative route employed electroless deposition of nickel as mentioned before. Nickel plating is followed by electroless deposition of palladium and Au film [48]. After obtaining Au film, Au nanostructures were grown on the electrodes. This is further discussed in section V-A.

B. Photolithography method for Au film deposition on Al electrodes

Another technique to deposit a Au film on an Al electrode is through photolithography. This involves chemical or physical vapor deposition of Au on the single chip or a full wafer through a mask followed by removal of photoresist by a chemical etchant. This method helps to obtain an adhesive coating of any metal layer on a substrate, however, it requires expensive instrumentation, trained technician to operate the machinery and the development of a mask to define the deposition pattern. Chromium and titanium have been commonly used as adhesive layers prior to Au deposition [49], [50]. Chromium has been used as adhesion layer because of its high affinity towards oxygen which helps to de-passivate many material surfaces.
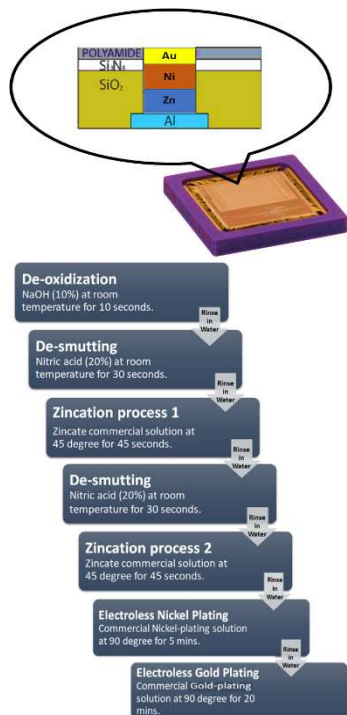
Fig. 3. Diagram of a Au coated pad on a CMOS chip. Schematic shows the steps of Au electroless deposition process via zinc/nickel route [46].

Table I
List of electrochemical sensors fabricated based on Au film coated on Al electrodes

Deposition Technique	adhesive layer	Analyte detected	Bioreceptor	Reference
Electroless	Zinc/Nickel	Potassium Ferricyanide	None	[45]
	Zinc/Nickel	HeLa cells	None*	[46]
	Palladium	DNA	DNA probe	[47]
Lift-off	titanium	DNA	DNA probe	[51]
	Chromium	Dopamine	None*	[52]

*Nanomaterial was used as bioreceptor

The deposition of chromium over the Al substrate is carried out using chemical vapor deposition. Titanium on the other hand, has been used as an adhesive layer for Au deposition because of its ability to form alloy with Au and providing a good base for the growth of Au films. It has been shown that a few nanometer thickness of titanium film is capable of providing a good ground for Au film growth [51]. The Au layer deposited using photolithography method provides better adhesion for post processing of the substrates due to high purity of the metals deposited [52]-[54]. The inert Au layer deposited have also been employed for electrochemical detection and Table I summarizes the electrochemical sensors fabricated based on Au films deposited on the working electrodes.

C. Pt film deposition on Al electrodes

This can be achieved using photolithography techniques with titanium as the adhesive layer [65], [66]. Unlike Au, there is no electro-less deposition technique in literature that has been employed for coating Al electrodes on CMOS substrates with Pt.

NANO-STRUCTURE DEPOSITION OVER ON-CHIP ELECTRODES

After deposition of an inert layer the nanomaterials can be immobilized on the surface. Alternatively, the Al electrode may be directly modification with nanomaterials. In sections V-A to V-F we review techniques for the deposition of nanostructures on Au or Pt coated electrodes or directly on Al surfaces. The nanostructures reported here based on the shortlisted articles are Au nanostructures, CNTs, Pt nanostructures, nano-polymers and metal-oxide/nitride nanoparticles.

A. Au nanostructure deposition on on-chip electrodes

Two main techniques have been used for the deposition of Au nanostructures on CMOS electrodes: (i) electrochemical deposition on Au coated electrode and (ii) templated electrochemical deposition on anodized Al oxide electrode.

Electrochemical deposition is a technique used to coat a conductive material on another metal through application of an electric current (galvanostatic) or a voltage (potentiation) using an electrolytic solution of the metal to be coated. This technique allows rapid deposition of metal atoms on the surface as well as the unique ability to selectively deposit a material on electrodes without needing a mask. Additionally, the amount of metal being deposited and its morphology can be altered by changing the electrolytic solution, deposition time and the amplitude of the applied voltage or currents to the electrode.

Any uneven surface charge or structural defects on the electrode leads to irregularities in the coating, limiting the controllability

Electrochemical deposition of Au nanostructures on Au-coated electrodes has been demonstrated in [48]. Au nanostructures were deposited over an electroless Au coated Al electrode using Au salt and hydrochloric acid as the electrolyte by applying various potentials (100 mV, 0 mV and -100 mV) for 125 seconds (results are seen in Fig. 4 (a)) . The electrode was then used to detect prostate cancer DNA using cyclic voltammetry technique. The addition of these nanomaterials was shown to lead to a 70% increase in the output signal as compared to plane Au as well as a faster response times. This can be attributed to the higher surface area and active sites on the surface of the nanostructure for immobilization of DNA probes to carry out DNA detection.

The templated electrochemical deposition of Au nanostructures directly over Al electrode surface using electrochemical deposition has been demonstrated by Olsen et al [56]. Here the electroplating of Au nanostructure is carried out over an anodized Al oxide layer. The anodized Al oxide on top of the
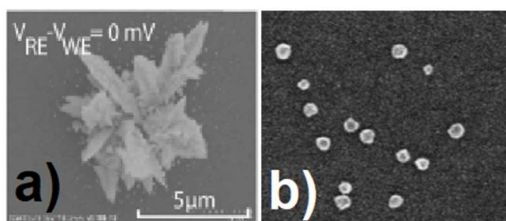
Fig. 4. SEM images of (a) Au Nanostructure grown on working electrodes at 0 mV potential, © [2014] IEEE [48], (b) Au nanoparticles deposited on Al electrode [56], Reprinted with permission from {J. Phys. Chem. B 2005, 109, 3, 1243–1250}. Copyright {2005} ACS.

Table II
Electrochemical sensors based on Au nanostructures deposited on Al or Au-coated electrodes

Base electrode material	Deposition Technique	Nanomaterial	Electrochemical deposition parameters	Analyte detected	Bioreceptor	Reference
Au	Electrochemical deposition	Au nanostructures	E= 0.1V, 0 V, -0.1V; T=125 secs; Electrolyte= Au salt and HCl acid	Prostate cancer DNA	DNA	[48]
Al	Templated electrochemical-deposition	Au nanoparticles	Anodized Al oxide = 4V DC; Electrolyte= Au solution sodium sulphate; CV= -0.7V to -1.3 V	Hexaamminerutheniu m(III) chloride	None*	[56]

*Nanomaterial was used as bioreceptor

Al electrode is obtained through the application of a high DC voltage (20-50 V) to the electrode when it is exposed to a mixture of phosphoric acid and chromic acid as electrolyte. Leading to the formation of a porous Al oxide structure [57]. One limitation of this method when applied to CMOS microchips is that such high voltages may cause irreversible damage to the electric circuits in the microchip. An alternative way to achieve an anodized Al oxide electrode using 4 V DC voltage has been shown in [58].

Once the anodized Al oxide structure is formed, the Au electroplating can be carried out using cyclic voltammetry technique (-0.7 to -1.3V) in a Au plating solution (Oromerse Part B) and sodium sulphate as the electrolyte [57]. During this process, the deposition of Au nanostructure occurs by formation of Au (I) sodium thiosulphate in the electrolyte solution, which is then reduced to deposit Au atoms on the electrode pores as seen in Fig. 4 (b). The electrodeposited Au nanoparticles led to increase in the surface area and conductivity of the electrode. Table II summarizes the fabricated sensors, bioreceptor element and analyte detected using the Au modified electrodes.

Prospects for CMOS integration: The methods described in this section provide parameters such as potential, time and electrochemical techniques employed for growth of Au nanostructures. These parameters can be used by the circuit designers to tailor the circuit in order to grow Au-nanostructures in-situ and/or on demand. The deposition parameters are highlighted in Table II.

The advantage of Au-nanostructures as electrode modifier is that they are biocompatible, increase the output signal due to more number of active sites and ease of bioconjugation with other bioreceptors such as DNA, enzymes and antibodies. The immobilization of the bioreceptors can be easily carried out via chemical means involving Au-S bonding, either using short thiol linkers or thiolated bioreceptor molecules.

B. Carbon Nanotubes (CNTs) Deposition on on-chip electrodes

CNTs are divided into two categories; single walled carbon nanotubes (SWCNTs) and multiwalled carbon nanotubes (MWCNTs). The SWCNTs are known for their conductivity which are dependent on the chirality whereas MWCNTs lose this property and possess better mechanical properties leading to more robust structure. CNTs have been deposited onto the CMOS based chips using two techniques: (i) micro-spotting and (ii) dip coating. In either ways, the deposition of CNTs onto the electrode surface requires them to be exfoliated in the solution to achieve proper immobilization. Exfoliation is the process of separating the agglomerated CNTs in the aqueous or other solution they are suspended in.

Microspotting - the micro-spotting technique is a contact-based method for transferring different material from solutions (with 50-80 μm diameters droplets) to solid surfaces using pins or capillaries using an instrument called a micro-spotter. This has been one of the widely used methods to deposit MWCNTs over Au coated electrodes on CMOS chips [53],[54],[59],[60]. The MWCNTs are first exfoliated in various solutions that are compatible with the spotting capillaries and then deposited on Au-coated electrodes. For example, MWCNTs were exfoliated

in an aqueous solution of nafion and ethanol which is micro-spotted on a Au electrode to detect various analytes [53],[54]. Another study used multi-working electrode chip was modified with nafion+ MWCNTs and medola's blue+ MWCNTs to detect dopamine and glutamate respectively [59],[60]. The solution of medola's blue and CNTs was prepared by mixing chitosan and meldola's blue (acting as a redox mediator to increase the output response) to exfoliate MWCNTs and was coated on Au-plated electrodes. This was followed my immobilization of glutamate oxidase on the deposited MWCNT to carry out glutamate detection [59],[60]. Nafion and chitosan have been used here because of their high viscosity and ability to stick to the capillaries of the spotter needle as well as to the surface of electrodes. Further, molecules like nafion, chitosan and meldola's blue also increase the selectivity of the modified electrode surface due to the presence of functional groups such as hydroxyl and amines. Incorporation of MWCNTs in the sensing platforms has been shown to lead to a lower noise and larger current range of the sensing compared to the other sensors mentioned in these studies [59],[60].

Dip coating- this method involves dipping of the substrate in a CNT solution and slowly removing it from the solution to get a CNT coated electrode. Although the technique does not provide a selective coating of CNTs on the electrode, it is a relatively low-cost technique.

Dip coating has been used to coat SWCNTs decorated with palladium on arrays of Au plated Al oxide electrodes to detect hydrogen [61]. SWCNTs were dispersed in a solution of 1,2-dichlorobenzene and substrate was dipped and pulled out of the solution at the rate of 3 mm/min. This solvent was used for SWCNTs solution because solvents get adsorbed on the surface of SWCNTs which helps them to separate each nanotube and form a well dispersed solution [62]. Additionally, the palladium-decorated-SWCNTs provided more catalytic sites in form of palladium, as well as rapid electron transport due to SWCNTs, which lead to fabrication of highly efficient receptor-less sensing electrode for hydrogen detection. Finally, Table III covers the fabricated sensors and analyte detected using the CNTs modified electrodes.

Prospects for CMOS integration: The methods that have so far been employed to deposit CNTs over the electrodes are contact-based incubations techniques, such as micro-spotting and dip coating, which make use of the chemical interactions between the electrode surface and CNT deposition solution. Both Pristine and modified CNTs can be deposited on CMOS electrodes using such techniques.
CNTs can be modified in two ways to achieve selective sensing: (i) modification/functionalization of CNTs before depositing over electrodes. CNTs can be modified/functionalized with a wide variety of organic and inorganic materials before carrying out deposition [63,64]. These modified CNTs can be deposited over the electrodes using contact-based techniques such as micro-spotting and dip coating.
(ii) Post-deposition modifications with polymers and metal nanoparticles. The method involves electrochemical deposition of metal nanoparticles and/or polymeric films to achieve tailored properties [65]. The main advantage of electrochemical deposition over contact-based is better adhesion of nanomaterials with the electrode resulting in a more robust modified electrode.

C. Pt Nanostructures deposition

Pt nanostructures can be synthesized in the form of nanoparticles, nano-rods, thin film or even porous 3-D structures and introduced to the sensing electrode. The deposition of Pt nanostructures on Pt coated and Al oxide electrodes have been carried out using either electrochemical deposition [66],[67] or template-based growth [68,69].

Electrochemical deposition of Pt nanoparticles is carried out using an electrochemical setup which utilizes Pt salt as electrolyte for deposition. Electrochemical deposition can be carried out using techniques such as linear sweep voltammetry (LSV) which works by employing a voltage sweep across a selected voltage window leading to reduction the metal ions in the electrolyte solution and its deposition on the electrode. The deposition of Pt nanostructures directly on Al pads has been achieved using sulphuric acid and Hexachloroplatinic (IV) acid as the electrolyte solution and LSV (with potential window of 0 V to 1 V with respect to Ag/AgCl reference electrode) resulting in spherical Pt nanoparticles as seen in Fig. 5(b) [66]. In another example, Pt nanoparticles were electrochemically deposited over Pt electrode by application of a working potential of -1.2 V as shown in Fig. 5 (c) [67]. The addition of Pt nanostructures increased the active surface area of the working electrode and also led to bioreceptor-less detection of redox active analyte [66],[67].

The template-based method utilizes templates to form a nano-porous structure in the Pt being deposited on the surface. Generally, the template structure is selected such that it is easy to remove after obtaining the nanostructures. To carry out electrochemical deposition of nano porous Pt film on Pt electrodes, a solution of octaethylene glycol monohexadecyl ether (OGME) (surfactant) and hexachloroplatinic acid hydrate was used as the electrolyte. Here, OGME was used as a template to achieve desired morphology for the

Table III
Electrochemical sensors based on CNT deposited on electrodes

Base electrode material	Deposition Technique	Nanomaterial	Analyte detected	Bioreceptor	Reference
Au	Micro-spotting	Nafion-MWCNTs	Glucose, lactate, glutamate	Enzymes	[53]
Au		Nafion-MWCNTs	Glucose, lactate, glutamate	Enzymes	[54]
Au		meldola's blue+MWCNT, Nafion+CNTs	Glutamate, dopamine	Enzymes	[59]
Au		meldola's blue+MWCNT, Nafion+CNTs	Glutamate, dopamine	Enzymes	[60]
Al	Dip coating	Pd-decorated SWCNTs	Hydrogen	None*	[61]

*Nanomaterial was used as bioreceptor

Table IV
Electrochemical sensors based on Pt nanomaterials deposited on working electrodes

Base electrode material	Deposition Technique	Nanomaterial	Electrochemical deposition parameters	Analyte detected	Bioreceptor	Reference
Al	Electrochemical-deposition	Pt nanostructures	LSV: 0-1V electrolyte : Sulphuric acid and hexachloroplatinic (IV) acid	Hydrogen peroxide	None*	[66]
Pt		Pt nanoparticles	Potential: -1.2V electrolyte : Sulphuric acid and hexachloroplatinic (IV) acid	γ-aminobutyric acid and glutamate	None*	[67]
Pt	Templated electrochemical-deposition	Nano-porous Pt film	Potential: -0.12 V electrolyte : Sulphuric acid and hexachloroplatinic (IV) acid	Glucose	None*	[68]
Pt		Nano-porous Pt film		Glucose	None*	[69]

*Nanomaterial was used as bioreceptor

electrodeposited Pt and hexachloroplatinic acid (H_2PtCl_6) was used as the Pt source for Pt deposition [68], [69]. The electrochemical deposition was carried out by applying a constant potential of -0.12 V vs. Ag/AgCl as shown in Fig. 5 (a). and a nano porous Pt plate was fabricated. Finally, Table IV covers the fabricated sensors and analyte detected using the Pt modified electrodes.

Prospects for CMOS integration: The electrochemical parameters for the deposition of Pt nanostructures can be incorporated in underlying electrical circuits on CMOS microchip to deposit Pt nanostructures in-situ and on-demand
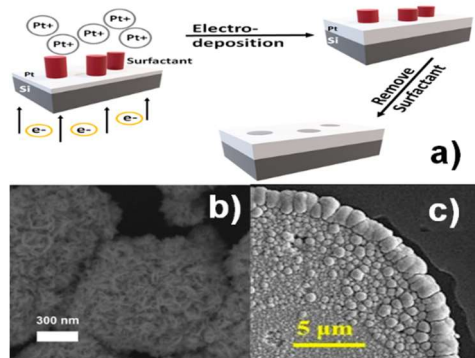
Fig. 5. (a) Fabrication of nano-hole arrayed Pt electrode in silicon substrate. Adapted from [68] (b) SEM of electrodeposited Pt nanostructures,© [2017] IEEE, [66], (c) SEM of Pt nanostructures on Pt electrode, © [2018] IEEE, [67].

over the on-chip electrodes without any external instrumentation.

Pt nanostructures, like Au nanostructures, have high conductivity and high surface to volume ratio which enhances the output electrochemical response of the system. Pt is more electrochemically stable and does not get etched easily by common chemicals typically used in electrochemical experiments such as sulphuric acid and redox couple like potassium ferrocyanide/ferricyanide. It also provides an enzymatic reaction towards compounds such as hydrogen peroxide. The disadvantage of Pt nanostructures is that immobilization of bioreceptors over them is not as convenient as compared to Au. Pt nanoparticles have been used as polymeric composites to deposit bioreceptors such as enzymes and antibodies [70].

Further, the aforementioned electrochemical deposition methods also make it possible to deposit Pt nanostructures over other nanomaterial (such as CNTs) coated electrodes. This can be used to improve the performance of their sensor as Pt nanostructures help in further enhancing the conductivity and surface area of the electrode.

D. Polymer deposition

In this section, we give an overview of polymer-based nanostructures in the form of hydrogels, conducting polymers, self-assembled monolayers (SAM) and three associated techniques for depositing polymeric nano-structures over Au or Pt electrodes. Such techniques although not directly developed on Al electrodes, are deemed to be compatible for application on Al electrodes after the Al surface is coated with Au or Pt following the techniques presented in section IV.

The first method for immobilizing hydrogels on substrate is the physical adsorption. This method uses forces such as van-der-wall interactions, hydrogen-bonding to adsorb a material on a substrate. Hydrogels have nano-porous structures which are synthesized by combination of various natural and synthetic polymers with interpenetrating networks. Hydrogels have been employed in various sensing and diagnostic applications [71]. For example, a hydrogel cross-linked with glucose oxidase enzyme was physically adsorbed on a Pt coated electrode on the CMOS chip as seen in Fig. 6 (a) for glucose detection [72],[73].

The second method employed for coating a polymeric film is electro-polymerization. It is a method of obtaining a polymer film on a substrate by applying a constant current or carrying out potential sweeps across a certain voltage range while exposing the electrode to an electrolyte that contains the monomer solution. This process allows controlling the thickness of the film coated on the substrate by controlling the number of scans or current applied.

For example, m-Phenylenediamine was electropolymerized over a Au coated electrode by performing CV across a potential window of 0.2V- 0.7V at a scan rate of 0.05 V/sec [74]. Then glutamate oxidase was immobilized on the electropolymerized electrode to carry out glutamate detection. This polymer layer was shown to help in reducing the unwanted interference from other molecules.

In another example of electropolymerization, conducting polymers have also been electropolymerized over working electrodes. These are polymer that can conduct electricity and have been extensively used for electrochemical applications

Table V
Electrochemical sensors based on polymers deposited on working electrodes

Base electrode material	Deposition Technique	Nanomaterial	Electrochemical deposition parameters	Analyte detected	Bioreceptor	Reference
Pt	physical adsorption	Hydrogel	-	Glucose	Enzyme	[72]
Pt	physical adsorption	Hydrogel	-	Glucose	Enzyme	[73]
Au	Electro-polymerization	m-Phenylenediamine	CV:0.2 - 0.7V, t=15min, electrolyte: m-Phenylenediamine in PBS	Glutamate	Enzyme	[74]
Pt	Electro-polymerization	polypyrrole	Potential: 0.85 V, t=800 secs, electrolyte: pyrrole in PBS	Glucose	Enzyme	[76]
Au	Sulphide bonding for SAM growth	SAMs (thioglycolic acid)	-	Glutamate	Enzyme	[79]

due to their selectivity and conducting nature [75]. The ease of electro-polymerization on various electrode surfaces makes conducting polymers a promising candidate for electrochemical applications. For example, polypyrrole was electropolymerized on a Pt electrode using pyrrole as the monomer as seen in Fig. 6 (b) [76]. The electrode was further immobilized with ferrocene labeled glutamate oxidase enzyme to carry glutamate detection.

The SAM is formed by self-assembly of a single layer of surface active material on a substrate. These are produced by spontaneous chemical interaction of the molecules with the substrate at the interface leading to a 2-D layer of molecular assembly [77]. One of the most extensively used SAMs in electrochemical sensing applications are thiols on Au electrodes. It is observed that sulphur (S) adsorbs onto the Au (Au) surface forming an Au-S bond via oxidation-reduction reaction, resulting in a SAM of thiol molecules [78]. following this technique, a glucose sensor was fabricated by growing SAM of thioglycolic acid on Au electrodes, followed by immobilization of glucose oxidase [79]. The advantage of using SAMs is the ease of coating due to self-assemble nature of the films, no external source is required to form the layer and secondly it makes attachment of any other biorecognition element over the electrode easier. Table V summarizes these polymeric nanomaterials coated CMOS based electrochemical detection systems.
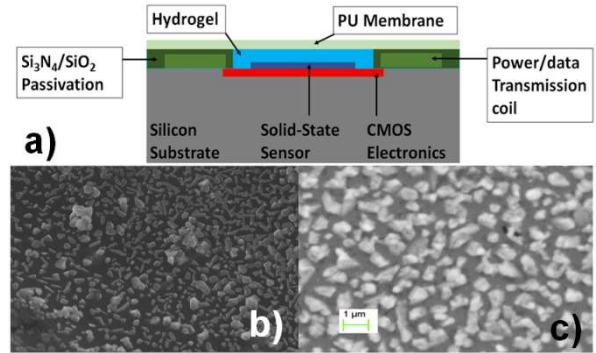
Fig. 6. (a) CMOS chip layout for electrochemical glucose detection, Adapted from [72] (b) SEM image of polypyrrole coating with enzyme immobilized, © [2015] IEEE, [76] (c) SEM image of protein matrix on the electrode, © [2010] IEEE, [79].

Prospects for CMOS integration: The polymers can be electropolymerized over electrodes allowing controllability and potential for in-situ and on-demand electrode modification (similar to the Au and Pt nanostructuring techniques).
Apart from the aforementioned polymeric materials, polymers such as aerogels, conducting polymers like polyaniline and self-assembled monolayers such as thiols and silanes can also be employed for electrochemical sensing applications. Conducting polymer can be synthesized with various structures and surface functional groups tailored to application. For example, co-electropolymerization of pyrrole and aniline was carried out for electrochemical applications [80]. In addition, the presence of functional groups eases the immobilization of bioreceptors to the polymer coated electrodes because it eliminates the requirement of any linkers as in case of metallic nanomaterials. On the other hand, thiol based SAMs with varying lengths are extensively used for immobilization of bioreceptors on gold surfaces [81]. These are terminated with various functional groups such as amine, biotin-streptavidin which help to immobilize bioreceptors via covalent or non-covalent interactions.

E. Metal oxide/nitride nanomaterials deposition
The main techniques that have been employed in literature to deposit metal oxide/nitride nanomaterials over Au-coated Al electrodes are (i) hydrothermal growth (ii) dip pen nanolithography, and (iii) lift-off.
Hydrothermal method employs growth of nanomaterials under controlled temperature and pressure conditions. The morphology and crystalline structure of the nanoparticles can be controlled through controlling the environmental parameters. The method is generally carried out in a hydrothermal autoclave setup where all the precursors are mixed, closed tightly and kept at high temperatures. For example, ZnO nanowires were grown over Au-plated Al electrodes through hydrothermal route to make an ethanol sensor [82]. Here, a ZnO seed layer was first sputtered on the electrode before it was placed in the hydrothermal setup containing zinc nitrate hexahydrate and hexamethylenetetramine at 90°C for 2 hours. This led to a well oriented growth of ZnO nanowires on the substrate as shown in Fig. 7 (a).
Dip pen nanolithography is a unique method of scanning probe lithography which makes deposition of various materials on

different patterns possible with sub-micron resolution. This technique can be used to deposit nanomaterials on an array of electrodes on CMOS chips. For example, ZnO nanorods (fig. 7 (b)) were deposited on Au coated electrodes to develop an ethanol sensor [83]. Here, ZnO nanorods were synthesized via wet chemical method and were mixed with terpineol to form a slurry (ZnO-95%, terpineol-5%). This was loaded in the cantilever tips and deposited on the electrodes with each drop volume ~10 pL per deposition. In another example, Au-tin oxide (Au-SnO$_2$) nanocomposite were synthesized (via wet chemical method) and deposited on Au coated electrodes on CMOS chip for ethanol detection [84]. These metal-oxide nanoparticle provide higher electroactive surface areas and allow a bioreceptor-less detection of analyte.

In another example, 3D titanium nitride based nanoelectrode array were deposited on Al electrode using the photolithography method for electrochemical detection of hydrogen peroxide [85]. The 3-D nanoarray of titanium oxide provided high chemical stability and the nano-electrodes behaved like cylindrical electrodes which led to higher current density as compared to the conventional rectangular microelectrodes. The focused ion beam SEM image for the 3-D nanoelectrodes is shown in the Fig. 7 (d). Another example employed electrochemical deposition of palladium nanostructures as shown in Fig. 7 (e), on Au-coated electrodes using palladium chloride and hydrochloric acid as the electrolyte by applying a constant potential (0 mV, -100 mV, -250 mV) for 150 seconds [86]. Finally, Table VI summarizes these metal/oxide nitride nanomaterials based sensors developed on Au coated electrodes.

Prospects for CMOS integration: The synthesis of composite nanomaterials such as ZnO, Au-SnO$_2$ with desired morphologies requires special conditions such as high temperature and/or via wet chemical synthesis (WCS) which may not be CMOS compatible. Such nanomaterials can be grown on top of electrodes via the bottom-up approach through
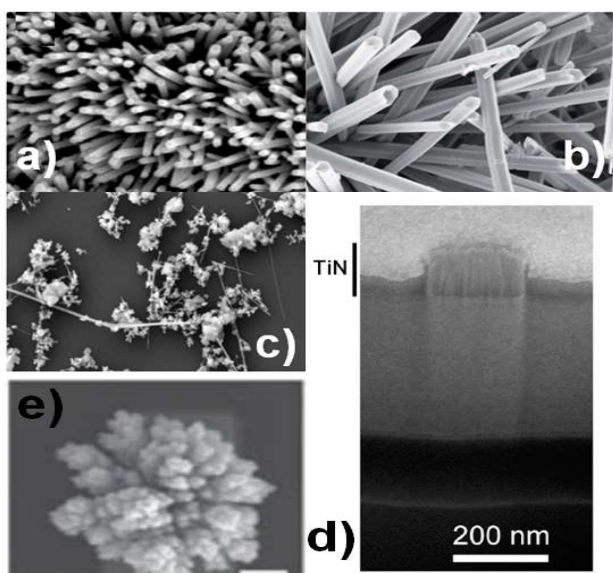
Table VI
Electrochemical sensors based on metal oxide/nitride deposited on working electrodes

Conductive electrode material	Deposition Technique	Nanomaterials	Analyte detected	Bioreceptor	Reference
Au	Hydrothermal Method	ZnO nanowires	Ethanol	None*	[82]
Au	Dip-pen lithography	ZnO nanorods	Ethanol	None*	[83]
Au		Au-SnO$_2$	Ethanol	None*	[84]
Au	Lift-off	3-D TiN nano array	Hydrogen peroxide	None*	[85]
Au	Electrochemical deposition	Palladium nanostructures	DNA copies	DNA probes	[86]

*Nanomaterial used as bioreceptor

WCS or they can be grown separately and then be deposited using other methods such as dep-pen nanolithography. Dip-pen nanolithography (DPN) The as it is based on physical adsorption, is a straightforward technique for deposition of hydrogels on CMOS. The DPN has been used to deposit various nanocomposite materials such as metal nanoparticles, CNTs, hydrogels and metal organic frameworks [87,88].

The lift-off technique, though well-established, requires customized masks for each deposition pattern and is limited to metallic materials. Therefore, it does not provide much flexibility to deposit a wide variety of nanomaterials as compared to other methods mentioned before.

SUMMARY AND CONCLUSION

An overview of nanomaterial deposition techniques for surface modification of microelectrodes made of Al, Pt-coated Al, or Au-coated Al, suitable for adoption in CMOS biosensors were given.

The techniques available in literature for the deposition of nanomaterials such as Au, Pt, CNTs, nano-polymers, and metal oxide/nitride nanomaterials on such surfaces have been reviewed with a focus on techniques that are CMOS-compatible. The modified electrode surfaces were either directly used for electro-catalytic detection or modified with DNA probes, enzymes to carry out sensing of biological entities such as cells, metabolites and DNA. A list of nanomaterials discussed in this review along with the general deposition technique along with their major advantages and disadvantages are summarized in Table VII.

It should be noted that there is only limited information in literature on the stability, life-time and reproducibility of the proposed nanomaterial deposition techniques even though these are key metrics in achieving a robust and reliable sensing platform.

Finally, although a variety nanomaterials have been explored and deposited on microelectrodes using CMOS-compatible techniques (as listed above), these are far fewer than the number

Fig. 7 SEM image of a) Hydrothermally grown ZnO nanowires [76], b) ZnO nanorods deposited on chip [77], c) Au-SnO$_2$ nanoparticles [78]. d) Focused ion beam SEM image of cross section view of a single TiN nanoelectrode. [79] e) Pd nanostructure on Au electrode [80].

Table VII
Nanomaterials and their deposition techniques covered in this review

S. No	Nano-Material	Deposition Techniques	Advantages	Disadvantages
1	Au	Electrochemical deposition	Cost effective, selective coating and thickness can be controlled.	Can be carried out only on selective substrates.
2	CNTs (SWCNTs, MWCNTs)	Micro-spotting/spotting	(i) Can be carried out on a chip with multiple electrodes for selective coating.	(i) The materials to be coated should be compatible with the spotter needle.
		Dip coating	(ii) Simple and rapid coating of multiple electrodes possible.	(ii) Not possible to carry out selective coating.
3	Pt	Electrochemical deposition	(i) Cost effective, selective coating and thickness can be controlled.	(i) Only can be carried out on selective substrates.
		Template based electrochemical deposition	(ii) Growth of controlled nanostructures with desired morphology.	(ii) Limited templates and templates cannot be grown on all substrates.
4	Polymers (hydrogel, polypyrrol, m-Phenylenediamine, SAMs)	Physical adsorption	(i) No large instrumentation required and rapid deposition.	(i) Weak adhesion of the film.
		Electro-polymerization	(ii) Rapid, selective coating and size of film can be controlled.	(ii) Requires external stimulus to coat the film.
		Self-assembled monolayers	(iii) Strong adhesive film deposition without any external stimulus.	(iii) Limited to selective surfaces such as Au.
5	Metal oxide/nitride (ZnO, Au-SnO$_2$, TiN)	Photolithography	(i) Strong adhesive film, can be deposited on variety of substrates.	(i) Large instrumentation required and complicated mask preparation.
		Dip pen nanolithography	(ii) Possible to coat multiple micro/nano sized electrodes with different materials on the same chip.	(ii) The material to be coated should be compatible with capillary of the instrument.
		Hydrothermal	(iii) Crystalline structure and desired orientation of nanomaterials obtained.	(iii) Can require high temperatures for growth of nanomaterials.

of nanomaterials that have been explored/deposited on macroelectrodes such as glassy carbon electrodes, paper based substrates, and glass substrates. Some of the techniques discussed in this review (e.g. spotting, electrochemical deposition, template based growth, incubation, and dip-pen nanolithography) can potentially be used for CMOS-compatible deposition of other nanomaterials and nanocomposites on microelectrodes as well, albeit following optimization of deposition parameters and chemical components involved.

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