Fabrication process and Performance analysis of Ion Sensitive Field Effect transistor Sensor (ISFET)

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By

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CERTIFICATE

This is to certify that the work entitled, “***Fabrication process and Performance analysis of Ion Sensitive Field Effect transistor Sensor (ISFET)***” submitted by ***Subhash Chandra*** in partial fulfillment for the award of degree of ***Master of Technology* in *Electronics and Communication Engineering*, Jaypee University of Information Technology, Solan**, has been carried out under my supervision. This work has not been submitted partially or wholly to any other University or Institute for the award of this or any other degree or diploma.

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ABSTRACT

Life science, healthcare and in the field of chemical science, detection and quantification of different chemical and biological species is a matter of central interests from the last many decades. It is required for the diagnosis of the disease, detection of dangerous and lethal epidemics, and detection of toxic gases in mines and in many other applications. However the direct and real time detection was the need in those areas. Solid state device sensors that basically comprise of semiconductor materials comes with a revolution in the field of biosensors. With lot of collective research work of physical science researchers and biomedical community these semiconductors sensors passed a lot many milestones in the way of selectively sensing the molecules and other chemical ions.

The use of Nanowire in these semiconductor sensors has made them capable of ultra-sensitive direct electrical detection, So these device became capable of detecting a very smaller concentration of target molecules in Femtomolar range. However they are still lagging in the sensitivity issues from the conventional label based detection with the sensitivity in Attomolar range. So here in this work we are going to present the two fabrication approaches of the Nanowire sensor i.e. top down and bottom up, with the detailed silicon nanowire growth method and use of that nanowire in the overall device fabrication. Then the sensitivity issues related with the geometries of the different sensors is analyzed with main focus on the nanowire cylindrical sensors, with this analysis we have tried to find the limitation of these nanowire sensors.

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Dated: (Subhash Chandra)

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Introduction

2.1 Motivation

As the man is moving faster in technological advancements, he is making the machines more artificially intelligent to serve his needs. Sensors are playing a vital role in doing so and they have the capability of changing our world.

We will see in next few decades that these technological advancements will provide us better health monitoring. Moreover using the faster sensors we would be able to rapidly test our blood, saliva, will be able to test the food we eat, the air we breathe so that any pathogenic threats could be avoided. We will be able to make our homes smarter enough which will tell us about any unwanted activity. We will secure our cities and borders from warfare agents and other dangerous viruses. These all technologies are based upon only a single principle of ability of detecting vanishingly minor specific particles. As there is a great history behind the detection of particles, but here we are going to talk about a small corner that consists of electronic field effect sensors and advanced nanowire sensors. This is also an area of device fabrication which is explored significantly and many sensors has put in applications but much scope remains there to improve the detection time and selectivity of sensors towards a particular sort of molecules.

Many protein detection methods are available today, and these methods can be divided in two categories depending on their technology. The first one is the Label based technique, which generally involve detection of fluorescence, chemiluminescence or radioactivity from a specific label following target-receptor binding. This is a conventional method, but these methods have got the sensitivity in Attomolar range. However, the high sensitivity in these methods are achieved by using two antibody receptor besides this labeling and other steps take time and cost. So these label based techniques are not good for real time applications. But this requirement was fulfilled by evolution of semiconductor devices, the solid state sensor devices. They can be operated at very low power supply, anywhere and at any time.

There are many semiconductor materials available, but to choose one, which will work efficiently as a sensor is also a challenging task. Silicon , silicon-germanium, indium oxide, gallium nitride etc. has already been demonstrated as sensor but silicon always prove to be the strongest candidate because of its naturally grown oxide which is very robust and environmentally stable, have reliable etchant HF and allows a good electronic control. Different fabrication approaches of nanowire sensors is also a matter of study as our mother nature always favors the Bottom Up approach, but scientist have already fabricated billions of devices over a small area as in our microprocessors by Top down approach.

Moreover sensors performance to detect targets also depends on dimensionality. Its radius, length should be optimum to respond quickly, various sensor geometries are also there which are affecting the sensing time and required concentration of the solution. Femtomolar concentration of target molecules in solution can be detected using these sensors.

2.2 Historical Background

Ion Sensitive Field Effect Transistor (ISFET) which was proposed by Prof. P. Bregveld in 1970, is working as ancestor for every semiconductor Biosensor.

2.2.1 The Basic ISFET

It was a planer FET, have the capability of detecting ions (protons) from the solution. It was a device similar to the MOSFET like shown in the figure 1-1 and figure 1-2.

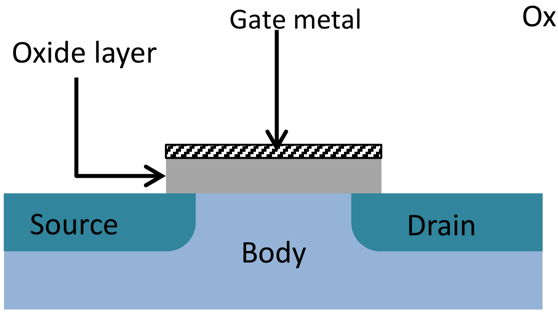


Figure 2-1 :- MOSFET

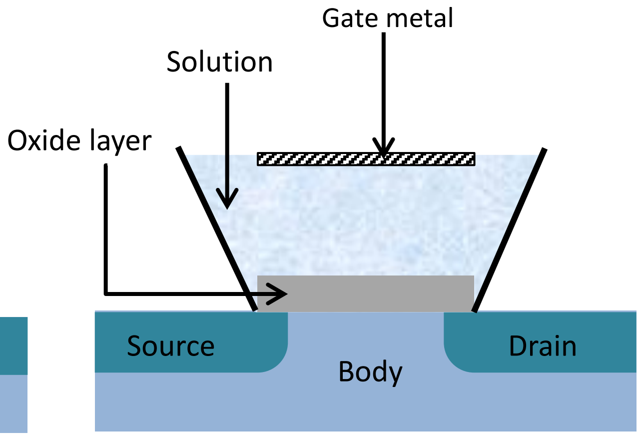


Figure 2-2:- ISFET

The only difference in case of ISFET is, the gate metal is separated from the whole device in form of reference electrode as shown in the figure (1-2). The separated gate metal behaves as reference electrode, which generally have 0V on it [1]. This device was firstly checked for hydrogen ion (pH value detection) sensing. It was also due to the limitation of SiO_2 which attracts only the positively charged ions. This is described by site bonding model [2].These insulators (SiO_2 etc.) have unsaturated dangling bonds of oxygen, which have partial negative charges. These negative charges attract positively charged hydrogen ions or hydroxyl ions from the solution. Due to this attraction these ions comes and bind with the surface of oxide layer forming a charge double layer. Now if we go in theory behind its working operation, it is as,

The accumulation of ions on the surface of the oxide is a kind of chemical equilibrium reaction that is given as :-

$$AOH \rightleftharpoons AO^- + H^+ \ \ and \ \ AOH_2{}^+ \rightleftharpoons AOH + H^+ \tag{1.1}$$

Here A is the base material of insulator like in SiO_2, it is Silicon.

So according to the reaction given in equation (1.1), the charge double forms and applying “The Gouy-Chapman-Stern model” this charge double layer creates a potential difference at the surface of the oxide layer or we can simply say that when positive hydrogen ions comes and accumulated over the surface of oxide [3], it behaves like a positive potential is applied over the gate .

The potential developed at the charge double layer or the surface of the oxide is given by Nernest equation.

$$\Psi_0 = const - \frac{RT}{F}\ln(a_i) \tag{1.2}$$

Where $R=8.314JK^{-1}mol^{-1}$ is the universal gas constant .

T is the temperature in Kelvin.

F is the Faraday constant (96,500 C/mol).

And a_i is the ionic activity, it is defined as ratio of forward reaction (K_f) constant to the backward reaction constant (K_b).

Due to this positive potential a vertical electric field will be developed towards the body of the ISFET, in response to that negative charges (electrons) starts to accumulate between the drain and source region .

The threshold voltage V_t of the MOSFET is given by:-

$$V_t = \frac{\emptyset_m - \emptyset_{Si}}{q} - \frac{Q_{ox}+Q_{ss}+Q_B}{C_{ox}} + 2\emptyset_f \tag{1.3}$$

Which remains constant throughout the operation, but in case of ISFET it depends on the solution applied for detection, so some extra factors of potential developed at the oxide solution interface, with the reference voltage applied on the reference electrode will come in the equation and it will be given as –

$$V_t' = E_{ref} - \Psi_0 + \chi^s - \frac{\emptyset_m - \emptyset_{Si}}{q} - \frac{Q_{ox}+Q_{ss}+Q_B}{C_{ox}} + 2\emptyset_f \tag{1.4}$$

Where, χ^s is the dipole moment of the solution, E_{ref} is the voltage at the reference electrode, Q_{ss} is the surface state charge and $\Psi_0 + \chi^s$ is the interface potential.

So a conductive channel appears between source and drain region, due to positive hydrogen ions. Now if we apply drain to source voltage current starts to flow, this current equation will be given by applying the modified threshold voltage and is given by:-

$$I_D = \mu_n C_{ox} \frac{W}{L}\left[\left(V_{gs} - V_t'\right)V_{ds} - \frac{1}{2}V_{DS}^2\right] \tag{1.5}$$

As this current is in the response of hydrogen ion accumulation on the oxide surface so detection of ions is occurred. Moreover current could be calibrated according to its values for the detection of hydrogen ion concentration or the pH value. After this device people started trying to detect any ion or any other molecule directly, because this ISFET was only for detection of pH values. They were thinking that how this device could be utilized in detection of other molecules. They had functionalized the surface of sensor by enzyme and successfully detected the penicillin and urea [4, 5]. Its name was then called as EnFET or Enzyme functionalized Field Effect transistor sensor.

2.2.2 The Immuno FET

In the next major advancement in ISFET detection was selectively detect the immobilize charge species. It was made possible by coating a specific antibody on the surface of oxide insulator. In 1978 Schenck suggested that the FET device can used to detect the surface polarization, as when a antibodies are immobilized over the surface of oxide and antigen molecules come they form a complex [6]. Investigations showed that the specific conductivity is higher than in the surrounding buffer, in an immunological precipitate deposited on the gate of an ISFET, caused by a high counter ion concentration in the precipitate with fixed charges (Schasfoort et al.,1989). It was concluded that the amount of protein charges in a precipitate can be measured by means of a change in local conductivity, However there are some disadvantages in applying this measuring technique practically because the effect depends on the thickness of the precipitate layer which furthermore can only be measured at a controlled low ionic strength of the electrolyte and at a pH far from the isoelectric point. The problem can be solved by applying some dynamic disturbance to the system, an electrolyte flow was applied along a column, which resulted in a streaming potential. This is a measure of the amount of protein adsorbed into the column.

Then an alternative method for monitoring an immunological reaction occurring in a porous membrane covering an ISFET is presented [7].

2.2.2.1 Detection Principle

When a membrane separates two compartments with different electrolyte concentrations a potential gradient can be measured. The different diffusion rates of anions and cations through the membrane set up a static membrane potential, which can be expressed by the Nernst-Planck equation [8] –

$$\emptyset_m = \frac{RT}{F} .X. ln\frac{a_2}{a_1} \tag{1.6}$$

Where $\emptyset_m$ is the membrane potential, a_1 *and* a_2 are the electrolyte activity in the respective compartments and X is the ratio of diffusion coefficients (D_+ and D_-) and given as

$$X = \frac{D_+ - D_-}{D_+ + D_-} \tag{1.7}$$

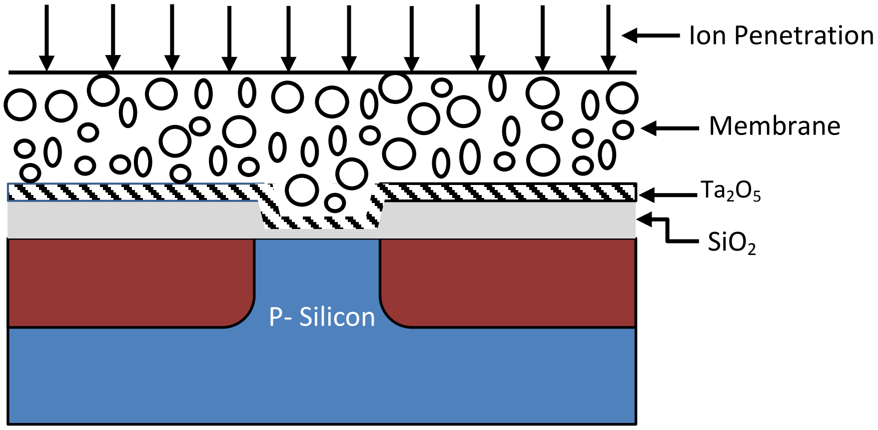


Figure 2-3 :- Immuno FET

If, at one side of the membrane, a stepwise electrolyte concentration change is applied, a transient membrane potential ($\emptyset_m$) exists, until the concentrations at both sides of the membrane are equilibrated. The amplitude of the transient membrane voltage, $\emptyset_m$ is a function of the difference in mobilities of the cations and anions flowing through the membrane, whereas the mobilities are functions of the membrane charge density [9]. A protein loaded membrane will have a pH-dependent charge density because of the amphoteric nature of the embedded proteins. This provides us with a method to modulate $\emptyset_m$ in order to measure charge properties of the embedded proteins. By applying ion-steps to the system with pH as a parameter, $\emptyset_m$, can be measured as, a function of pH. But these method fails in practice because the interfacial dipole charge cannot be detected due to screening of the charges at equilibrium by small inorganic ions present in the sample.

2.2.3 Thin Film ISFET

The close relationship between ISFETs and MOSFETs makes it highly desirable to fabricate both devices monolithically on the same wafer [10]. The monolithic fabrication of ISFETs and MOSFETs is difficult due to the following reasons:

(1) ISFETs eliminate the Polysilicon gate used for the alignment of source-drain implants,

(2) The thick silicon oxide layer used for isolation of Polysilicon and aluminum must be eliminated from the gate area while leaving an exposed thin gate dielectric.

A good approach for monolithic fabrication is to add as a post-processing the ISFET sensing layer on the metal gate of a MOSFET. The study is based on the Floating Gate Electrolyte Insulator Semiconductor (FGEIS) capacitor, which is the parallel structure to the Metal Oxide Semiconductor (MOS) capacitor found in MOSFETs.

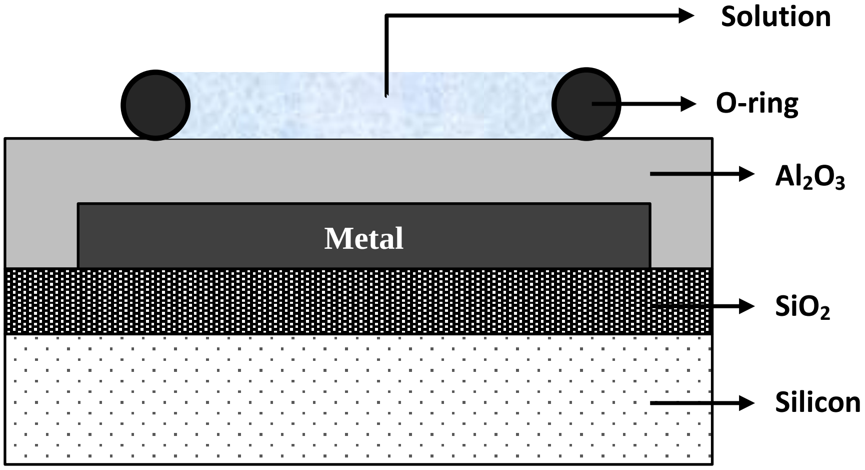


Figure 2-4:- FGEIS capacitor or Thin film ISFET

The floating gate consists on an aluminum layer on silicon dioxide covered by a sensing layer of aluminum oxide or silicon nitride. Both layers are widely used to obtain pH sensitivity.

The devices are studied through Capacitance-Voltage characteristics, using a buffer electrolyte with pH=7. The results show good consistency regarding layer thickness and substrate characteristics. A large hysteresis of -1.lV at flat-band capacitance is observed in the case of the silicon nitride layer. **A** smaller hysteresis of -0.15V is measured for the aluminum oxide layer [10]. In order to enhance the coupling of electrical signals, the thickness of the sensing membrane has to be continuously decreased. Thermally grown SiO_2 membranes, which were first proposed as ISFETs, have been a very attractive material in view of easier growth, good interfaces for gate oxides, and coupling with biomolecules. However, the thickness threshold of reliable SiO_2 has constantly caused controversy because an SiO_2 membrane can be seriously damaged by ions in electrolyte for long-term usage. Si_3N_4 is one of the promising materials for the alternative to SiO_2 in terms of excellent sensing. So to overcome the limitations of SiO_2, an engineered sensing membrane to improve sensitivity and stability by stacking SiO_2/HfO_2/$Al2O_3$ (OHA) layers for field-effect ion-sensitive devices [11]. The OHA sensing membrane shows higher quality characteristics in term of the hysteresis phenomenon, drift effect, sensitivity, and linearity than those of other layers. It is found that the proposed OHA stacked layer has good thickness uniformity, a low trapping characteristic, a low leakage current, and a large capacitance. The OHA membrane in the EIS pH sensors exhibited better performance such as a lower drift effect, a lower hysteresis phenomenon, and higher sensitivity than the O and ON sensing membranes.

Another advancement in the thin film ISFETs, is the development of flexible ISFETs, in which glass base is replaced by polyethylene naphthalate (PEN) plastic [12]. As the glass or the silicon base restrict the range of diagnostic applications in which the biosensor must come in direct contact with human tissue, or in direct contact with food or drink, where the ISFET biosensor may need to be conformable or shatterproof.

2.2.4 The Nanowire ISFET

In 2001, Lieber’s group reported the first use of a semiconductor nanowire as both an ISFET pH sensor as well as an Immuno FET. They have presumably claimed that-

> *Binding to the surface of a nanowire (NW) or nanotube (NT) can lead to depletion or accumulation of carriers in the "bulk" of the nanometer diameter structure (versus only the surface region of a planar device) and increase sensitivity to the point that single molecule detection is possible* [12].

The downsizing of silicon electronic components from the micro- to the nano-scale has steadily progressed in the past decades and nanoelectronics, bionanosensors and nanophotonics have tremendously benefitted from it [14, 15].

Before starting in the Nano scale range we should have a question in our mind that, Why do we need nanoscale devices for Bio or Chemical sensor development? The answer lies in the dimensionality of these devices that raise the sensitivity of the sensor (due to the high-surface-to volume ratio) [16] and in combination with the range of methods for surface functionalizations (especially for silicon-based devices), these feature offer an ideal platform for highly sensitive and better selective sensors.

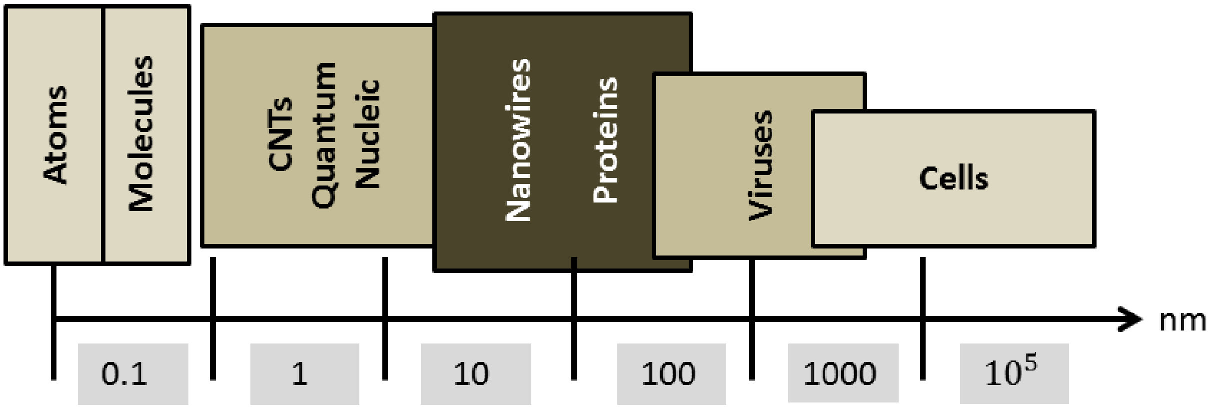


Figure 2-5:- A scale bar comparing the size of Nano devices and other molecular entities required for nanowire sensor

A NW-based device which has at least one of its dimensions in the 1-100nm range has a high-surface-to-volume ratio typically 1000 times. This provides a large interaction area for a small footprint (for increased response) and confines charge carriers in a very thin structure that is almost one-dimensional. Therefore, changes generated by the interaction of the bio-species at the NW surface are more significant, can be detected with higher sensitivity for small concentration and higher output resolution or signals. This sensitivity of nanowires can also be explained as when a bio molecule of nano scale dimension comes and bind with the planer ISFET having very larger surface area compare to the molecules. The effect produce by that molecule will be small and if the molecules will very few in number like one or two then, the effect will be negligible. So these nanowires offers ultrahigh sensitivity detection possibilities for very low concentrations of a sample and at the same time providing label-free, fast and realtime detection, which is not available in corresponding micro-scale sensing devices. Besides possessing a high-surface-to-volume, NWs are also relatively comparable in size to the species of interest such as proteins, cells, viruses and other biological entities, making NWs an ideal platform or interface between the biological samples.

2.2.4.1 Nanowire Biosensors: Principle of operation

The basic working principle of nanowire sensor is a combination of planer ISFET and Immuno FET. Binding of specific molecules, ions or ligands onto the chemically modified surface of a NW will induce some extra positive or negative charges, results in altering the electrical charges inside the NW, thus changing its conductance [17]. Due to conductance change the current flowing through it will also change. Moreover, transducing the signal change can be divided into two schemes: the resistivity and the Field Effect Transistor (FET) scheme, as schematically depicted in Figure 1-6. The resistivity scheme applies mostly to the metallic NW-based sensors (Figure 1-6), while the FET scheme is used in semiconductor NW-based sensing devices (Fig. 1-7 (a) and 7 (b).

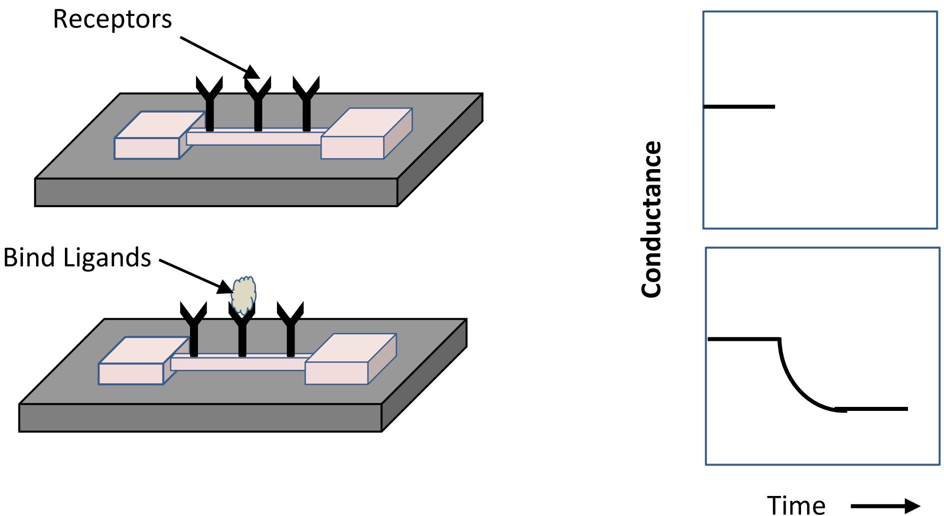


Figure 2-6:- Binding of ligands or target to the nanowire and change in conductance

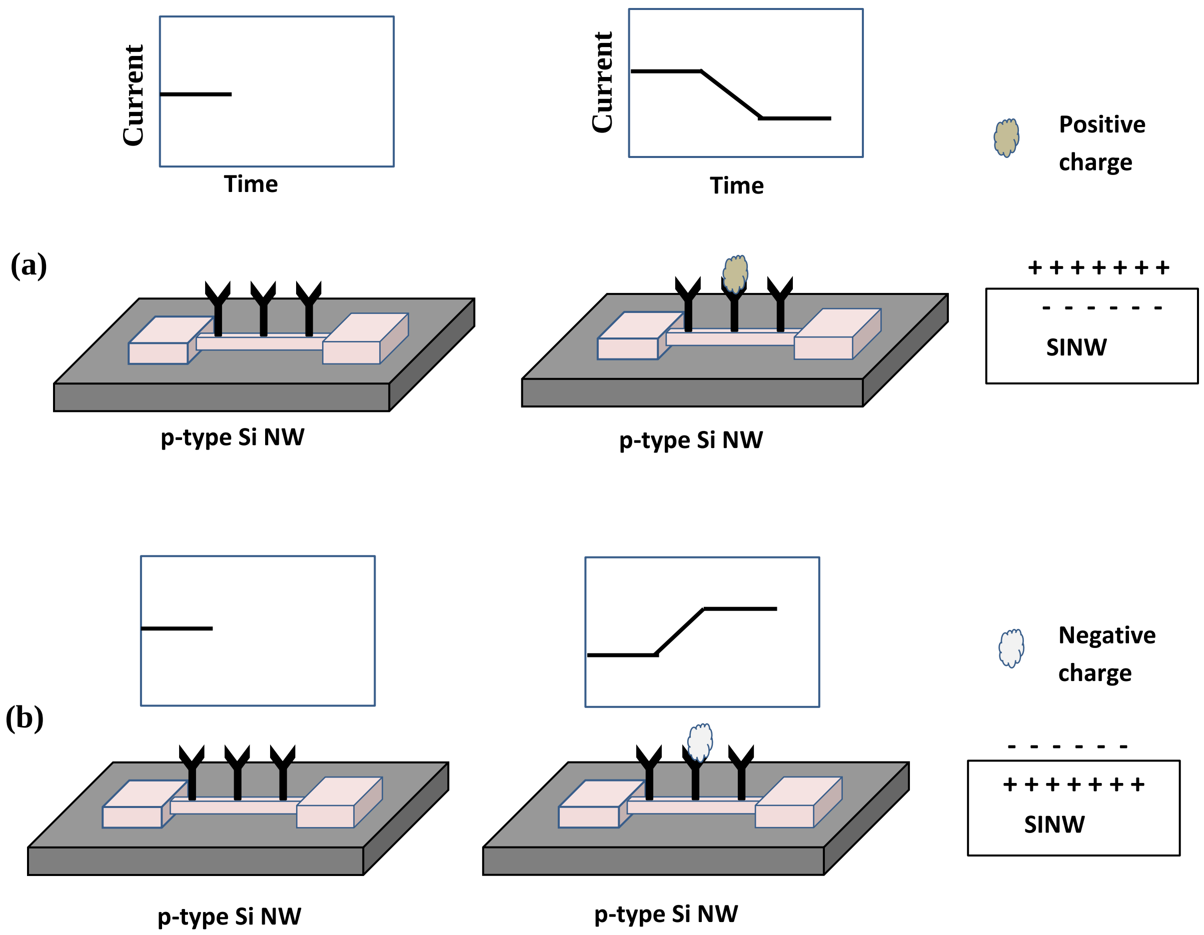


Figure 2-7:- Ligand binding and change in the current according to nature of NW.

In the resistivity scheme the metallic NWs act as metal resistors and any changes (e.g. the binding of targeted species which is either positively or negatively charged) on their surface will alter the conductance inside the NWs which is either p-type or n type. Depending on the polarity of the targeted species, these charged molecules will increase or decrease the signal relatively to the previously measured signal (Figure1.3(a)). Therefore, a signal change indicates the presence of targeted species. It should be noted that no extra biasing is required in operating these devices.

The change in conductance due to ligand or target ion (molecule) binding can be well understood by the above figure (1-7). In figure(1-7)(a) the p-type nanowire is bind with the positive charged ligand which will deplete the charges from the nanowire bulk and conductance will be less. But in figure (1-7)(b) due to negative target binding the positive charges will induce and enhance the conductivity of nanowire.

As the scaling law suggests that the sensitivity of nanowire increases as the diameter decreases or in other word it can also be said like as the surface to volume ratio increases the sensitivity increases.

Consider a cylindrical nanowire of length L ,diameter d and with uniform doping density N_D. The conductance of this wire is given by:-

$$G = q\mu\pi d^2 N_D / 4L \tag{1.8}$$

Where μ is the electron mobility. In this case, the potential is assumed to be uniform throughout the wire (ignoring whatever is outside the wire), hence the mobile charge in the channel equals the doping density. The wire may be considered as an n-channel depletion mode FET in the linear region of operation. If we now introduce a constant surface charge density, σ, to approximate the charge due to molecular conjugation, the nanowire will be accumulated or depleted by an equal amount of charge:

$$\Delta Q = \sigma\pi d L \tag{1.9}$$

The change in conductance is given by:-

$$\Delta G = \pi d \mu \sigma / L \tag{1.10}$$

As the sensitivity is defined as ration of change in conductance to the total conductance, so from equation (1.10) and (1.8). It is given as:-

$$S = \frac{\Delta G}{G} = \frac{4\sigma}{q d N_D} \tag{1.11}$$

So from equation (1.11) it can be suggested that the sensitivity is inversely proportional to diameter d. Here for the sensitivity calculation the assumption taken are, 1) constant potential in radial direction, 2) current is only due to drift and the diffusion current is zero and, 3) No screening effect is there.

The cross sectional view of a Silicon Nanowire sensor is given in figure (8), In this figure the source and drain region are highly doped n-type region and the channel is the nanowire which

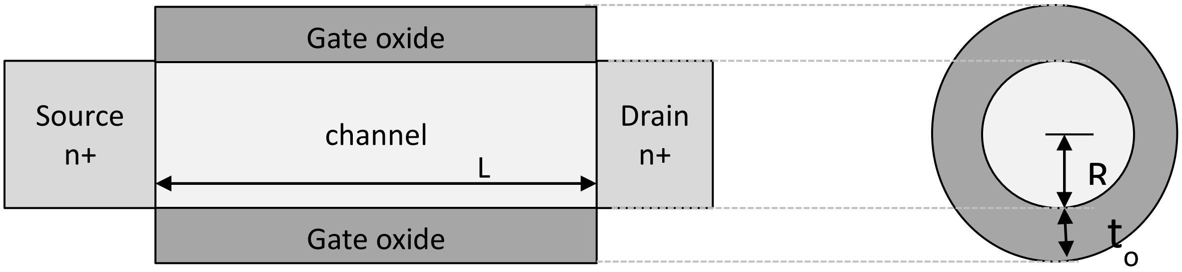


Figure 2-8 :- The cross sectional view of a nanowire sensor

Could be lightly doped n-type region , the radius of the nanowire is R and the oxide layer over the bulk NW have the thickness of ,$\mathbf{t_{ox}}$..Several analytical solution have been developed to find current on cylindrical surrounding Nanowires in terms of mobile carrier concentration [18-20].

2.3 Application of Nanowire sensors

In Protein Detection

Cancer marker proteins have been detected in a multiplexed format down to the Femtomolar concentration level with near-perfect selectivity using nanowire sensors modified with monoclonal antibody receptors [21]. In contrast to many optical assays, the detection process is dynamic and reversible, which enables (i) concentration dependent data to be acquired and (ii) cross-binding reactivity to be studied for each device during an experimental run. A potential limitation of the protocol is that the field-effect device detection Sensitivity will depend on solution ionic strength. Experiments to date have achieved good response for ionic strengths up to the millimolar level, although the highest sensitivity measurements were carried out in 1–10 μM ionic strength solutions. It is, however, possible to analyze biological samples with minimal sample preparation.

In DNA Detection

SiNW field-effect devices have been used for the detection of single-stranded DNA, where recognition of the DNA target molecule was carried out using complementary single-stranded sequences of peptide nucleic acids (PNAs) [22]. PNA was used as the receptor for DNA detection in this work since the uncharged PNA molecule has a greater affinity and stability than corresponding DNA recognition sequences at low ionic strength where nanowire sensitivity is greater. Studies with silicon nanowire devices modified with a PNA receptor designed to recognize wild-type versus the DF508 mutation site in the cystic fibrosis trans membrane receptor gene showed that selective detection of wild-type sequences versus sequence with the DF508 mutation site could be achieved to the 10 femtomolar level [22]. SiNW sensors have also been used in nucleic acid–based marker assays involving the detection, activity and inhibition of telomerase [21].

The nanowire telomerase assay is remarkably simple: the presence or absence of telomerase is determined by monitoring the nanowire conductance following delivery of a sample cell extract to the device array, and activity is monitored through an increase in conductance resulting from the incorporation of negatively charged nucleotides near the nanowire surface.

Detection of Small Molecules

Identification of organic molecules that bind specifically to proteins and macromolecular complexes is central to many areas of the life sciences, and thus represents an important target for sensors. A broadly representative example in this area has been the identification of molecular inhibitors to tyrosine kinases [23]. Nanowire sensor devices were configured for screening small-molecule inhibitors to the kinase Ab1 by linking Ab1 to the surface of the nanowire, and subsequently monitoring the binding of ATP and competitive inhibition of

ATP binding with organic molecules [24]. Data recorded from Ab1-modified SiNW devices showed the expected reversible, concentration-dependent increases in conductance upon introducing solutions containing ATP, and importantly, exhibited reversible decreases in conductance because of competitive inhibition of ATP binding by the different small molecules [24].

Virus Detection

SiNW sensor arrays have also been used to selectively detect viruses at the level of a single virus particle13. Delivery of very low concentration influenza A virus solutions, in the order of 80 Attomolar (50 viruses per microliter), to p-type SiNW devices modified with monoclonal antibody for influenza A produced well-defined, discrete conductance changes characteristic of binding and unbinding of single positively charged influenza virus [25]. Definitive proof that the discrete conductance changes observed in these studies were due to detection of a single virus binding and then unbinding was obtained from simultaneous optical and electrical measurements using fluorescently labeled influenza viruses, which showed that as a virus diffuses near a nanowire device the conductance remains at the baseline value, and only after binding at the nanowire surface does the conductance drop in a quantized manner similar to that observed with unlabeled viruses; as the virus dissociates and diffuses from the nanowire surface the conductance returns rapidly to the baseline value.

Other Applications

Apart from applications in biology, SiNWs FET also have been reported to be used as a piezoresistive-based pressure sensor [26-29]. Pavel et al. reported the construction of SiNW FET at the base of a cantilever. By modulating the whole structure with an electric field, a giant piezoresistive effect was observed with two orders of magnitude increase compared to the bulk value [30], thus, enhancing the sensitivity of the piezoresistive pressure sensor. It is noted that not all applications require the FET effect, for example grown bundles of SiNWs are also reported to be used in fuel cell and solar cell applications [31,32]. Chan et al. reported performance improvement in lithium-ion batteries that uses a stainless steel anode covered with SiNWs for faster charging and discharging and size reduction of the battery [33]. SiNWs offer also new possibilities in solar energy conversion as reported by Peng et al [32], owning to the large surface area and strong light absorption with efficient charge separation [31]. Furthermore, SiNWs also have been reported for possible integrated nanophotonics application [34].

Chapter 2

Fabrication Process Top down Approach

The fabrication of nanowire ion sensitive sensor involves two different approaches one is top down approach and the other is Bottom up approach, both the methods are suitable but they have their own advantages and disadvantages like bottom up approach is cheaper compare to top down, but top down approach can make very perfect structures.

3.1 Top Down Approach

Top-down approaches are mostly derived from integrated circuit processing. Instead of building complex structures starting from the atomic or molecular level, top-down processing is often associated with steps for example deposition, patterning, growth (oxidation) of different materials and subsequently removal of the patterned region through etching by a plasma or by a chemical solution [35].

3.1.1 Step 1. Selecting the Wafer

To start with top down approach, the very first step is to choose the wafer on which we will make the device. Moreover in the fabrication of nanowire sensors we are dealing with very small dimensions in nanometer range so problem like drain induced barrier lowering and leakage current may occur so to avoid those problems we should take SOI (Silicon on Insulator) wafers.

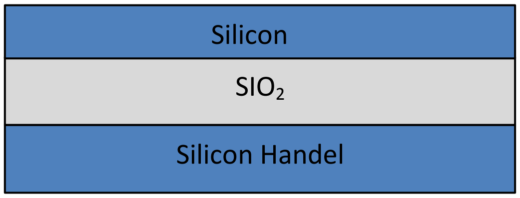


Figure 2-1:- Silicon on Insulator wafer

There are three layers in the SOI wafer, an insulator (SIO_2) layer is sandwiched between two silicon layers. The above layer is called the active silicon layer and the lower layer is called the silicon handle layer. This layer is there to provide robustness to overall structure.

RCA (Radio Corporation of America) standard chemical cleaning process is followed to avoid greasy substances and heavy metallic contamination from the wafer.

3.1.2 Step 2. Making the active layer P-type or N-type.

To make the upper active silicon layer more conductive we have to dope that layer by p-type or n-type impurity. For making it p-type we can dope it by Boron, and for n-type we will use Phosphorous as dopant material.

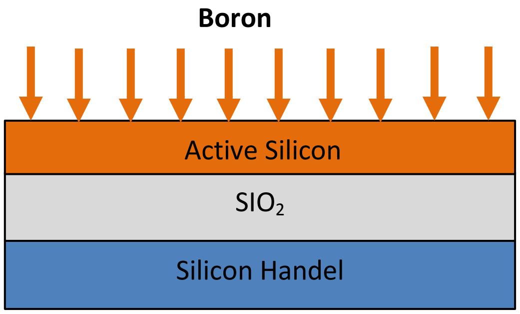


Figure 2-2:- Boron doped Active Silicon layer

3.1.3 Step 3. Deposit a silicon nitride layer by LPCVD at 800^0C .

First we thinned down the active silicon layer according to our requirement. Its thickness should be same as the thickness of nanowire required, as we will make

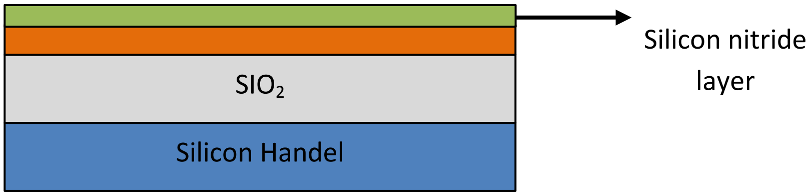


Figure 2-3:- Silicon nitride layer

the nanowire in the upper layer only. Then we deposit a 20-25nm silicon nitride layer using LPCVD (Low pressure chemical vapor deposition) techniques.

3.1.4 Step 4. Deposition of Polysilicon for gate conductor

After silicon nitride layer we will deposit another layer of Polysilicon which will act as conductor for gate. It will be deposited by LPCVD technique.

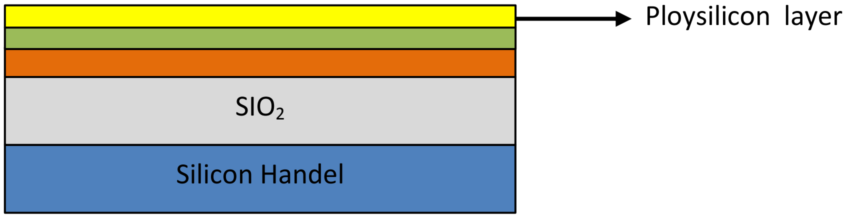


Figure 2-4:- Polysilicon layer

3.1.5 Step 5. Pattern alignment marking

For making in the structure we have to use mask or e-beam lithography and in making some complex structures this step may repeat several times, so to align those masks we have to make some alignments marks .The pattern was aligned to the flat of the wafer as closely as possible to ensure that all lithographic patterns are aligned to the crystallographic axes of the wafer. This is extremely important later in the process because of an orientation dependent etch.

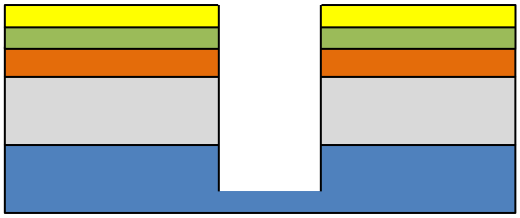


Figure 2-5:- Alignment mark

The alignment pattern was transferred into the wafer by reactive-ion etching. First, the pattern was etched through the active layer using a CF4 RIE process. Second, the pattern was etched through the BOX using a CHF_3/Ar RIE process . Finally, the pattern was transferred into the handle wafer to a depth of 3-4 microns using a silicon deep-RIE (Bosch process, Unaxis 660 ICP, CNF). These alignment marks can readily be seen during all the subsequent processing steps for ease of alignment.

3.1.6 Step 6. E-beam lithography to define nanowire FET channel.

For defining smaller dimensions e.g. of 10nm or sub 10nm in the Nano-world, people generally use Electron beam lithography or focused ion beam lithography (FIB). Patterns are made on a resist layer by manipulating the focused electron or Ion beam. Then by etching, this pattern can be transferred into wafer material. Many research groups have already used this E-beam lithography in defining the nanowire structure. Li et al [36] who demonstrated the precisely controlled fabrication of sub 10nm Silicon NW devices using E-beam lithography on Silicon on Insulator (SOI) wafers.

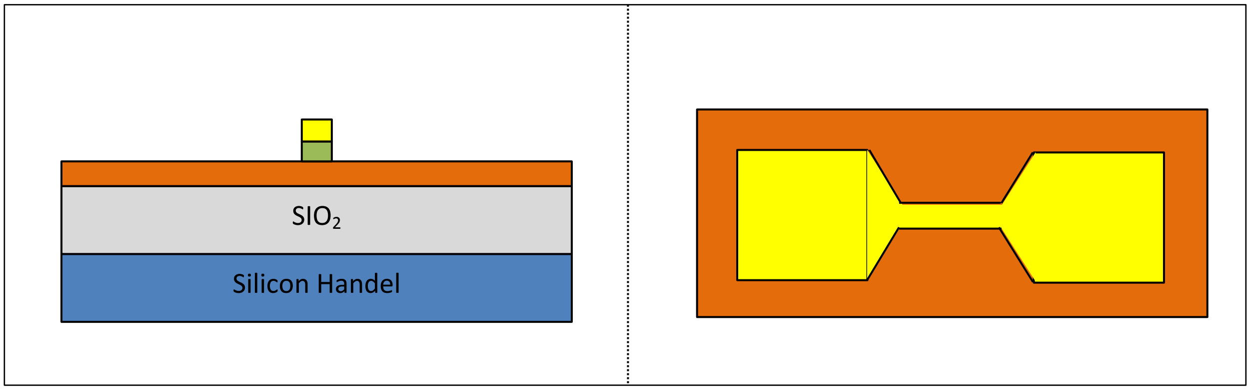


Figure 2-6:- source drain and nanowire patterning

However, these types of patterning (E-beam and FIB) are very slow, time-consuming and expensive compared to conventional optical lithography. It is believed that conventional optical lithography in combination with a size reduction strategy may provide a simple and more economic solution to realize SiNWs for commercial devices [16].

3.1.7 Step 7. HSQ layer deposition over gate stack by e-beam lithography.

In this second round of e-beam lithography, Hydrogen Silsequioxane (HSQ) is applied on the wafer by spin-coating to yield a 150 nm thick layer. Then HSQ is exposed at 100 KeV using doses ranging from 500-2500 uC/cm^2 depending on the size of the feature and proximity to other large features. The critical features are exposed at a beam current of 2 nA. Large features can be exposed with higher current at the range of 20 nA, to make the step time efficient. The unexposed HSQ is developed, around 4 minutes in a tetra methyl ammonium hydroxide based developer (AZ 300-MIF) until visibly cleared. The HSQ is then annealed by Rapid thermal annealing (RTA) at 900 °C for 5 minutes in an oxygen atmosphere. This treatment drives any remaining hydrogen out of the HSQ and yields a dense SiO_2-like material with good wet and dry-etch resistance. This pattern was transferred into the gate stack using the same etching processes as the previous step. During the CF4 RIE process, the active layer surrounding the source and drain pad structure was etched down to the BOX (Buried oxide layer i.e. SiO_2 layer) .

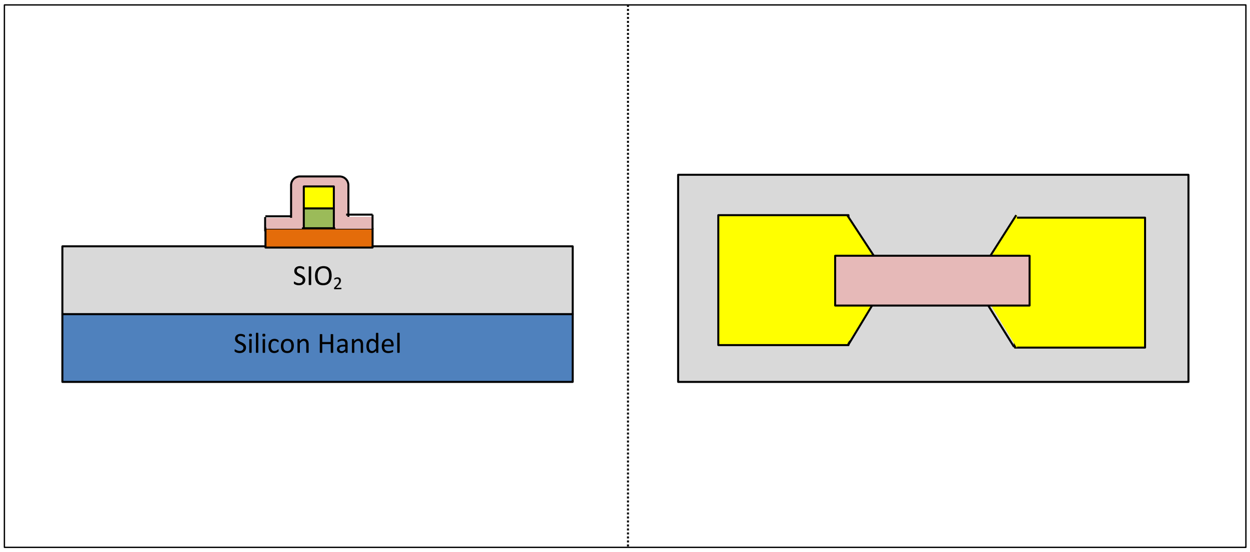


Figure 2-7 :- HSQ layer deposition

3.1.8 Step 8. Ion implantation to make source and drain region.

The source and drain regions of the devices are required to doped by ion implantation (see appendix B). The wafers are patterned with positive photoresist (Shipley 1813) and contact lithography is used to expose only the source and drain regions. These regions are doped by low-energy ion beam. Boron difluoride ions are implanted at about 7-10 KeV to a dose of 5 x 10^{15} for p-type contacts and arsenic ions are implanted at the same energy and dose for n-type contacts. At this specified energy range, These species had a projected range of 10-12nm, as calculated by SRIM [86], and suggested that most of the dopant would remain in the active layer at this energy. After Ion Implantation the HSQ layer is removed by etching in Buffer HF(Hydrogen fluoride) solution 10:1.

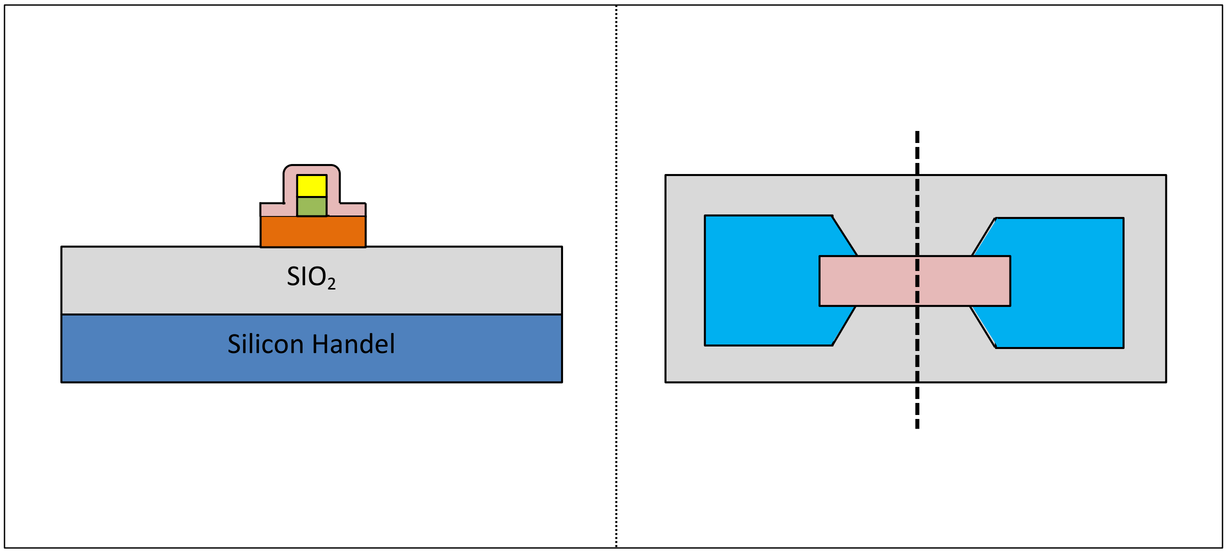


Figure 2-8 :- ion implantation for surce drain region

3.1.9 Step 9. Deposition of dielectric layer for isolation

Now we apply a dielectric layer of about 150-200 nm thickness using PECVD (plasma etched chemical vapor deposition), so that source drain and gate contacts could be electrically isolated. Contact lithography can be used here to open windows on drain, source and the nanowire gate regions. But the etching of these windows is a crucial task specially the nanowire gate window, As the window over the nanowire is very small so we start with RIE and etch upto 80%, and remaining 20% is done using wet etching i.e. using 10:1 BHF solution. The BHF solution is here used so that etching could be stopped at the Polysilicon layer and active silicon layer on source drain regions.

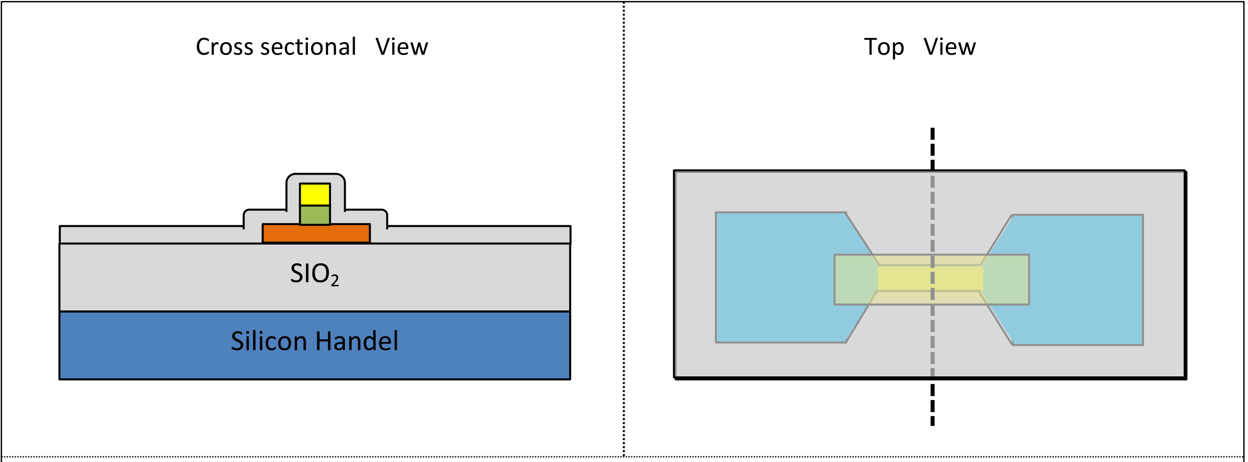


Figure 2-9 :- SiO_2 layer over the whole surface

3.1.10 Step 10. Patterning windows in SiO2 layer.

This window is opened here is the SiO_2 layer so that the solution to be sensed could be put here and the nanowire could be open to environment.

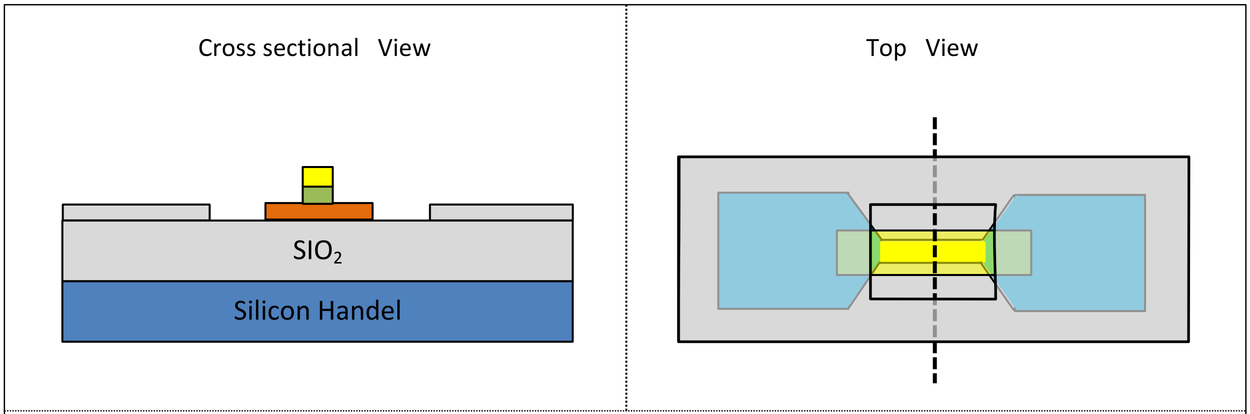


Figure 2-10 :- Open window over the whole nanowire

3.1.11 Step 11. TMAH etching

Silicon active layer which was opened by window is again etched by TMAH (Tetra methyl ammonium hydroxide) at 50^0C for 8-10 minutes.

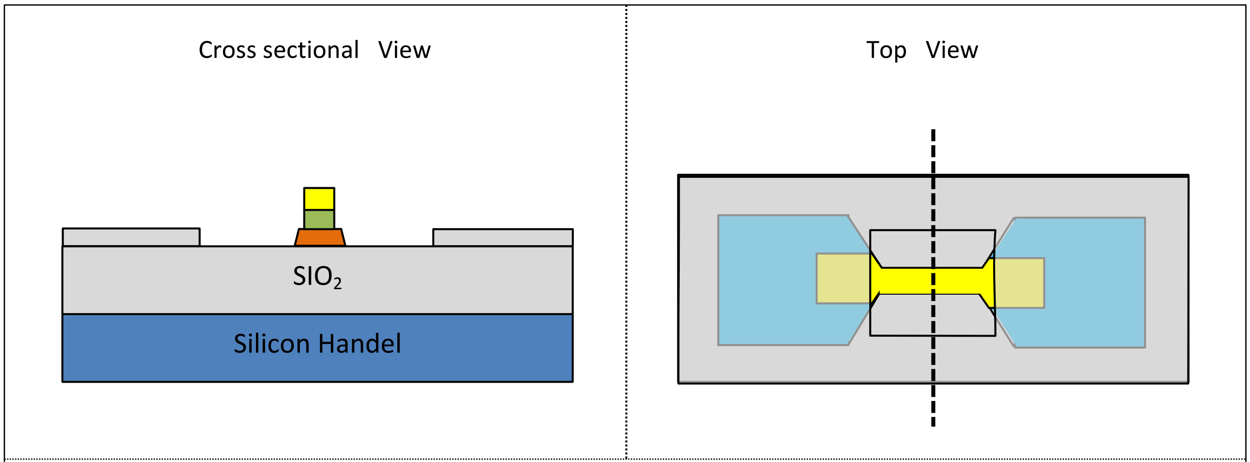


Figure 2-11:- Open window over the whole nanowire

3.1.12 Step 12.Opening ways for contact.

For making electrical contacts on source, drain and gate (Nanowire) we have to make openings in the deposited dielectric layer using contact lithography. Etching of these ways is processed in the same way as of window opening.

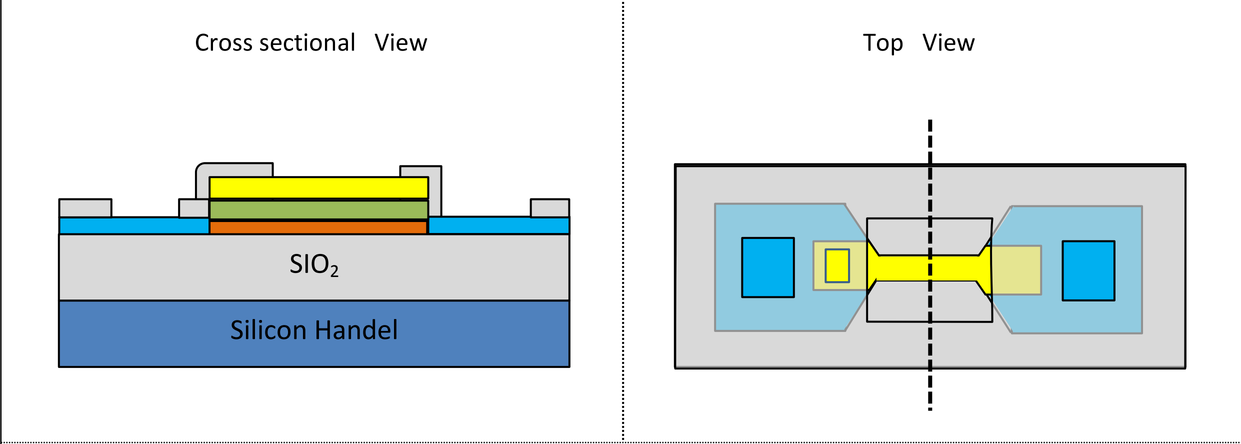


Figure 2-12:- Opening ways for electrical contacts

3.1.13 Step 13. Metallization

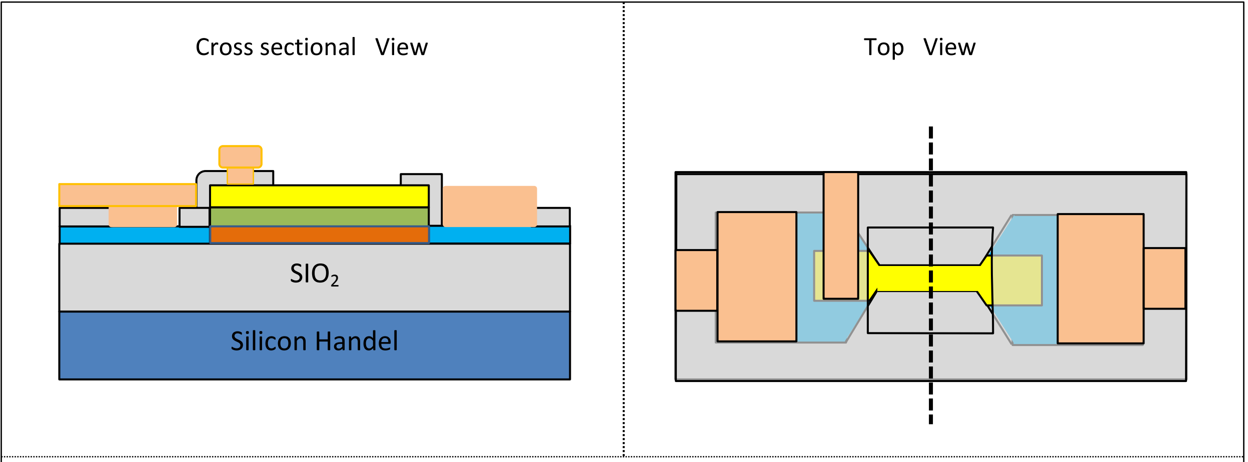


Figure 2-13:- Metal contacts

After opening the windows for the metal contacts, we put the this chip in metal thermal evaporator to deposit the metal in the contact window. A vacuum of 10^{-7}mbar is maintained inside the chamber of evaporator and then metal is heated to melt. The metal particles come and deposited over the whole surface then by lift off process we remove the metals from unwanted places.

Chapter 3

Fabrication Process: Bottom up Approach

Bottom up approach of nanowire growth is inspired from “Nature”. As in nature everything starts from its very basic building block and continuously grows in complex, larger, functional structures. This could be understood by an example, as in zoology similar type of cells combine to form tissues, and many tissues of same kind combine to form the stem of the tree and in the same manner the whole tree. The above given conceptual technique could be utilized in making synthetic nanostructures e.g. nanowires. In true sense the process of nanowire growth is a chemical synthesis kind of process, in which atomic and molecular species of same specific material are continuously added to form a more complex structure [37, 38].

A nanowire (semiconductor nanowire) is a solid rod like structure whose cross section could be circular, rectangular or may be triangular with radius approximately 100-200 nm or less[39]. These nanowires could grow using one material or using many material too, according to the need. The lower limit of radius of nanowires is hard to define because people are working hard to make radius lesser. Radius of 5nm is already reported.

Several methods are reported in literature of growing nanowire with bottom up approach, the three main techniques are: -

(1). VLS (vapor Liquid Solid)

(2). Vapor -solid

(3). Template based electrochemical deposition.

The overall growth of nanowire involves two steps synthesis and isolation of nanowire. For the synthesis we will discuss only the VLS method in detail here, as it is the most efficient method and radius and material could be changed according to our need. The isolation is to remove the nanowire from the substrate into a solution suspension e.g. ethanol etc. The uniformity of nanowire diameter is checked by Scanning Electron Microscopy (SEM).

3.2 Vapor liquid Solid Process (VLS)

In this process the supersaturated solution of specific material is precipitated to form a crystalline material. Here the crystalline material is the nanowire and the solution is of that material of which we are trying to make nanowire. But this growth involves lot of chemistry in it. This growth process is initiated by a specific catalyst for each specific material. So choosing a correct catalyst is also a crucial task. The selection of catalyst depends on the binary phase diagram of the material. The temperature and the catalyst conformation for growing nanowires can be determined, by inspecting the phase diagram of the specified material for nanowire, as reported by Duan et al. [40].

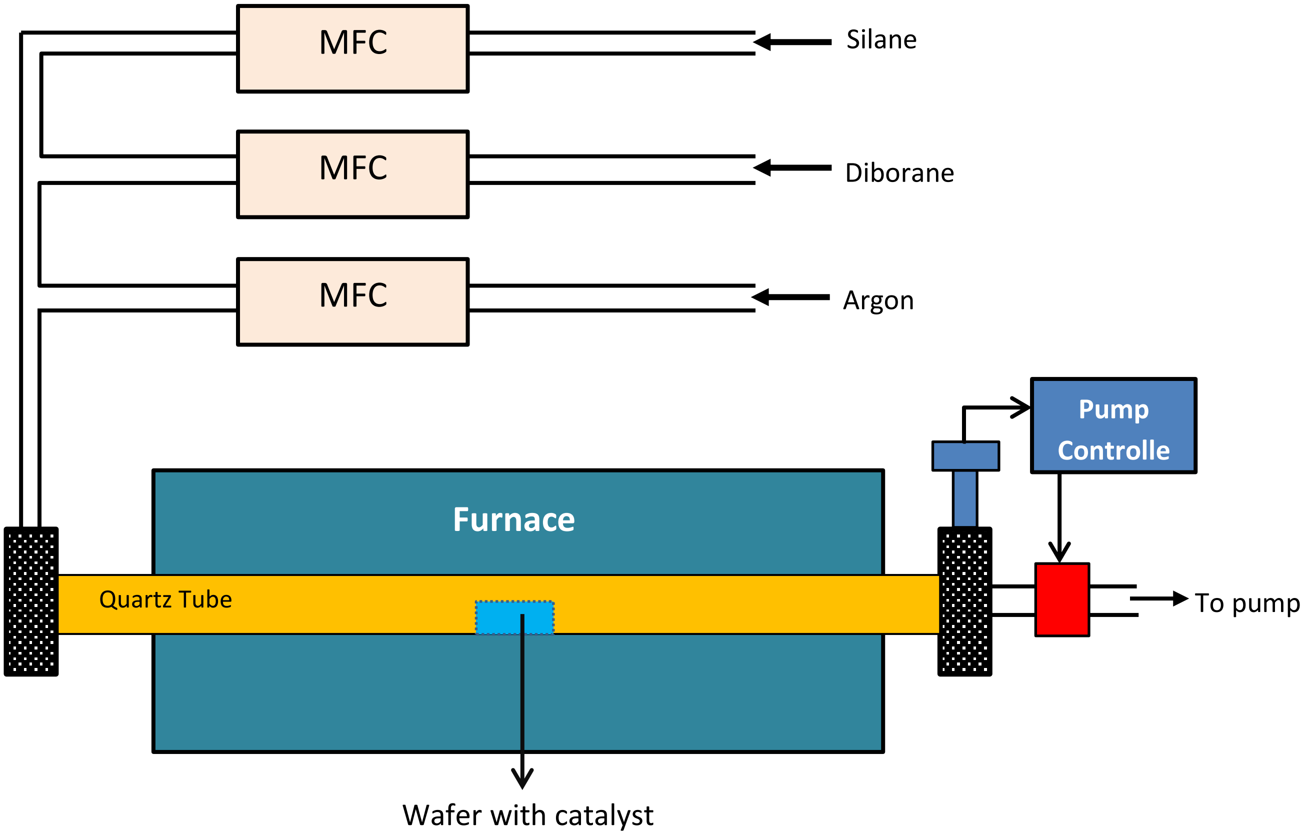


Figure 3-1:- A block diagram of nanowire synthesis system by VLS process

The detailed steps of VLS process is given as follows, and the whole fabrication of Nanowire sensor by bottom up approach is divided in two parts with several steps [41].

3.3 Part 1: Process Flow for Silicon Nanowire growth.

3.3.1 Step 1. Selecting the wafer.

We will take a silicon wafer with area 1-2cm^2, clean the surface of that wafer by oxygen plasma for 200 seconds. Organic residues and other dust particles are removed by this plasma treatment and surface of the wafer becomes hydrophilic.

The dose of this plasma treatment is given like at 100w 40 sccm (standard cubic centimeters per minute), 1 sccm = 1.7×10^{-8} m^3 s^{-1}.

Figure 3-2:- A silicon wafer

3.3.2 Step 2. Surface modification by Poly-l-lysine.

After cleaning the surface, we will coat a layer of Poly-l-lysine on the wafer. The poly-l-lysine is a polymer; it is used as charge enhancer of the surface . The process of coating is, use a 0.1% solution of Poly-l-lysine and allow the solution to stand for 4 min. It tends to improve the binding of other substances with the surface. After that we will remove the Poly-l-lysine by rinsing it in dH_2O (De-ionized water, resistivity above 10MΩ) and make its surface dry using gentle nitrogen flow for 8-10s.

Figure 3-3:- Surface modified wafer

3.3.3 Step 3. Cover the surface by catalyst nanoparticles.

For the silicon nanowire growth the gold material can be used as catalyst. So we will cover the Poly-l-lysine treated surface by gold nanoparticles solution containing particles of varying diameter up to 20nm. Here the critical step is, solution should be prepared freshly and wafer should be put in the solution for 8-10s for deposition otherwise the particles will aggregate and form particles of larger diameter. So after allowing the solution to stand for 10s it should be cleaned by rinsing in dH_2O, dry the surface by a gentle stream of nitrogen gas. In this process the negatively charged gold nanoparticles will bind with the positively charged Poly-l-lysine particles.

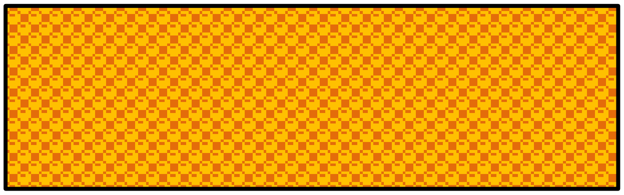


Figure 3-4:- Growth wafer surface with gold nanoparticles

After this we again clean the growth chip with oxygen plasma for 5 min at 100w and 50 sccm. It allows a uniform nucleation and nanowire growth.

3.3.4 Step 4. Growth of nanowire.

Now we will put the cleaned growth chip inside the quartz tube in the middle(so that temperature remains same at every part of the chip) as shown in the figure (10) for the growth of nanowire. This quartz tube (reactor) is part of CVD furnace. Vacuum is created at 3mtorr in the inside the quartz reactor by evacuating the air, temperature of the furnace is raised up to 460^0C then argon (Ar) gas starts to flow to make the environment of the reactor inert. when temperature of the reactor becomes stable we starts to flow Silane (SiH_4) which is the silicon source and if we would like to dope the nanowire by either p-type or n-type we have to flow Diborane (B_2H_6) gas for p-type and phosphine(PH_3) for n-type impurity. The detailed mechanism of nanowire growth in the CVD furnace is given in figure (3-1). Catalyst material i.e. gold nanoparticles here, melts at the temp of 460^{0}C.

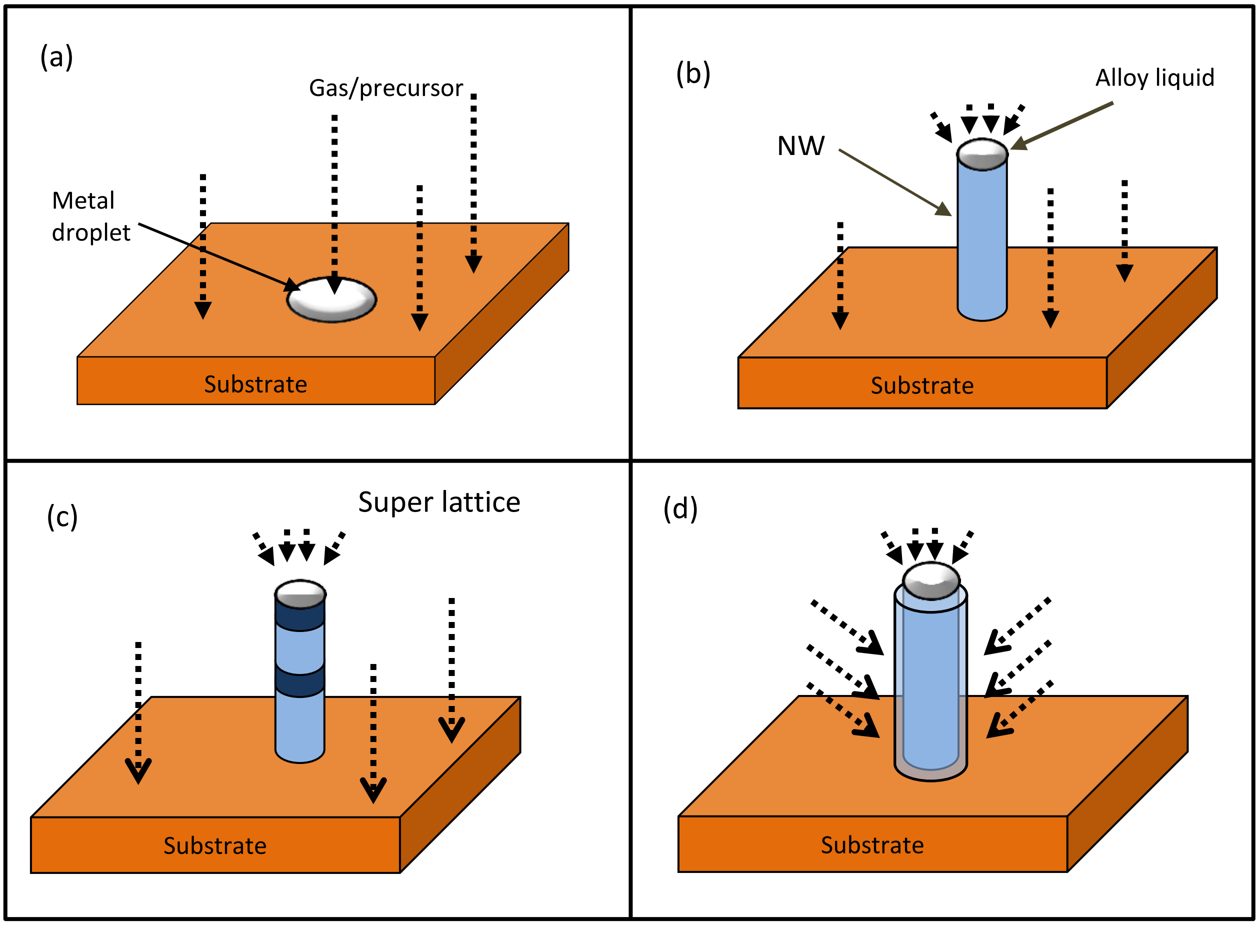


Figure 3-5:- Process of nanowire growth by VLS method

In this condition when we start to flow the gas (gas precursor) of desired material, Material atoms from the gas e.g. silicon from the silane starts to fall on the melted droplet of gold figure 3-5 (a). As after melting the surface of droplet become parabolic in geometry and its sticking coefficient is higher than that of lower part of droplet. The concentrated assimilation of the material atoms will lead to hypersaturation of the material. In this way due to cooling and precipitation nucleation of material and alloying take place, and nanowire starts to grow figure 3-5(b).

We can develop heterostructures either by adding different material layers in the length or radially to get different radius nanowire using this VLS process as shown in figure 3-5(c) and (d). only we have to change the precursor material or the gas. After development of nanowires from this VLS process. We will get the nanowires on the wafer very densely populated as shown in the figure.

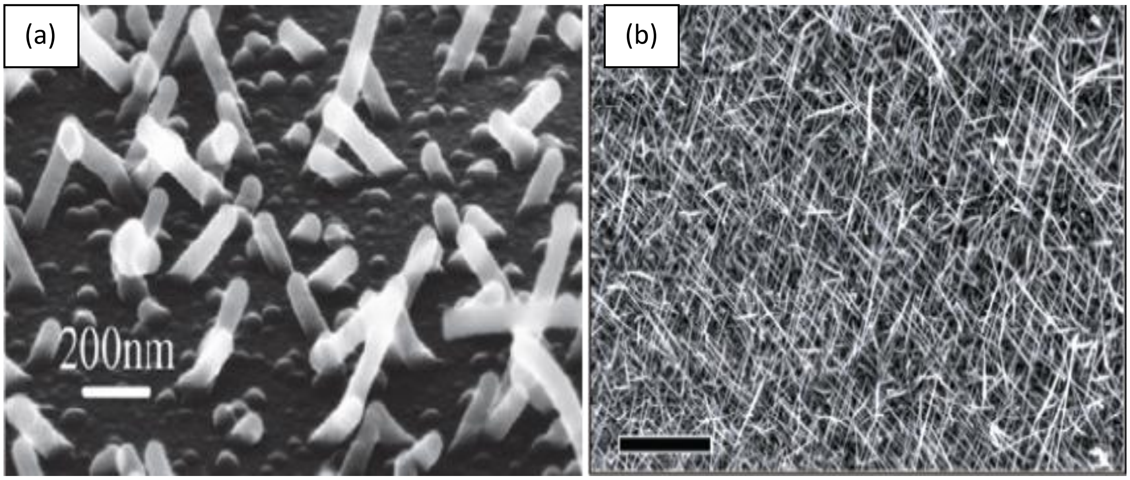


Figure 3-6 :- (a) The nanowires after the growth using VLS process, and LPCVD technique is used for making catalyst nano particles [16], (b) SEM Image of n-type GaN nanowires grown using nickel Nano clusters [42].

3.3.5 Step 5: Removing Nanowire from the Growth Chip.

In this step we will remove the nanowire from the growth chip and suspend it in ethanol (solution) .This removing is also a critical process because these nanowires are very tiny and

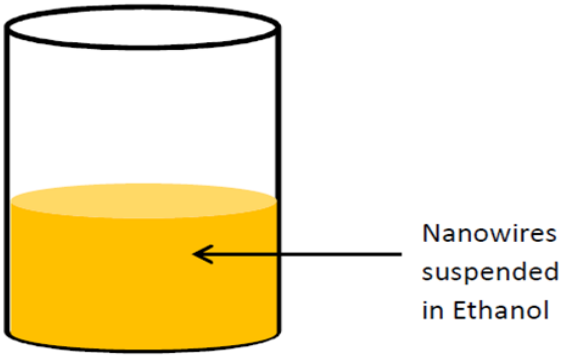


Figure 3-7 :- Nanowires suspended in the ethanol solution we have to remove it from the chip in such a manner that a whole nanowire separates from the chip and it doesn't get broken. So for this the technique which is used, is called as sonication (ultra sonication). In this process the growth chip is immersed in the ethanol solution and this solution with the growth chip is then kept on the sonicator machine for 5-10 seconds. Which generates ultra sonic waves, due to the effect of these waves the solution vibrates with its frequency. These vibration are very small but they are enough to remove the nanowire from the growth chip. So the nanowires from the growth chip removes and suspend into the solution. This nanowire solution can be for 1-2 weeks, but the nanowires degrades with time.

3.4 Part 2: Process for the device Fabrication using the grown NWs

Now after getting the NWs, we have to use them in device i.e. our nanowire sensor fabrication. As we have grown the nanowires by bottom up approach, now our task is to use that NW as a channel between the source and drain region. So we will follow the top up approach of fabrication.

3.4.1 Step 1. Deposit two layer of Photoresist for contact pads.

Deposit a two-layer photoresist consisting of LOR3A and S1805 onto the sensor chip by spin coating: (i) Deposit 0.5 ml LOR3A by spinning at 500 rpm for 5 s then 4000 rpm for 40 s. After the spin coating this wafer is baked at 185^0 C on a hotplate for 5 min so that the polymers in the photoresist solution makes their proper bonds and its moisture could be removed.

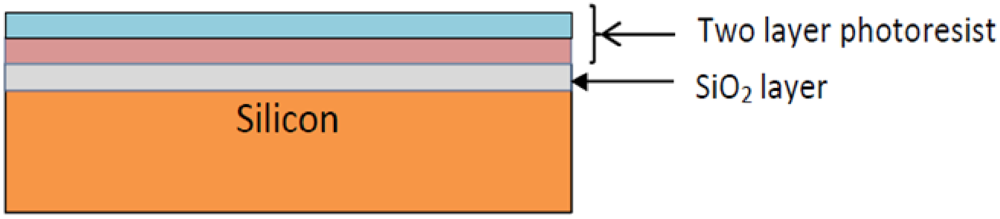


Figure 3-8 :- Two layer photoresist coated SiO_2 surface

The LOR3A layer thickness should be approximately 300 nm. The thickness of the photoresist plays its role when photolithography happens, according to its thickness we will increase or decrease the exposure time. (ii) Then again we will deposit 0.5 ml S1805 by spinning at 500 rpm for 5 s then 4000 rpm for 40 s, followed by baking on a hotplate at 115^0 C for 90 s; the S1805 layer thickness should be approx. 500 nm.

3.4.2 Step 2: Defining the outer contact pads by Photolithography

Now after coating the two layer of photoresist we have to define the outer contact pads ,from there the fabricated devices will connect to the outer world. So we use contact lithography (Photolithography) wavelength (350-430nm) and exposure time 0.8 sec. Using the quartz mask ,which is have already these contact pads designed. The mask is also of two kinds one is positive resist and other is for negative resist. So if we want to design some pattern using positive mask, the exposed portion under ultraviolet (UV) light will become softer or technically the polymer chain of resist breaks due to photonic energy of UV light.

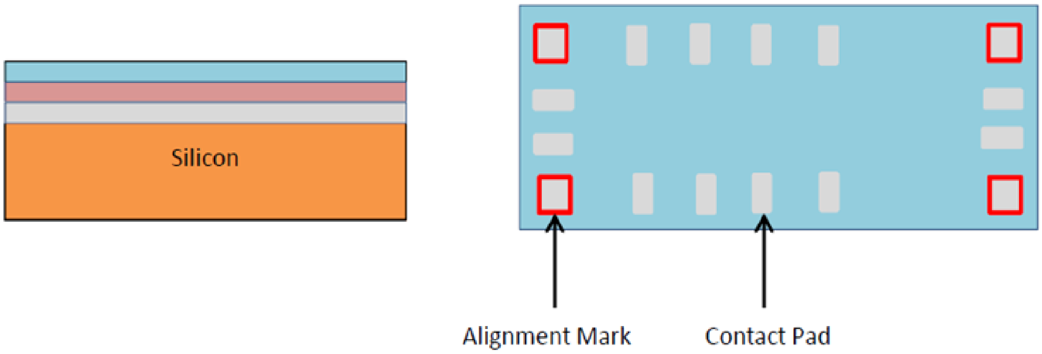


Figure 3-9:- Contact pads defined using Photolithography

After exposure immerse the whole chip in developer solution for 1 min and rinse it in dH_2O for 2 min, immerse the chip in dH_2O and shake gently .Take the chip out from the deionized water and dry it in the flow of nitrogen gas.

3.4.3 Step 3:- Depositing metals on the contact pads.

After defining the contact pad region, we have to deposit metal in those regions . For the contact we can deposit gold, silver or aluminum, but as gold have highest conductivity, so gold is a better option. But before depositing gold one should be careful because gold's adhesion is not good so to avoid any failure chromium is deposited before deposition of gold.

It will prevent the gold to go inside the silicon. For depositing the gold and chromium, these material are put on the coils of evaporator, then evaporator is evacuated to a pressure of 10^{-7} bar, after this vacuum achieved coil starts to heat melting the material kept over it. So first that coil is heated at which the chromium is kept. At this vacuum level when Cr melts its molecules spread in the chamber of evaporator and covers everything inside that, except this a high DC voltage is applied between the coil and the wafer base, so due to this potential molecules of Cr attracts towards the wafer.

Cr deposits at a rate of 0.1nm per second, a 5nm Cr layer is deposited and then gold coil is heated to deposit a 50nm layer of gold in the same way as the Cr is deposited, both these metals are deposited in a single evaporator just one after the other.

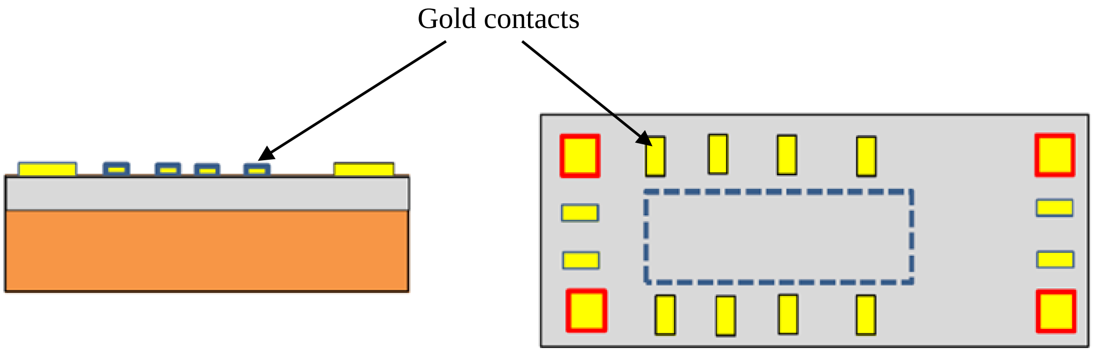


Figure 3-10:- Gold deposited over the contact pads.

Dissolve the remaining photoresist by heating it in the respective specified solvent for 30 minutes and at 70^0C. Then rinse the chip in acetone and then in ethanol for 10s each by flowing them from the chip using squeeze bottle. Then dry the chip by flowing nitrogen gas flow.

3.4.4 Step 4 : Deposition of NWs from the suspension and their alignment.

Now after making contact pads, NWs should be deposited on this chip and source drain pads should be made. For this, the very first step is to deposit the NWs on the fabrication chip and their alignment. This step of NW deposition and their alignment could be done in many ways as flow induced alignment or Langmuir Blodgett method, these methods need larger number of NWs, I will discuss only the Langmuir method.

3.4.4.1 The Langmuir Blodgett method of alignment of NWs:-

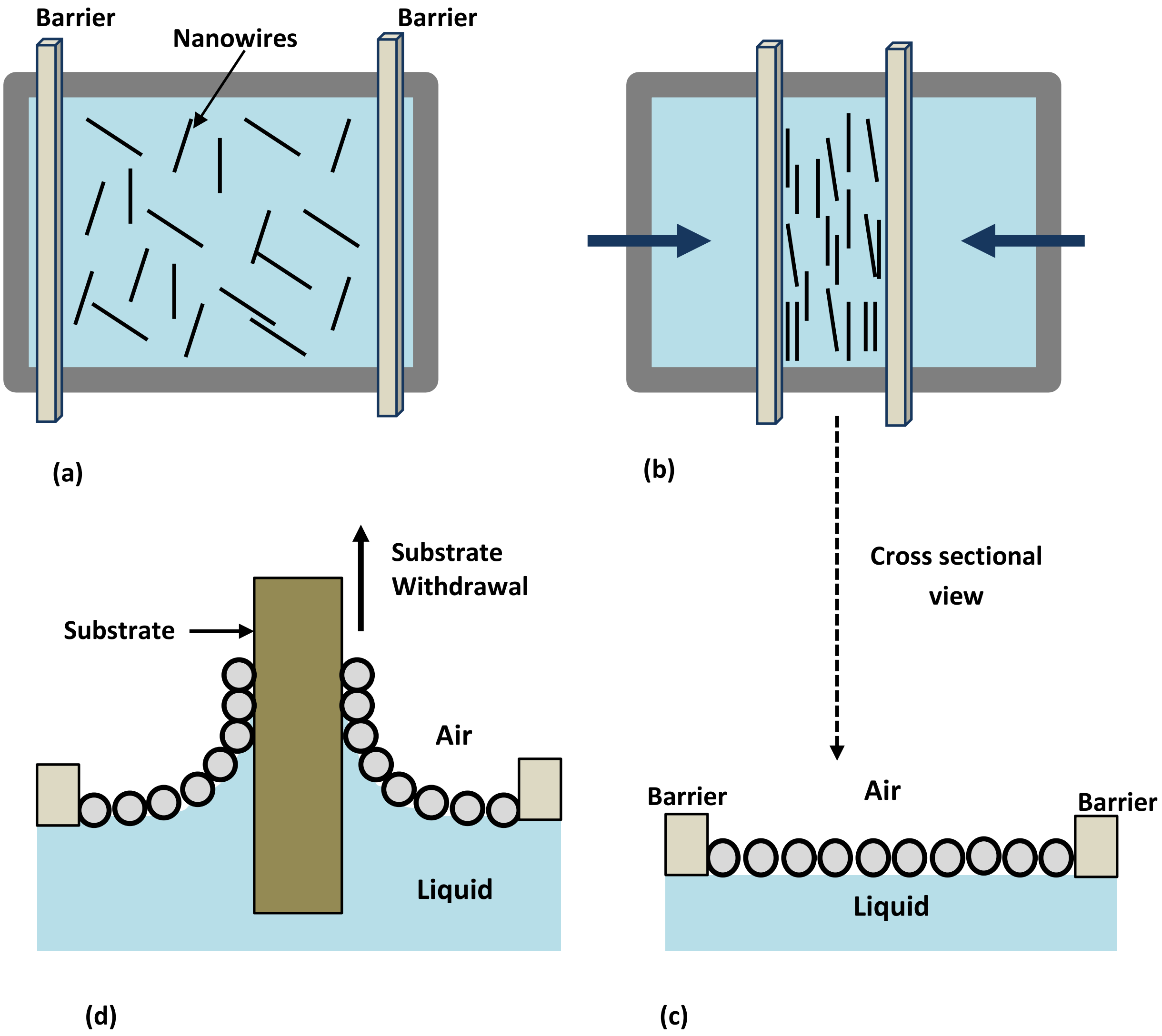


Figure 3-11:- A Langmuir Blodgett method overview [39], (a) The LB trough and the nanowire spreaded over the solution, (b) The barriers compressed, (c) the cross sectional view of the compressed nanowires, (d) The substrate immersed and withdrawal, and NWs are sticking with it.

In this method a LB trough is there, in which dH_2O is filled and from the solution one or two drops of NW containing ethanol solution is droped.so from the solution these NW spread over the solution interface with air, after they are compressed from both the sides by barriers as shown in the figure (3-11).

Due to compression, nanowires get a closed packed group in order to minimize the energy. Then dip coating is used to transfer the NWs on to the substrates.

So by using above given Langmuir Blodgett method, the chip at which the contact pads are already made, the NWs from the ethanol solution will be transferred in an aligned manner. Then the chip will look as given in figure 3-12.

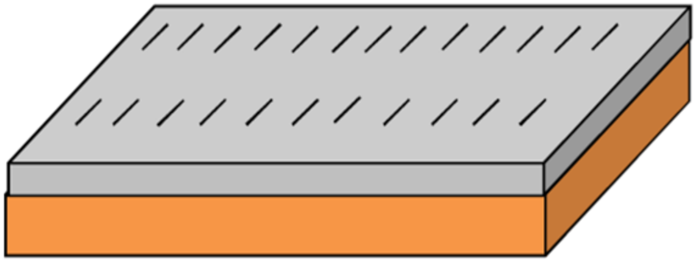


Figure 3-12 :- Aligned Nanowires using Langmuir Blodgett method

Now we have got the Nanowires on our chip, we have to do source , drain patterning now.

3.4.5 Step 5: Deposit two layer of Photoresist.

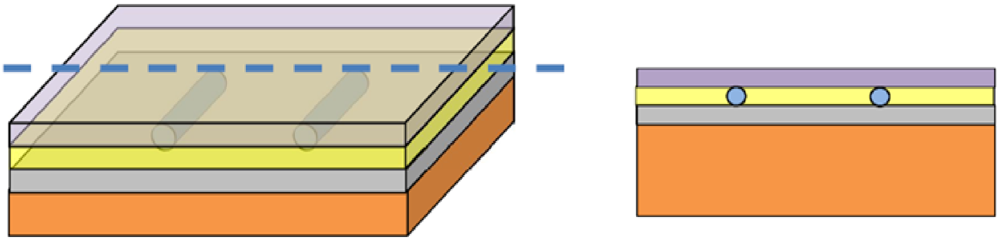


Figure 3-13:- two layer of Photoresist coated over the surface of the chip with NWs

Then we deposit a two layer of photoresist by spin coating, so that all the nanowire on the surface of chip should be covered in the first layer only as shown in the figure (3-13). Then again another a layer of photo resists is coated over the previous one.

3.4.6 Step 6: Defining the source drain region.

Now after the two layer coating of Photoresist, we have to open the window for source and drain regions in this two layers using contact lithography .So applying mask on the surface we will put this chip covered with mask below the optical lithography system.

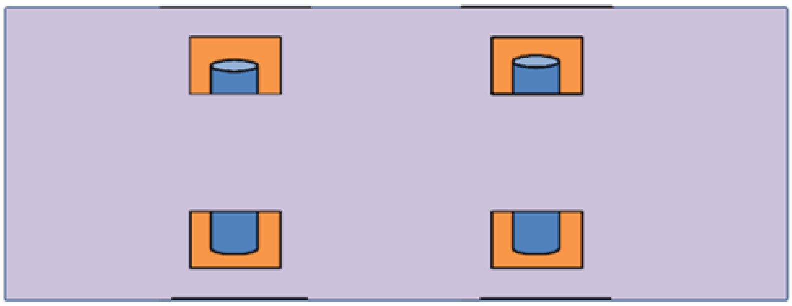


Figure 3-14:- Opened window in two layer of Photo resist for source and drain

Then after lithography we will dip this chip in the developer solution so soft area, of resist will get dissolved in the solution

3.4.7 Step 7: Depositing Nickel (Ni) for the source and drain pads.

For the making source and Drain we will only deposit nickel (metal) in this opening of the photoresist. This nanowire containing chip will be loaded in the metal evaporator, this evaporator will be evacuated to a vacuum level of 10^{-7} torr range. Then the metal is heated to evaporate and deposition starts. 60nm thick layer of Ni is deposited for the contact pads at the rate of 0.1nm s^{-1}.

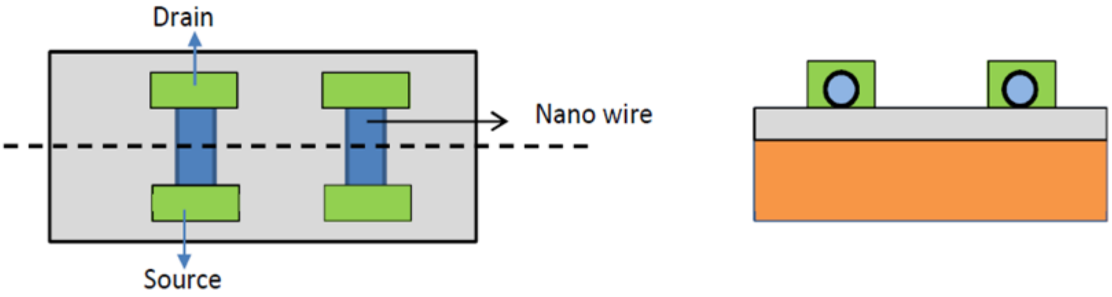


Figure 3-15 :- Source and Drain pads are deposited by thermal evaporation

After this metal deposition it should be annealed so as to make a good ohmic contact between the metal and the nanowire. So the sensor chip will be loaded in the RTA (rapid thermal anneler) at temperature 380^0C for 2 minutes.

This is the overall sensor fabrication process by bottom up approach which takes less time compare to top down approach, as it avoids the e-beam lithography process.

Chapter 4

Performance Analysis of Nanowire Sensors

4.1 Introduction:-

In life science and chemistry many measurements are taken when any target particle reacts with any surface or some surface bind receptors, e.g. when DNA is detected by protein microarrays [43]. This is the basic phenomenon behind any surface dependent sensors. Many times we encounter with problems of detecting some specific molecules from a very small fluidic volume of sample and very precious samples with very less concentration of analyte particles generally in Femtomolar (fM) range. To meet these needs scientist are exploring the minimization of dimensional properties of sensor so as samples could be analyzed very efficiently, rapidly and better selectivity could be maintained. Examples of micro scale sensors are ISFET these are silicon field effect transistor sensor in which OH^{-} ions can directly be sensed by the dangling bonds on the SiO_2 surface, microelectromechanical cantilever (MEMS) sensors which converts the molecular binding into mechanical bending and electrochemical sensors are also explored.

But if move towards Nano scale sensors like “Nanowire (NW) sensors” they require very few target molecules for detection, a few target molecules are more than enough to work for a nanowire sensor, example: if we take one Femtomolar solution, it contains one target molecule per Nano liter.

As we have reached to extremely small size for sensing very dilute solutions. So obviously some questions arise in our mind like, when the dilution limits of the solution reach?, or what are the limitations of the sensor size e.g. length or radius in case of NW sensors?, if we have applied such dilute solution how much time will it take to bind the first target molecule?, or how a better and faster sensor system could be designed?, but to answer these questions we have to go through the mathematical analysis of the conjugation and diffusion phenomenon.

However difficulty in analyzing theses system is that, they exhibits extremely varied behavior and multiple effects which tries to dominate each other with the variation of conditions. Diffusion of target molecules are random ,they may bind with other entity surfaces in ambiance, temperature of the system or the solution may also effect positively or adversely, bind molecules may dissociate from the surface etc. are such effect which should be analyzed by mathematics. Exact solution for these problems are not available but by making some approximation and simplification we could apply these for our sensor parameters.

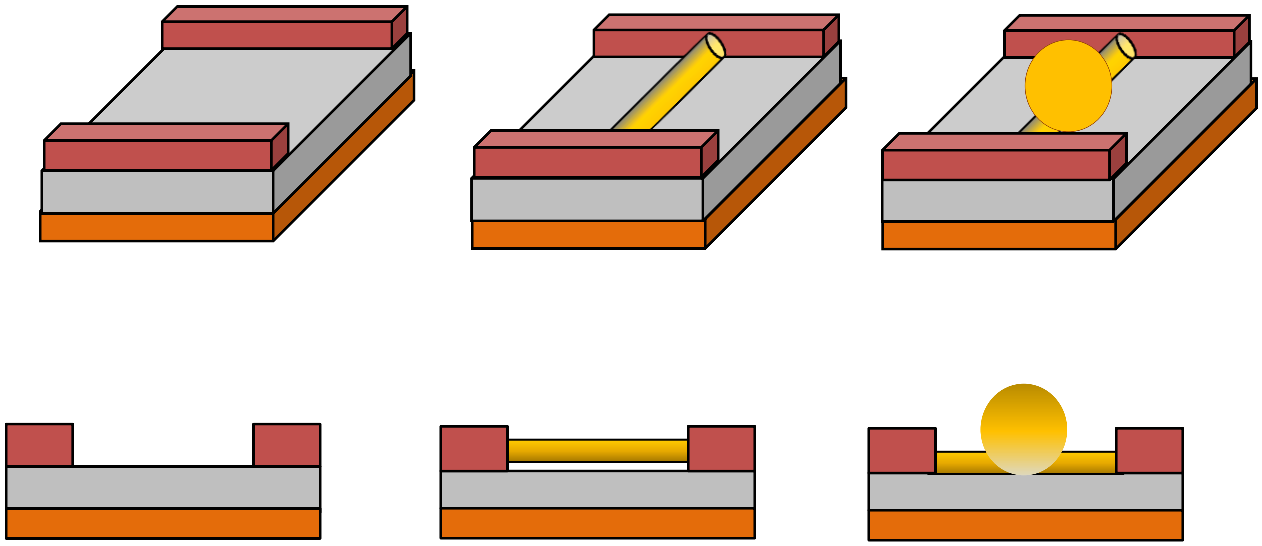
To build the sensing system easily understood we start with simplest possible target molecules diffusion through the solution. As the target molecules wander in the solution and whenever they encounter with the sensor surface they immediately bind with that. The sensor's geometry also plays role in this process as the diffusion distance is different for different dimensional system. How reaction kinetics will affect the sensor parameters based on geometrical variations will be our main focus. Radius dependent solution concentration , conjugation time detection time.

4.2 Sensor Geometries

As we are dealing with the sensor geometries , we can think of three very frequent come in all structures .

(i) Planer Sensor (1D)
(ii) Cylindrical Sensor (2D)
(iii) Spherical Sensor (3D)

These above given sensors in figure (4-1) are called 1D, 2D or 3D, conferring to their sensing directions. As in the figure (4-1)(a) i.e. planer sensor or it is termed as 1D because it always senses from only one direction, from the upper planer area. The sensor in the figure (4-1)(b) is the cylindrical or the nanowire sensor ,about which we have talked in previous chapter, its NW senses from two direction, means if we talk in the terms of cylindrical co-ordinates it is always fixed in z direction.



(c) 1D Planar ISFET

(b) 2D cylindrical ISFET

(a) 3D spherical ISFET

Figure 4-1:- Three ISFET geometries

For a particular NW its length is always fixed. The last one is the spherical sensor that can senses from its all directions, so it is also called as 3D sensor. It has a nanosphere as the sensor part as nanowires in the cylindrical. According to the sensor geometries their performance also varies. Variation of sensing area , radius of nanowire or Nano sphere, length of nanowire etc. have great effect on sensitivity of the sensor.

4.3 Kinetic theory of detection

As the detection of molecules or ions by a sensor is a chemical equilibrium type of reaction, so its kinetic analysis is also required. When any sensor is immersed in the solution containing target molecules its time to capture the specific target and the settling time (t_s) is a matter of concern as the sensitivity and detection time are important parameters in the case of sensors. So to start with reaction kinetic analysis, for simplicity the First order Langmuir kinetics is assumed [43]. If an isolated sensor is immersed in a solution containing target molecules, with the sensor surface functionalize with particular receptor for target. The target-receptor conjugation rate is given by-

$$\frac{dN}{dt} = k_{on}(N_0 - N)C_s - k_{off}N \tag{4.1}$$

Where N is the density of conjugated receptors, N_0 is the density of receptors on the sensor surface, k_{on} and k_{off} are the capture (forward) and dissociation (backward) constants.

Binding of molecules depends on the concentration of target at the sensor surface i.e. C_s and the unbound sites $N_0 - N$.

The above target- receptor conjugation model is a linear differential equation of first order and can be solved by manipulating it in the form.

$$\frac{dN}{dt} + \left(k_{on}C_s + k_{off}\right)N = k_{off}N_0 \tag{4.2}$$

And putting a boundary conditions i.e the conjugation of target-receptor will be zero at time t=0.It can be assumed that practically when we immerse the sensor in the solution at that particular time there will be no conjugation.

$$N(t) = 0 \qquad\qquad at \qquad\qquad t = 0$$

We will get a solution of this equation as

$$N(t) = \frac{k_{on}N_0}{k_{on}C_s + k_{off}}\left(1 - e^{-(k_{on}C_s + k_{off})t}\right) \tag{4.3}$$

The above equation gives the number of target – receptor conjugation $N(t)$ at any given time t. here if we define a new constant as K_D as the ratio of association and dissociation rate which appears as the natural concentration scale.

$$K_D = \frac{k_{on}}{k_{off}} \tag{4.4}$$

The equation number (4.3) can be manipulated in the form of this constant K_D, and taken one assumption that is the convection and diffusion transport phenomenon, transport the target particles and at sufficient rate ,so as the given kinetic model is reaction limited only .Then $C_s \approx C_0$,and the equation could be given as-

$$\frac{N(t)}{N} = \frac{C_0/K_D}{1+C_0/K_D}(1 - e^{-(k_{on}C_s+k_{off})t}) \tag{4.5}$$

From the above equation (4.5) we could find the fraction of bound receptors at equilibrium ,it is not a matter of concern here that how much time the sensor will take to be in equilibrium ,and it is given as-

$$\frac{N_{eq}}{N} = \frac{C_0/K_D}{1+C_0/K_D} \tag{4.6}$$

For concentrated solution $C_0/K_D \gg 1$, or equivalently we can say that $C_0 \gg K_D$, and from the analysis of this statement it can also be shown, as K_D is the ratio of association to dissociation constant and if association constant is greater than dissociation constant ,this statement will come true, and if association constant is more it means there are large number of target molecules in the solution, leads to higher concentration.

But if $C_0/K_D \ll 1$, or $C_0 \ll K_D$, in this case the solution is dilute and only a fraction of molecules will binds with the sensor ,that leads to

$$N_{eq} \sim \frac{C_0 N}{K_D} \qquad \ll N \tag{4.7}$$

Which means the equilibrium concentration of conjugated receptors is less than the receptors initially, or in other words it few receptors are filled with target and others are unfilled. This conclusion leads to many arguments as what should be the concentration for at least one reception, or how much time will it take to sense the molecules.

One more thing that could be evolved from the equation (4.3) is the time required for the sensor to come in equilibrium state.

$$\tau_r = (k_{on} C_s + k_{off})^{-1} \tag{4.8}$$

When concentration is more $C_0 \gg K_D$,in this case nearly all the receptors sites will be occupied by the target. So $N_{eq} = N$, It specifies that how long the association kinetics takes to provide sufficient molecules to the sensor surface. But if the other case comes in which concentration of the very less, and conjugated sites are very few, at equilibrium the conjugation flux and the dissociation flux requires canceling each other. But in low concentration the target particle if binds, have enough time to unbind.so the equilibrium time will be decided by the off state kinetics$\tau_r \sim {k_{off}}^{-1}$.

4.4 Diffusion Theory of Detection

Except the Kinetic theory of reaction, the diffusion of the target molecules also plays a crucial role in the detection by the sensors. As in the solution the target particles do Brownian motion and moves randomly any where. Diffusion is a random motion of the particles or any molecules in some medium due to thermal energy [17]. If the diffusion of molecules is in the direction of sensor due to some reason e.g concentration gradient or temperature, it will leads to a good detection by the sensor, but if they are not diffusing towards the sensor then it will be difficult and problem gets bigger if the solution have very less concentration.

As we have three geometries of sensors, we have to first look for how these particles diffuses in these dimensions. So we have to check first for the diffusion lengths in all the three directions , so that we could do further analysis of what are the effects of diffusion rate on detection and effects of dimension and temperature variations.

As we know that if any particle have some absolute temperature T, the kinetic energy associated with that is given as

$$K_E = \frac{kT}{2} \qquad (4.9)$$

And if this thermally generated kinetic energy is compared with the kinetic energy of a particle of mass m and average velocity v_x in the direction of x-axis $m{v_x}^2/2$.

$$\frac{m{v_x}^2}{2} = \frac{kT}{2} \qquad (4.10)$$

From the above equation the root mean square velocity of any particle is given as-

$$< v_x^2 >^{1/2} = (KT/m)^{1/2} \qquad (4.11)$$

With this much velocity particles moves in any solution, but as they are immersed in a solution so have lots of collision with other particles of the solution and they bounce back after every collision. As a result they are forced to wander around and execute Brownian motion.

Now to analyze the diffusive spreading of the particles, we should start with is one dimensional motion. As shown in figure if any particle starts at t=0 from the position x=0,

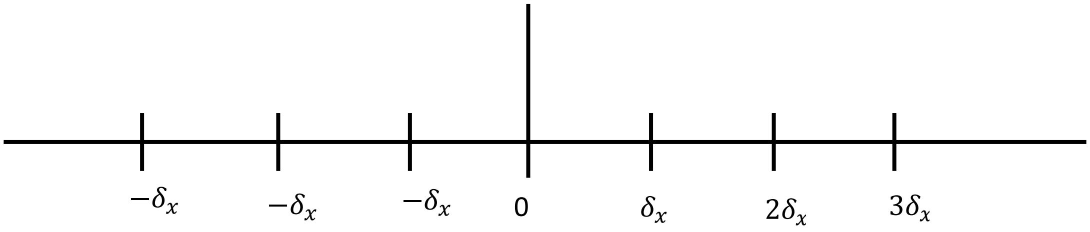


Figure 4-2:- any particle executing a random walk, from the origin and occupying the position $\pm\boldsymbol{\delta}$, $\pm\boldsymbol{2\delta}$ ….etc.

In random walk these particles follow some rules.

1. Each particles starts from the origin and moves one step either in left or in right direction with a velocity $\pm v_x$ at every τ seconds, travells a distance$\pm\delta = \tau v_x$.
2. Probability of moving either left or right is $1/2$, after collision with solution molecules they forget what they did in last step of their journey.
3. Each particles moves independent of each other, they generally do not interact with other, if the suspension is dilute.

If we have N particles and $x_i(n)$ be the position of i th particle after n th step. The position on particle will differ from its $(n-1)$ th position by $\pm\delta$.

So the position of the particle is given as-

$$x_i(n) = x_i(n-1) \pm \delta \tag{4.12}$$

And the mean displacement of n particles are given by

$$< x_i(n) > = \frac{1}{N}\sum_{i=1}^{N} x_i(n-1) \pm \delta \tag{4.13}$$

The mean position remains the same i.e. origin , but the particles spread in both the direction symmetrically about the origin.

But how much do the particles spread? A appropriate measure is root-mean –square displacement. So we will take the square of the equation (4.13) and then the mean of that.It will come as-

$$< x^2(n) >=< x^2(n-1) > +\delta^2 \tag{4.14}$$

For n = 0,1,2……n , we get $< x^2(0) >= 0$, $< x^2(1) >= \delta^2$, $< x^2(1) >= 2\delta^2$…..and for n it is $< x^2(n) >= n\delta^2$.

So from here we can conclude that mean square displacement increases with step number n, and if the root of displacement is taken then it will be proportional to root of n. As we know from the rule number 1, that any particle will take time $t = n\tau$ for moving n steps.so from this conclusion we can say that n is proportional to t, for the mean square displacement. If we take the root of mean square displacement it will be proportional to root of t.

From the above we can say that $n = t/\tau$, so if we put this in the n^{th} mean square displacement it will become-

$$< x^2(t) >= (t/\tau)\delta^2 \ = (\delta^2/\tau)t \tag{4.15}$$

The diffusion coefficient is defined as the $D = \delta^2/2\tau$ with the unit cm^2/sec.so the above equation could be written as-

$$< x^2(t) >= 2Dt \tag{4.16}$$

And the root of this

$$< x^2(t) >^{1/2}= (2Dt)^{1/2} \tag{4.17}$$

The above is root mean square displacement for one dimensional motion called as the diffusion length at time t. The Diffusion coefficients (D) characterize the migration of a given sort of particle at a given temperature. Generally depends on structure of medium, particle size and its absolute temperature.

In the figure (4-3), it is shown there the equilibrium analyte distance from the sensor surface, after the conjugation starts on the surface a depletion zone starts to create because the molecules near the sensor surface have been already collected by the sensor.

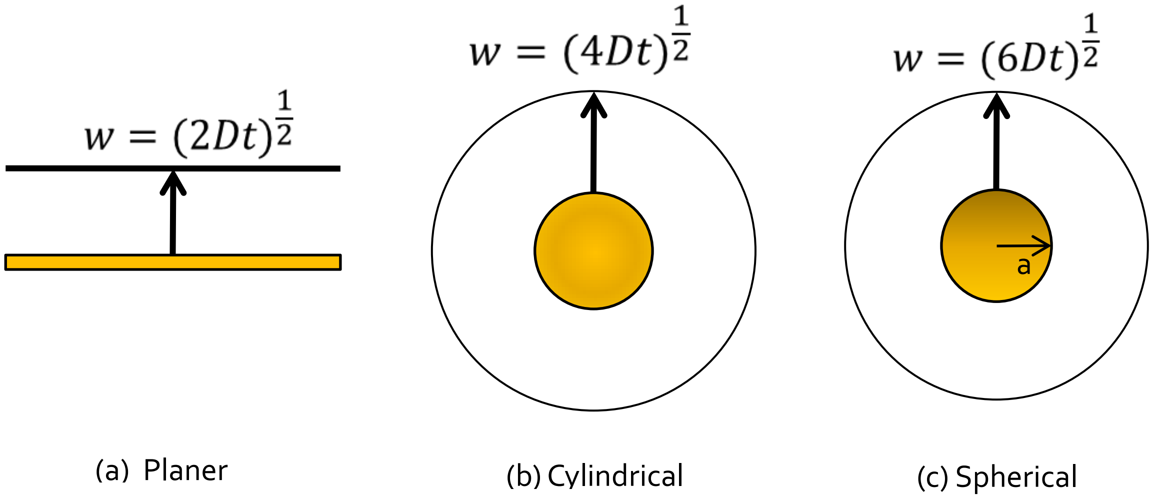


Figure 4-3:- The three sensor geometries ,where w is the equilibrium analyte distance.

So at equilibrium which comes after time ,the equilibrium distance is given by the root mean square displacement as given in equation (4.17) for planer surface sensor (1D).

Similarly this equilibrium analyte distance for the 2D cylindrical and 3D spherical sensor can also be given. For 2D and 3D sensors we have y and z directions also except the x direction. As for $< x^2 >= 2Dt$, it will be same for each direction $< y^2 >= 2Dt$ and $< z^2 >= 2Dt$ .But in 2 dimension the distance is given as $r^2 = x^2 + y^2$ therefore,

$$< r^2 >= 4Dt \qquad or \qquad < r^2 >^{1/2}= (4Dt)^{1/2} \tag{4.18}$$

In three dimensions this distance is given by $r^2 = x^2 + y^2 + z^2$ and,

$$< r^2 >= 6Dt \qquad or \qquad < r^2 >^{1/2}= (6Dt)^{1/2} \tag{4.19}$$

As the diffusion of the Target molecules is set by concentration gradient then this diffusion is governed by the Fick’s diffusion equation –

$$\frac{dC}{dt} = D\nabla^2 C \tag{4.20}$$

Which states that time rate of change of concentration is proportional to the curvature of the concentration function and the proportionality constant is D.

At equilibrium $dC/dt = 0$, so the above equation (4.20) is reduced to

$$\nabla^2 C = 0 \tag{4.21}$$

The above equation is three dimensional Laplacian. For different geometries which we have to change the co-ordinate systems for the solution of the above equation.

For the case of Nanowire sensors we have to consider the cylindrical symmetry of NW, and the above equation (4.21) can be given like-

$$\frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r} = 0 \tag{4.22}$$

And for the spherical sensors with spherical symmetry conditions it will be given like-

$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right) = 0 \tag{4.23}$$

The solution of the above equation is given as

$$C(r) = C_1 + \frac{C_2}{r} \qquad (4.24)$$

The concentration variation can be considered from the sensor's axis and taking the radius of the spherical and cylindrical sensor to be a. The boundary conditions are given like, when $r = a$, at the surface of the sensor concentration $C = C_s$ and at distance $r = a + w$ at equilibrium analyte distance the concentration will be initial i.e.$C = C_0$. Putting these boundary condition we get the solution of the above equation (4.24).

$$C_r(r) = C_s - \frac{C_S - C_0}{\frac{1}{a} - \frac{1}{a+w}} (\frac{1}{a} - \frac{1}{r}) \qquad (4.25)$$

As the above given equation denotes the concentration variation, the flux due to this concentration variation is given by, $J_r(r) = -D\, \partial C/\partial r$.

So the flux for spherical symmetry problem is given by using the above equation –

$$J_r(r) = \frac{D}{r^2} (\frac{C_0 - C_S}{\frac{1}{a} - \frac{1}{a+w}}) \qquad (4.26)$$

So the over all particles adsorbed by the spherical sensor is given by-

$$I = J.A_S = \left(\frac{4\pi D}{\frac{1}{a} - \frac{1}{a+w}} \right) (C_0 - C_S) \qquad (4.27)$$

In the above equation if we replace the D by ∈ in the term in the first bracket, the first term will become the capacitance given by a spherical cell of inner radius a and the outer radius $a + w$.

Similarly if we can find the above relation for the Cylindrical nanowire case as-

$$I = J.A_s = \left(\frac{2\pi D}{\log\left(\frac{w+a}{a}\right)}\right)(C_0 - C_s) \tag{4.28}$$

And for the planer sensor case similarly-

$$I = J.A_s = \left(\frac{DA}{d}\right)(C_0 - C_s) \tag{4.29}$$

In the above two equations in (4.28) and in (4.29) if we replace D by ∈ in the first term in bracket, they are the capacitance by cylindrical shell and a parallel plate capacitor respectively.

So in general we can write the above three equation of over all flux on the surface as

$$I = JA_s = C_{Ds}(C_0 - C_s) \tag{4.30}$$

Where C_{Ds} is the diffusion dependent capacitance. This capacitance due to diffusion is also dependent on the w which is the equilibrium analyte distance that depends on time , so this C_{Ds} is also time dependent so we can replace it by $C_{Ds}(t)$.

Now for the equilibrium to achieve the diffusion generated flux should be cancelled be the receptor-target conjugation flux of kinetic theory [46] given in equation (4.1). For large value of $K_D \sim 10^5$ and N_0 the equation (4.1) could be written as-

$$\frac{dN}{dt} \sim k_{on} N_0 C_s \qquad (4.31)$$

So for the equilibrium to be achieved the equating equation (4.30) and (4.31) we get the result-

$$N(t) = C_0 t \ \left(\frac{A_s}{C_{Ds}(t)} + \frac{1}{k_{on} N_0} \right)^{-1} \qquad (4.32)$$

This equation is an important result for the sensors of different geometries, it predicts that concentration of solution grows linearly in time under steady state conditions .we can find some results about the expected time of detection by different sensors with different geometries as this equation involves the geometry dependent diffusion capacitance term.

4.5 Results

In the figure (4-4) we can see the tradeoff between settling time and different detectable concentration, as we can analyze that at the concentration of 1000fM that is a quite less concentration. In this case also the spherical sensor can detect the first molecule in 10 to 20 seconds and the cylindrical sensor can take about 1000 sec to detect. However we can see that the planer sensor with larger surface area has the detection time about 10^{10} seconds. This is quite impractical kind of time for detection by a sensor. Therefore we can say from this graph that cylindrical NW and the spherical sensors have the detection limit five to six times higer than that of the planer sensor. As this result is plotted for the cylindrical and spherical sensor of radius 20nm, but if we plot it for 10 nm radius or sub 10nm range the detection time will become more lessor in 10 and 100 of milliseconds.

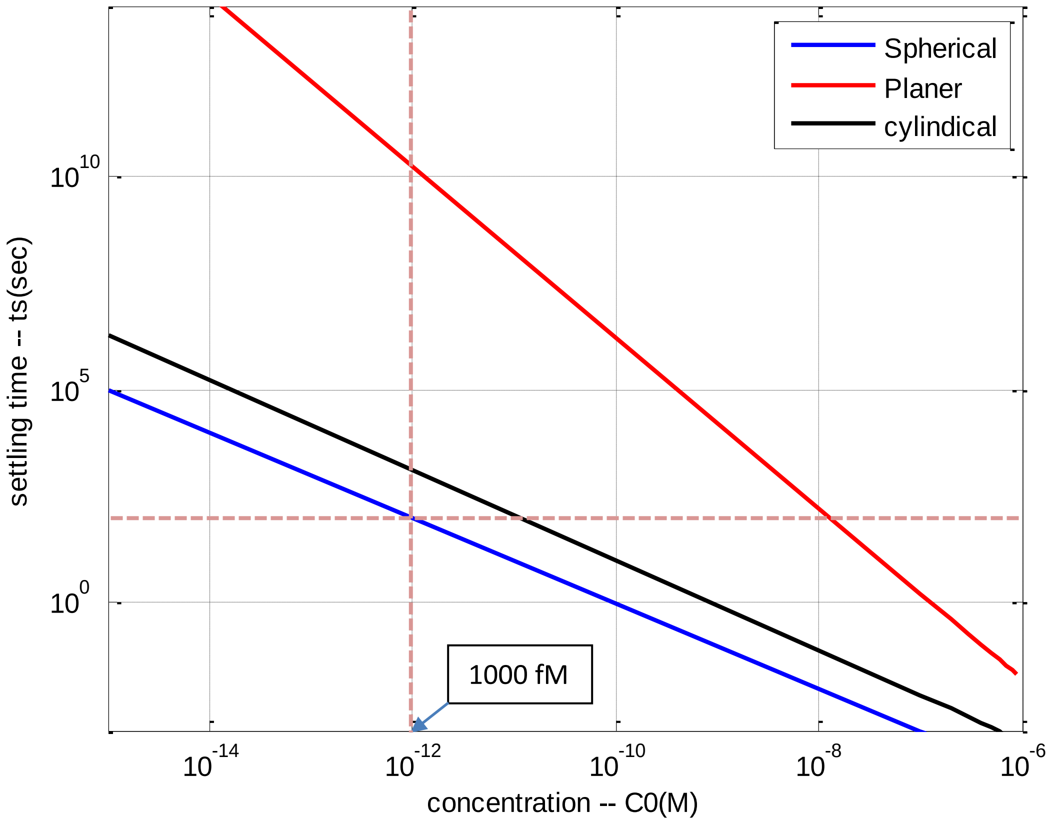


Figure 4-4 :- Settling time of detection graph for different concentration for different sensor geometries, the graph is plotted for the radius of 20 nm.

We can check the nanowire sensor performance for the variation in the diffusion constant ,for different target molecules and for different solvent the diffusion constant could vary ,except this temperature also effects the diffusion constant. So from figure (4-5) it can be analyzed that is the

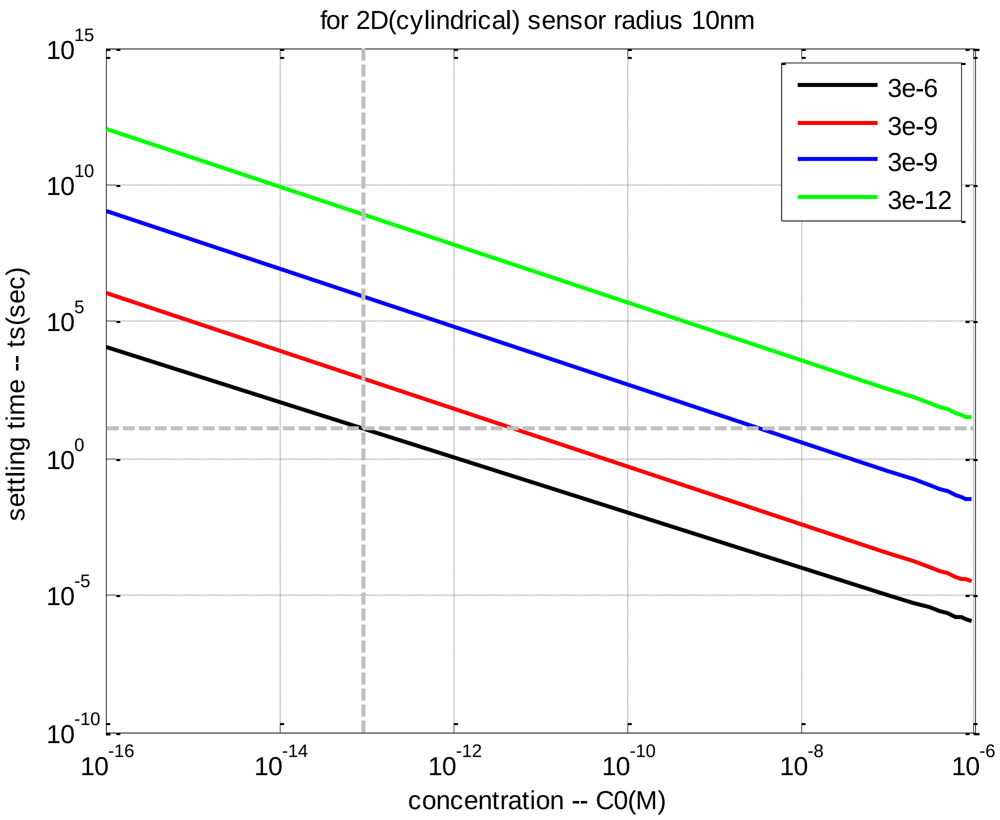


Figure 4-5 :- The plot of concentration and settling time of cylindrical sensor radius 10nm , with varying diffusion constant

The Diffusion coefficient is more the detection time will be less, as molecules diffuses faster to the surface of nanowire sensor . We can see in the figure (4-5) that 100fM concentration can be detected by a 10nm radius nanowire sensor within 10 seconds, that is a good performance for a NW sensor. But if the diffusion constant decreases the performance of these NW sensors also reduces.

The most important analysis is the radius variation of nanowire sensors in geometrical analysis we should have the thing in our hand is radius of nanowire as it can also be analyzed that "if the radius will be less the sensor's sensitivity will be more". This statement can also be analyzed in the by figure (4-6) , that the nanowire with radius 5nm can even sense the 10fM concentration

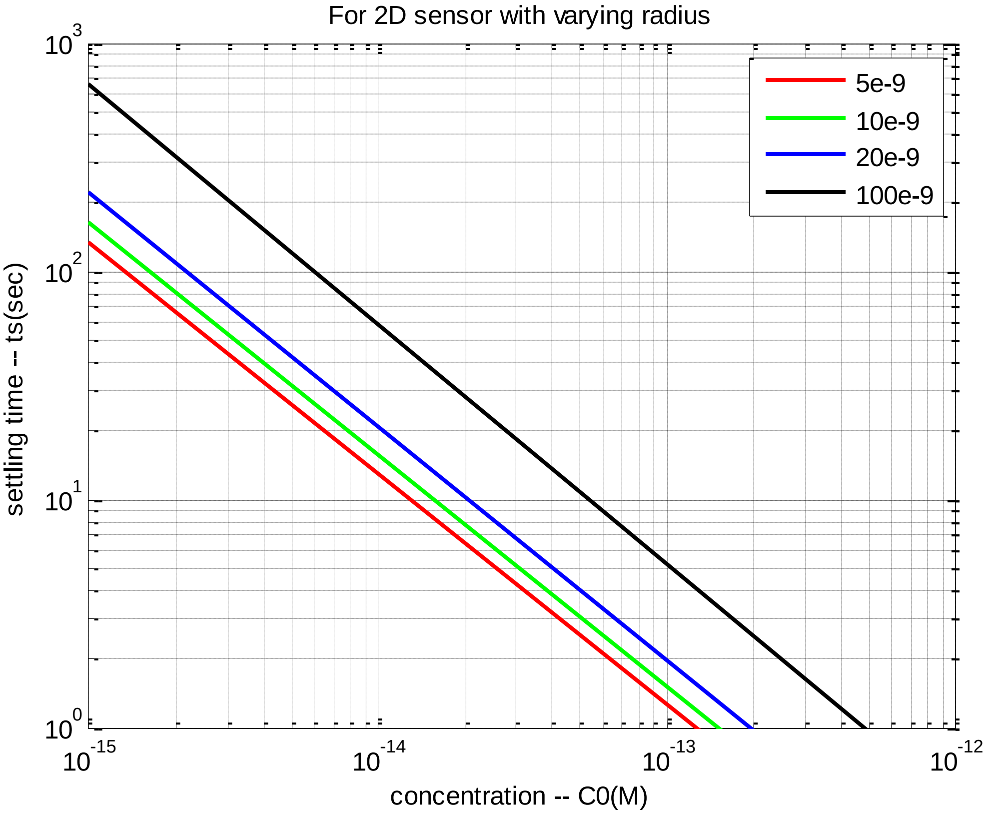


Figure 4-6 : - A plot of concentration and settling time for different radius of the Nanowire

Solution with a small detection time of 10-13 seconds. Moreover a 100fM solution can be detected with 1-2 seconds time. A similar result for spherical sensor with the radius variation is given in appendix (A). So clearly it can be generalized that reducing the radius will increase the sensitivity of the sensor for lower concentration detections. However in case of radius reduction the for radius less than 10 nm, the forward reaction constant start to play role and below 5 nm if we increase the reaction constant sensitivity increases.

Chapter 5

Conclusion and Future work

There are two approaches of fabrication of these semiconductor nanowire sensors are available one is Top down and the other one is Bottom up approach, but in today's scenario mainly top up approach is preferred. As this approach has a long background and its technology is quit matured, this approach is strongly recommended in case of packaged and integrated device application. It is due to improved quality of electrical characteristics found by top up approach e.g. the Ohmic contacts between nanowires and metal contacts is better than the bottom up approach. On the other hand the bottom up approach is better in sense of reducing the time requirement and cost reduction. However this technology is not quite matured, that we could grow any device of any architecture. As in our case sensor fabrication by bottom up approach we have seen that after growth of nanowire by bottom up approach , we have moved to the top down approach for further processing. But it has its own advantages also like in case of Top down approach we cannot make a nanowire with circular cross section but by Bottom up approach using VLS process it is quite simple. E-beam lithography in the top down is a quiet time consuming and costly process. So analyzing all this, it can be concluded that those methods should be searched for fabrication, which involves the both the approaches top down and bottom up and it will be cost and time effective.

As the sensitivity achieved until by these sensor is in Femtomolar range which is still lagging from the conventional label based method, by using porous nanowire and smaller radius nanowires it could be achieved . In our analysis we have shown that as the radius of nanowire is reducing it sensitivity is increasing but fabrication of nanowires with radius less than 5nm is still a matter of research because of limitations of e-beam lithography. Spherical sensors can be used in place of nanowire sensors as they show better sensitivity but a making a nano sphere and then processing on it is a very tedious task. But one can go for the technological improvements so that this Nano sphere fabrication could easily be achieved, and using these Nano spheres we could achieve higher sensitivity and direct real time detection.

Appendix. A

The plot of Nano sphere sensitivity with varying radius and accumulation time in seconds. It shown there the first molecules detection for 100fM concentration of target in solution.

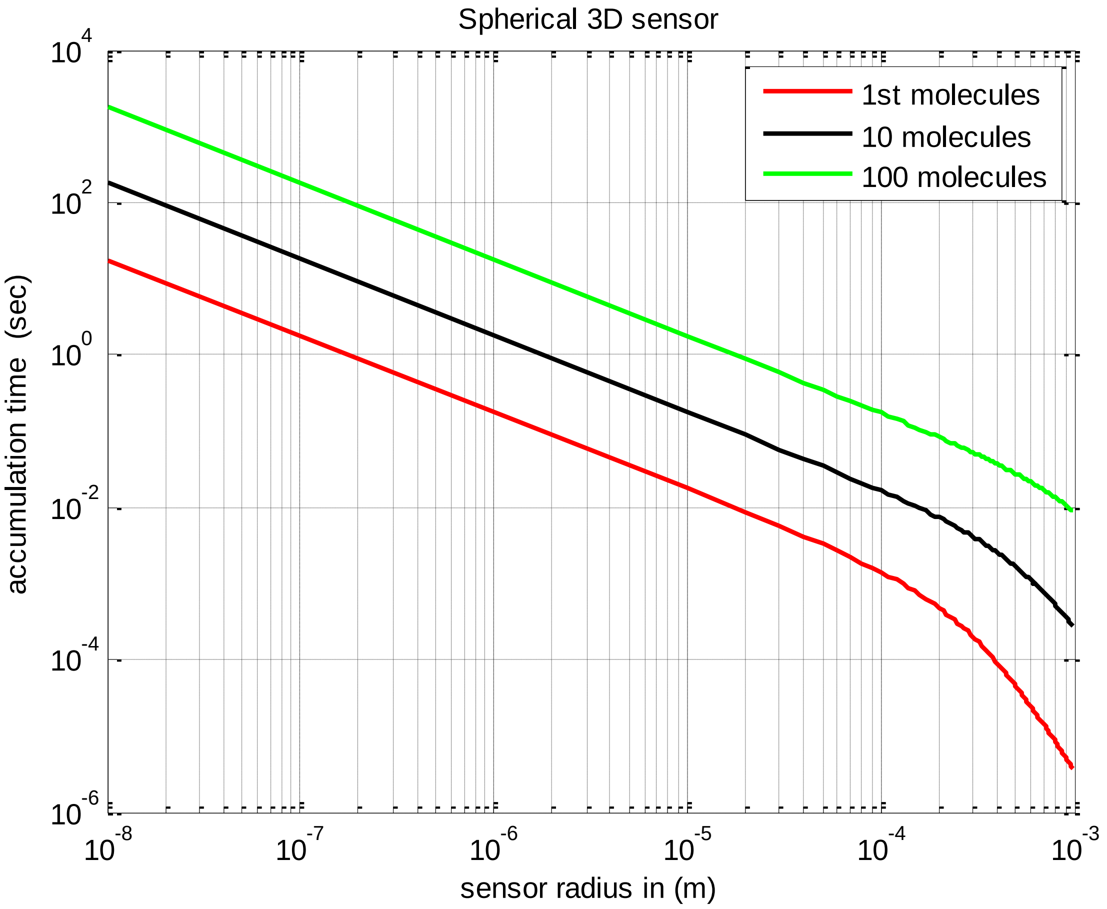


Figure A.1 – A radius verses accumulation time graph for Nano Sphere sensor [46]

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