Nanofabrication Techniques for Wireless, Real-Time Fully Integrated Sensing Platforms

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ABSTRACT

Designing small scale integrated systems for sensing and actuation has gained lots of interest in recent years. Currently, subsystems are fabricated separately and then bonded together to form an integrated platform. This poses a fundamental limit on the size and design of such systems and also on their longevity and performance. Here, we present methods of designing and fabricating such systems using standard fabrication techniques on standard electronic substrates to result in very small, fully integrated systems. These techniques provide a set of tool to convert such electronic systems into complete sensing/actuation platforms which can then be used for many different applications. Furthermore, the CMOS-compatibility of these techniques makes it possible to integrate these processes in commercial CMOS foundries to reduce the complexity and hence cost of fabricating such systems. Finally, we will show results of sensing using the devices fabricated with these techniques.

Keywords: Real-Time, Integrated, Wireless, Nanofabrication, CMOS compatible

1 INTRODUCTION

Fully wireless implantable sensors have the potential to revolutionize health care problems. These systems can be used by both the patients and the health care providers and can be effective in plenty of health care situations [1]. By taking advantage of the secure data communication networks already present, these systems can form a global network of health care.

Significant effort has been made in designing these systems. However, there are some very challenging issues towards this end. For example, the main problem has been biocompatibility due to the large size of the devices. This creates a substantial damage to the body after implantation resulting in biofouling and scar tissue formation [1] and finally the rejection of the foreign body by a complex foreign body response.

Micro/Nano scale structuring of electrodes has been used in sensing and energy storage for quite some time. Such structuring of electrodes can provide high output signal and enhanced selectivity. However, the techniques employed for their fabrication are typically bottom-up growth which compromises control of their properties and robustness, leading to uncontrolled variation in electrode properties if their size is small. Also, the methods of fabricating these electrodes are not compatible with current CMOS technologies and need specialized post-processing and extra on/off chip circuitry and equipment leading to low yield and high costs and a high lower bound on the system size.

Real-time operation of sensors is very critical for many applications where immediate action should be taken to avoid complexities. For example, fast response sensors are very important for preventing hypoglycemic complexities and for long term hyperglycemic damages between glucose readings taken using discrete (e.g. finger pricking) methods. A miniaturized sensor with very thin layers (which are needed to control response of the sensor), with minimal scar tissue around it and with direct access to filtered blood can provide very fast real-time results in similar situations.

It has been proposed that miniaturizing these sensors and controlling their interface with the body are key steps towards making these devices very close to practical applications. The small size (few hundred microns in the largest dimension) has many advantages including minimal implantation damage and foreign body response, and ease of implantation and ex-plantation. Top-Down Micro/Nano technologies are very promising to achieve these key objectives. In the next sections, we will show how this can be done with modern fabrication techniques.

2 SYSTEM DESIGN

A completely wireless system is needed to avoid the risk of infection and damage involved in the currently used tethered systems. Due to the small size, such systems can't use large batteries and hence need to generate their own power on-chip. This can be achieved by making on-chip Photovoltaic cells which generate power from an external light source. Communication with external reader is also done optically using a vertical cavity surface emitting laser (VCSEL), integrated with the system. These optical components have very small footprints. Control and signal processing circuitry is also required to control the on-chip sensor and to coordinate the operation of whole system. This is designed using CMOS process (TSMC 0.25um offered through MOSIS) which can make very small and robust devices made of mostly biocompatible materials.

Our system has all of these subsystems integrated on-chip, as shown in figure 1. The main focus of this paper is

the on-chip integrated electrochemical sensor and the interface with the body.

2.1 Sensor Design

The proposed electrochemical sensor consists of on-chip electrodes, all or some of which can be patterned at micro/nano scale to improve their performance. It is important to use minimum on-chip area for these electrodes to keep the cost low and overall device size small. The number of electrodes is decided based upon system requirements. Three electrodes design is more stable due to separate reference (RE) and counter electrode (CE) and hence minimal ohmic (iR) losses between RE and Working Electrode (WE).

The parameters of micro/nano patterning (e.g. depth/height of electrodes) depend upon the specie being sensed, the environment, sensor size etc. and are optimized through a parametric sweep simulation.

2.2 Interface with the body

The other novel feature in this system is the way these devices interact with the body, which is similar to the way different subsystems in the body interface with each other. The technique is to grow a system of vessels through the devices that will exchange the constituents of blood with the sensing system through capillary wall diffusion [2]. Hence, the foreign body response only needs to be suppressed for the initial growth period of these capillaries (by using thin biocompatible layers which eventually break down in any system) and by local release of drugs which further suppresses such responses. Once the capillary bed has grown, the sensor has its integrated interface with the body and hence its performance does not depend upon the thickness of scar tissue and other encapsulations.

3 FABRICATION

Fabrication of these systems involves both micro and nano fabrication techniques on CMOS and other platforms which already have electronic or other functional units on the same substrate. Hence, all processes need to be done taking care of no to expose the substrate to some harsh (e.g. high temperature) processing steps. Our chosen techniques are described now.

3.1 Lithography

Lithography on such substrates is challenging owing to their typically small size (100's of microns range). One solution is to get a bigger overall die size and do the photolithography on it for post-processing. Backside mechanical/chemical polishing is then used to thin these down and then these can be scribed and broken into individual devices. Scribe lines can be defined in the CMOS process by using the pad layer without having any structure underneath. This exposes the CMOS substrate which can then be scribed easily. If this is not an option, a handling wafer can also be used. We have also used this technique successfully. However, this requires very careful bonding and deboning of the actual die to the handling wafer to get reliable lithography results later on.

Photolithography is done using both positive (S1813) and negative (AZ5214E) resists using an MA6 mask aligner. Lift-off resist (LOR10A) is used with positive resist for effective lift-off, whenever needed. Electron-beam lithography is done using PMMA 950A4 resist in a Leica EBPG 5000+ system.

The circuit is also insulated lithographically by patterning some stable insulator (e.g. SU8 or Polyimide) to create isolation on other parts of the circuit. This also helps create wells (to hold the functionalization chemistry near the sensors) for functionalization of the sensor later on.

3.2 Etching

Dry plasma etching is used for micro/nano patterning on such substrates.

Hard alumina mask is used for fabricating patterned sensor at nanoscale. Dry etching using near room temperature (15^{o}C) pseudobosch etch (utilizing a mixture of SF6 and C4F8 plasma) in 380 etcher is used to get high aspect ratio structures in Si [3], shown in figure 2. For etching Aluminum pads on a CMOS substrate, a Unaxis RIE based system utilizing a mixture of Boron Trichloride (BCl_3), Chlorine (Cl_2) and $CHCl_3$ plasma is used, with parameters optimized for almost vertical sidewalls, as shown in figure 3.

For micron scale features, the resist (S1813) itself is used as etch mask. Low temperature (-130C) etch using oxford instruments 380 etcher utilizing an ICP-RIE plasma with a combination of SF6 and O2 gases is used. Top metal Pads in most of the CMOS processes are made of Aluminum. Weak hydroxide solutions (e.g. TMAH) are used to pattern CMOS pads at micro scale. Micro resist's ma-N resist is used as etch mask in this case. Negative resist and lift-off were used to get hard alumina mask for fabricating through the devices holes for the sensor interface with the body. Cryo etching was used to etch the holes, as shown in figure 4. Etch parameters were adjusted to get substantial etching as the holes become deeper.

3.2 Surface Treatment by Plasma

Surface oxidation is required to isolate underlying material (e.g. Si, Al) to coat the electrodes with a more suitable material (e.g. Pt) and/or to make multiple electrodes. Normally this is done by thermal oxidation. Another method is to use low temperature oxygen plasma. For integrated substrates like CMOS, this can be done at much lower temperatures and can result in good quality films without damaging other components. Oxygen plasma is also used to de-scum the resist layers before depositing

next material layer. Plasma treatment can also be used to do surface reactions in a clean manner. For example, Ag electrodes are exposed to chlorine plasma to convert the top layer into AgCl. This avoids the need of any wet processing for reference electrode formation which becomes hard and non-repeatable at such small scales.

3.3 Deposition

Electron-beam evaporation, thermal evaporation and sputtering are used to deposit the sensor materials (Pt, Ag) on the electrodes. Alumina is used to insulate electrode surface before any deposition. This also avoids interference/corrosion between any exposed metal areas and deposited electrode material.

Focused ion beam assisted deposition has also been used to deposit Pt on selective areas (e.g. sensors). This Pt, although in general considered to be less pure than Pt deposited by other methods, did show a very clean layer as verified by X-ray analysis in an FEI Sirion microscope, as shown in figure 5. Hence, it can also be used as sensing electrode material. We also coated nano patterned electrodes with this method and the resulting coating seems pretty conformal (figure 6), although not as good as sputtered one. However, this shows that this scheme can be used, at least, for fast prototyping of these sensors.

Sputter coating was done in an Argon Plasma under high pressures (around 20mT) to get thin conformal layers of Pt or Gold on nano patterned electrodes with a thin layer of Ti (10nm) as adhesion layer, as shown in figure 7.

3.4 Functionalization

In situ functionalization techniques are best suited for such small systems and are done using some multifunctional coating material. For example for glucose sensing, glucose oxidase mixed in bovine serum albumin hydrogel is pipetted on the electrodes and the mixture is gelled at room temperature for about 15 minutes. The sensor is then rinsed in water and is optionally cleaned in oxygen plasma, using a stencil mask. Electrochemical polymerization is another method in which the enzyme is mixed in the monomer solution (e.g. pyrrole) and gets incorporated in the polymer (poly-pyrrole) layer. For nucleic acid functionalization, sensors are soaked in the right solution in a beaker for some definite time period (few hours).For capillary growth, the required chemistry (described in [2]) is included in the hydrogel which is used to coat the holes array in a similar manner

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4 RESULTS

Electrochemical testing of the sensors was performed by using a CH Instruments CHI 7051D Potentiostat/an on-chip CMOS Potentiostat. Electrodes were either immersed in the solution or small droplets were pipetted on these.

Nano patterned sensors provided very promising results and outperformed their planar counter parts in all the tests. As one particular example, Nanopatterened sensors provided high sensitivity towards glucose detection even at 100um^2 electrode size, as shown in figure 8 whereas the planar electrode had very small signal (data not shown). Finally, the CMOS circuits were tested before and after all the processing and the circuits were still working fine and hence these techniques are nondestructive to other sub-systems in the integrated platform.

5 CONCLUSION

This work showed the feasibility of using large scale fabrication techniques to solve the challenges of integrated electrochemical sensor design and interfacing it with the body, at micro and nano scale. We showed that these techniques can be easily adapted so as to achieve the goals for sensor optimization without damaging rest of the components of the system.

6 ACKNOWLEDGMENT

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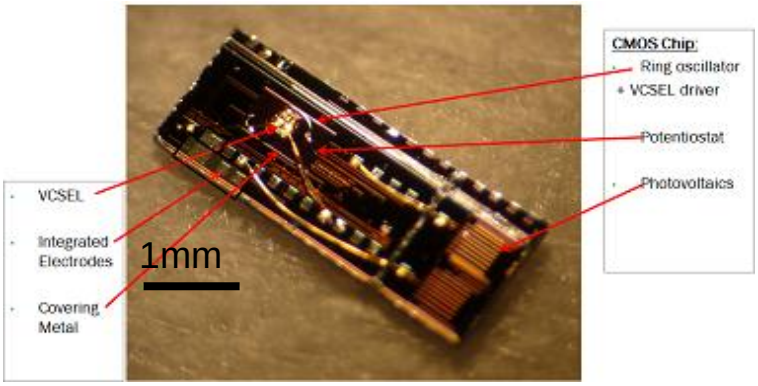
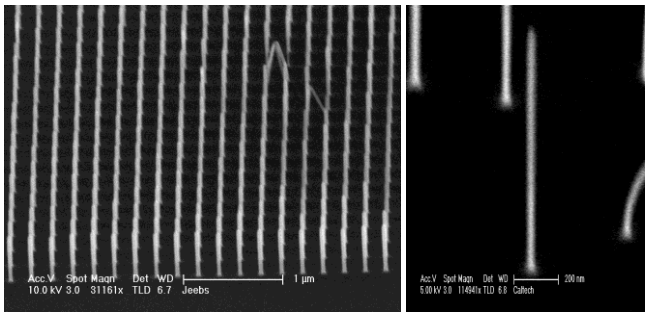


Figure 1: Picture of the Integrated System containing all subsystems, and wiring with test (bonding) Pads



(a) *(b)*

Figure 2: Nano pillars etched in Si Substrate (a) Pillar array (b) Sparse Pillars

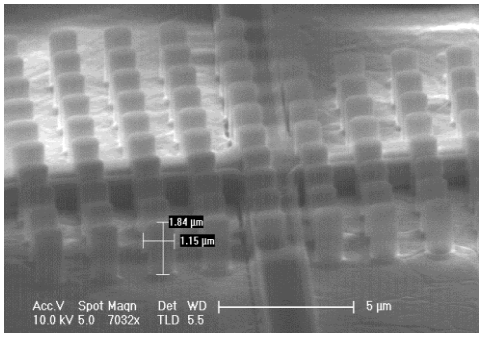


Figure 3: Nano pillars etched in CMOS Aluminum Pad

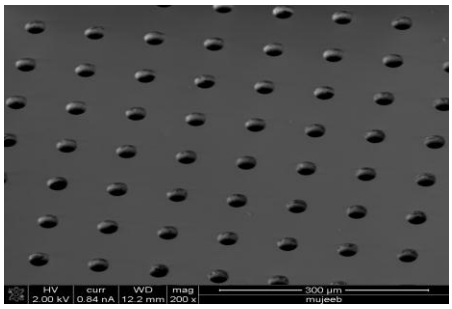


Figure 4: Through holes etched for capillary growth

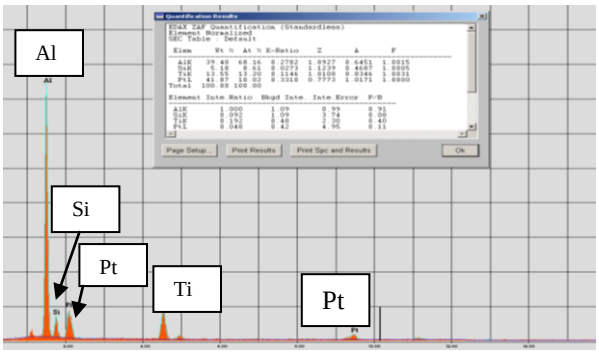


Figure 5: Spectroscopic analysis of FIB deposited Pt thin film on CMOS Aluminum Pads

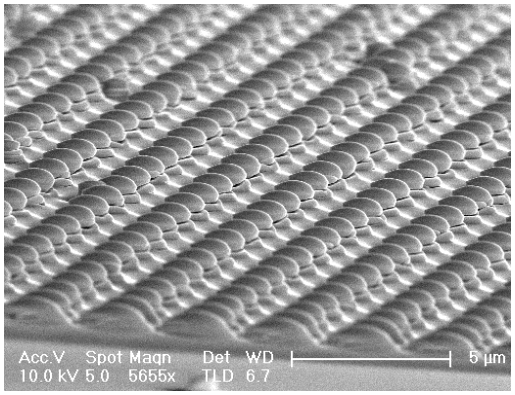


Figure 6: Nano pillars after FIB deposition of 100nm Pt

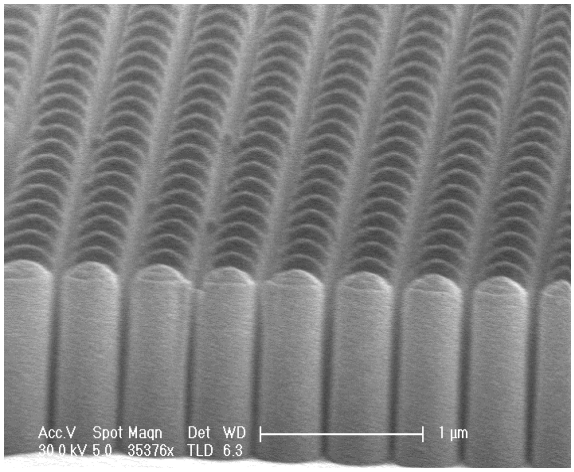


Figure 7: Gold Sputtered Nano pillars

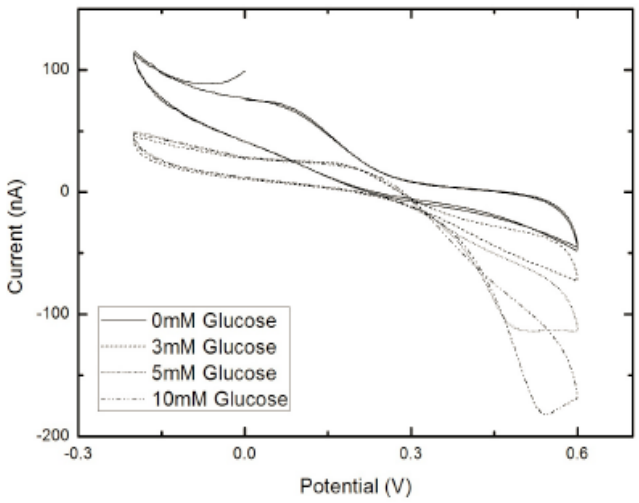


Figure 6: Glucose Sensing Results (in vitro) using Glucose Oxidase immobilization on a 100um^2 Pt electrode

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