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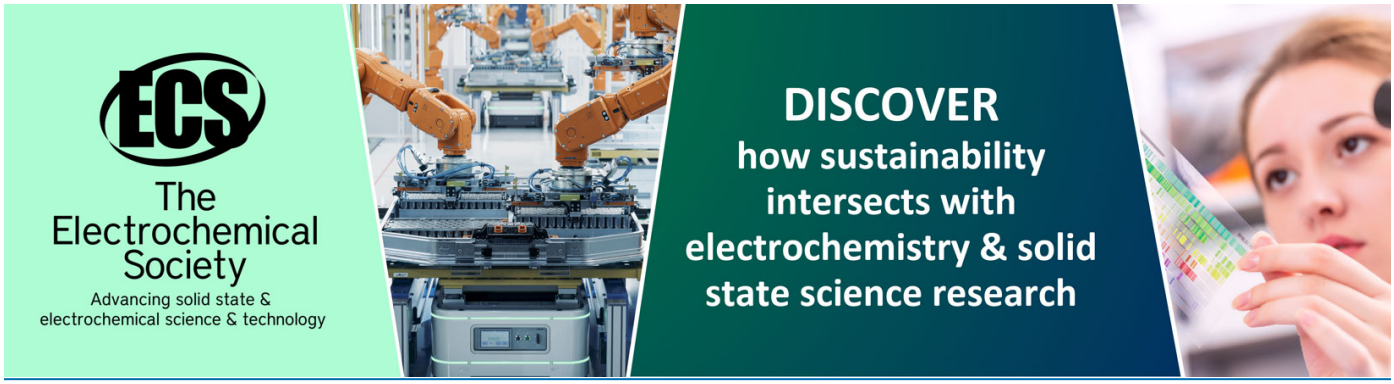


Investigation of Graphene as a Sensing Layer for Future Prostate Cancer Biosensing Applications

A Sarkar[1,4], M Sreenath[2], K Srinivas[1], N V Teja[3]

[1] Electronics and Communication Engineering, Vishnu Institute of Technology, Bhimavaram, Andhra Pradesh, India-534202
[2] Electronics and Communication Engineering, Audisankara College of Engineering & Technology, Gudur, Andhra Pradesh, India - 524101
[3] Electronics and Communication Engineering, Sree Vidyanikethan Engineering College, Tirupati, Andhra Pradesh, India - 517102

E-mail: argha15@gmail.com

Abstract. The work proposes simulation, characterization and synthesis of sensing layer for bio sensor application. So far no curable treatment is there for prostate cancer if it is not treated at earlier phase i.e. in right time. So biosensor is having major impact on detection at initial phase. Next generation sensor (NGS) includes graphene. This paper proposes biosensor and in the regard of graphene, and same will be analyzed for sensing layer. Chirality (associated with chiral indices and chiral angle) and electrical properties of grapheme along with some key properties are also simulated in ninithi software and comparison of mathematical model is also reported. So we have followed a substrate free easy way to produce graphene at atmospheric pressure. This process could be an easy and comparatively inexpensive method for preparing graphene. Finally the synthesized graphene is characterized by Scanning Electron Microscope (SEM) and the crystal growth is visualized through X ray diffraction (XRD) which are thriving implementation for a biosensing platform.

Keywords — PCa (Prostate cancer), Graphene, Chirality, Synthesis, PSA (Prostate specific antigen).

1. Introduction

Prostate cancer (PCa) is a disease which only affects men. This is a kind of disease which must be detected at the early stage otherwise it may cause death. The word "prostate" is derived from Medieval Latin prostate and Medieval French prostate. The ancient Greek word prostates means "one standing in front", from “proistanai” meaning "set before". The prostate is so called because of its position - it is at the base of the bladder.[1] Prostate cancer is mostly seen in men in the UK. It is observed that over 40,000 new cases are diagnosed every year. In Canada one in eight men will be diagnosed with the disease in their lifetime. [2] The life style, food habits are changing day by day as the globalization is going on. It causes the rise of Non communicable disease (NCD) like diabetes, cardiovascular problem, cancer etc. Prostate cancer (PCa) has become a great concern of present days. It is associated with the intake of vitamin E, selenium, lycopene, vitamin C etc.[3] PCa is one of the leading cause of men death from the variety of causes[4]. Now a days, it is not restricted to western countries, Asian countries like Inida is also suffering from prostate cancer as per the report of population based cancer registries (PBCR)[5]. It is mostly occurs in the elderly men around 65years of age, and the chances of occurrence is rare before the age of 40 [6]. Sensing of prostate cancer detection using nanoelectric sensor is done

by a field effect transistor where graphene will act as a semiconducting channel [7]. When the surface of graphene absorbs specific bio molecules, then conductance changes rapidly. Since graphene is featured with high level of adsorptive capacity, incraesed surface to area ratio and quick response time, it may be used as sensing element. Thus the electrical properties like conductance capacitance changes appreciably for ionic cells.[8] So the graphene is synthesized and the investigation is made on graphene for the sensing channel as well as the transducer element.

2. Prostate Cancer and Biosensor

Prostate cancer is fatal when the growth and division of prostate cells becomes uncontrollable. In vast cases it is termed as adenocarcinoma. A prostate cell is cancerous when,

- Growth becomes uncontrollable
- Abnormal structure
- Ability to change position from one part to another part of the body.

Prostate cancer is a slow growing phenomenon. Having prostate cancer one can live many years without even knowing that he is having cancer. 80% of all men I their sixties die of prostate cancer but nobody knows. Sometimes it is dangerous also. If it is not detected at right time it becomes impossible to diagnosis. Prostate cancer initiates with little change in shape and size of the prostate gland cells, which is called Prostate Intraepithelial Neoplasia (PIN). Most of the men of around 50 years of age have PIN. But all the cases are not same. Main concern is that whether prostate gland cells are changing with high grade or low grade. High grade implies abnormal and low grade implies more or less normal. But strict monitoring with time to time is necessary. A patient having high grade PIN means he has a greater risk of having cancer cells. Prostate Specific antigen is also a great issue to detect cancer at early stage.

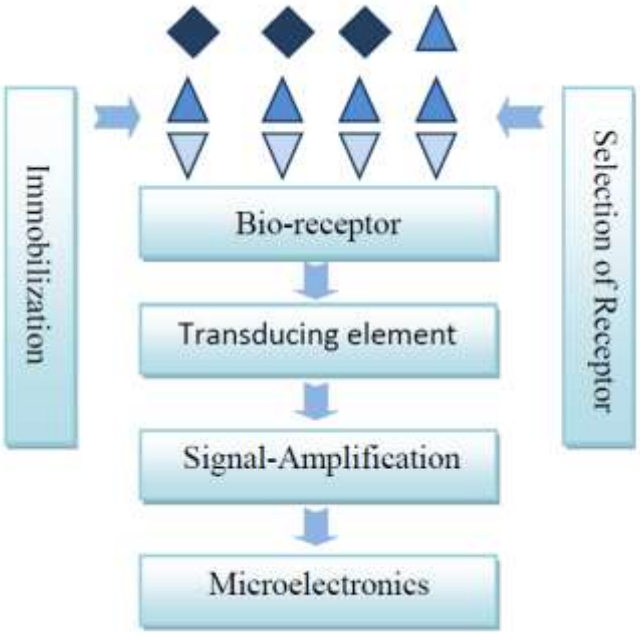


Fig.1 Schematic Block Diagram of Biosensor

PSA (Prostate Specific Antigen) is a protein which is produced by the epithelial cells of the prostate gland. Main function of PSA is to keep semen in the liquid state. PSA is a great concern for cancer issue. Some PSA also goes to the blood stream. So man's blood should be checked, that means if a sensor can be designed which will measure the PSA levels in the blood stream. The sensor output will tell whether PSA levels of men is high or low, and according to that chance of prostate cancer condition can be determined. Prostate cancer should be identified at the early stage, once it is spread

diagnosis becomes impossible. High PSA level does not always implies cancer has taken place. It indicates something may be going wrong in the prostate, so that one can take care of that and if there is a chance of caner then proper treatment can e started from the initial stage. Male hormones like testosterone affect the growth of prostate and the amount of PSA produced. At the time of adolescence the prostate gland is slowly grown. If the male hormones are low at that time, the prostate gland will not grow to proper size. On other hand, if the secretion of male hormone continues to grow, specially the part around the urethra. As a result, urine cannot be passed properly and urethra collapsed. In this way, prostate gland becomes too big and it is then called Benign Prostate Hypersia (BPH). BPH is not cancer but medical care should be taken [9].

The PSA concentration in the serum normal (0-4ng/ml), decides the critical stage [10]. So, it is very significant to detect PSA concentration to understand the cancer stage. The graphene could be one of the ultra-sensitive materials to detect and differentiate various forms of isoforms and it can be used as a sensing layer for field effect transistor biosensor [11]. Bio-receptor and transducer are the two fundamental part of a bio-analytical device. The bio-receptor functions for recognizing the target analyte i.e. the reaction with the cell or molecule of the analyte (shown in fig.1). The purpose of using the transducer is to convert the biological reaction into a computable signal. To design a sensor, it is very crucial to ensure the sensitivity, selectivity and specificity for real time environment.

3. Simulation and Structural Characterization of Graphene

The simulation of different graphene structures have been visualized and characterized in Ninithi, from nanohub. The corresponding analysis has also be done using this tool where the graphs shows electrical behavior [12]. Graphene is basically planer sheet of carbon atoms and the structure of the planer sheet seems to be a honeycomb and here each C atom is chemically bonded with another three C atoms. It is sp3 hybridized. Nanoribbon is the selective portion of grapheme sheet. The term chirality is very much relevant to characterize the graphene structures and it is represented by chiral indices (n,m). Equation 1 is the equation of chiral vector which is the fundamental equations to describe the chirality. Chiral vector and its associated chiral angle, chiral indices are projected on a plane sheet of simulated graphene in the figure 2.

$$C_h = n\bar{a}_1 + m\bar{a}_2 \quad \text{.....(1)}$$

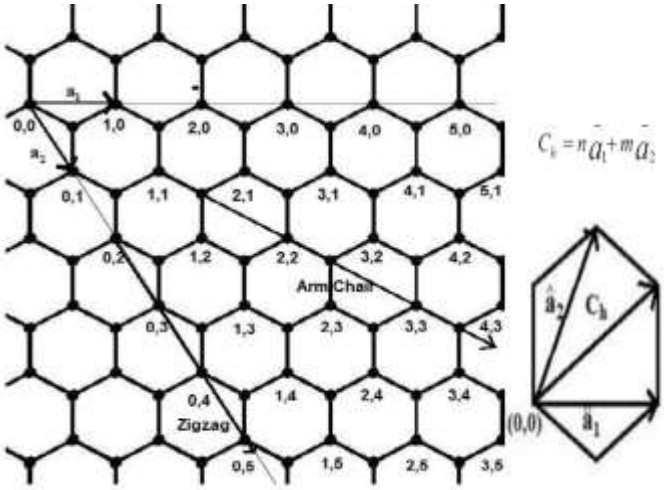


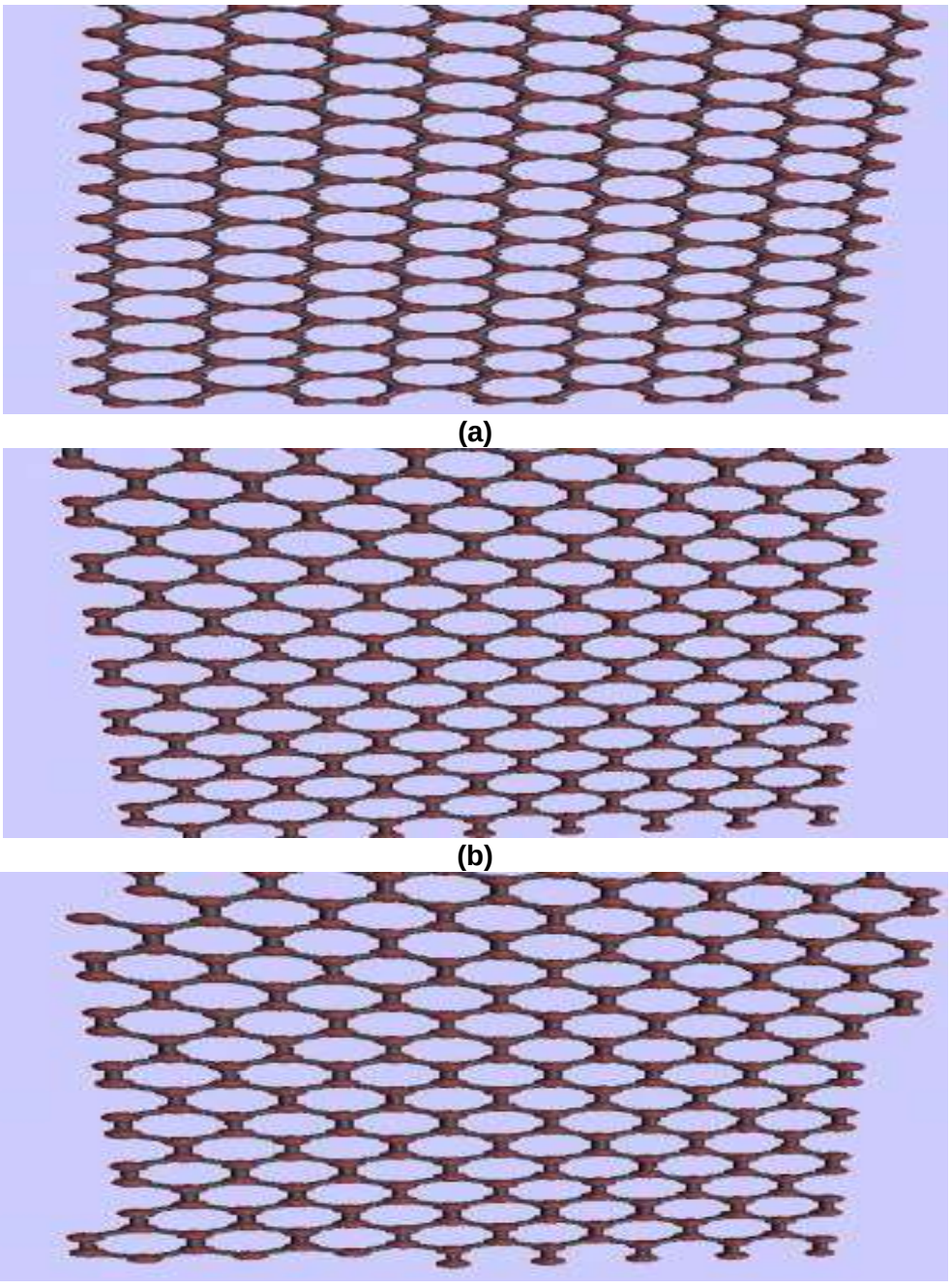
Fig. 2: Hexagonal lattice structured graphene sheet

Where, $\bar{a}_1$, $\bar{a}_2$ represents 2D graphene lattice vectors. The chiral angle manages the chiral indices and the chiral angle is denoted as [13].

Mathematically,

$$\theta = \tan^{-1}\sqrt{3}m/(2n+m) \quad \text{.....(2)}$$

Depending on the chiral angle & chiral indices, arm chair, zig-zag or chiral is simulated. A careful observation of figure 3 provides a significant understanding of the different structure of outer end of the tubes like zig-zag, arm chair etc.



(a)

(b)

(c)

Fig.3: Structural variance in the outer end of the tube and the formation of (a) Zigzag (0, 13) (b) Armchair (13, 13) (c) Chiral (13, 11)

Again from figure 3 and figure 4 we can observe the structural similarities. Mathematically the different types of graphene like zigzag arm chair are plotted and simulated by ninithi maintaining same chiral indces. It is observed that same structure is obtained for the specific chiral values.

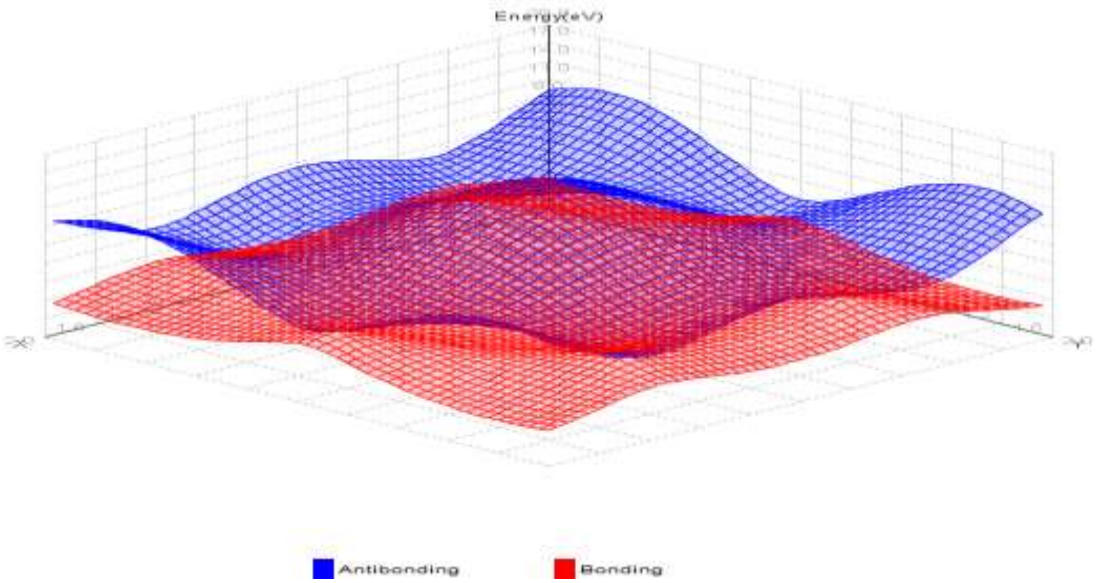


Fig. 4: E-K diagram of grapheme having C-C transfer energy 3.013 eV

The energy (E) – wave momentum (K) diagram is very much essential to realize the mathematical energy – wave momentum formalism for carriers and band structure into useful investigation of about the energy levels of electrons in the simulated or synthesized graphene. Figure 4 shows the band structure of graphene and the bond length 1.42 angstrom, C-C transfer energy 3.013 eV. The overlap integral is set to 0.129 and site energy of 2p orbital is zero. Here blue colored portion signifies the antibonding bands and the red colored portion signifies the bonding bands. It is reviewed that the graphene posses higher conductivity which is very much meaningful to choose as a sensing material [14].

4. Synthesis of Graphene

PECVD, Microwave PECVD are the common method to form nanostructures of graphene. Graphene generally formed on the substrate, bulk layers of graphite or three dimensional carbon structures. But here the new process of synthesizing graphene does not involve substrate. Whole process is done in gas phase at atmospheric pressure. [15]

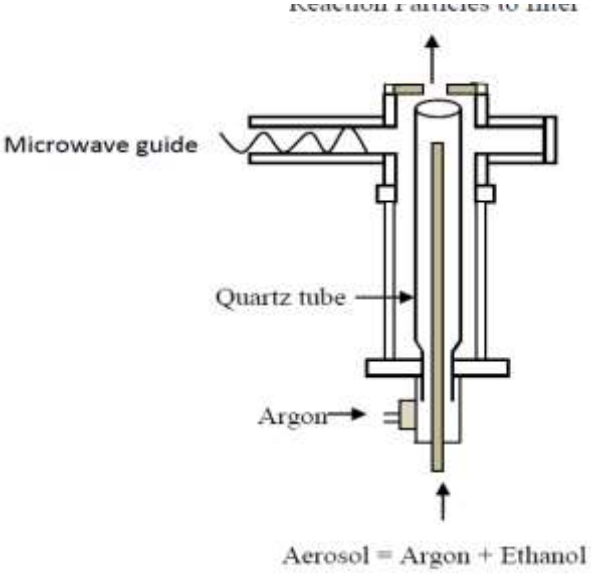


Fig 5. Schematic diagram of microwave plasma reactor.

The experiment is done at atmosphere pressure using a microwave plasma reactor whose operating frequency is about 2.5GHz. The experimental set up for plasma reactor is shown in figure 5. To produce argon plasma, flow of argon gas is needed. From argon gas cylinder it is passed through quartz tube which is placed within the reactor. The tube is having 20mm diameter. The flow rate of argon is 1.7L/Min. A comparatively smaller tube of alumina is placed concentrically within the quartz tube which is having diameter almost 7 times of alumina tube. The purpose of putting the alumina tube is to pass an aerosol (argon gas 2 L/min and ethanol droplets 4*10-4 L/min) to the argon plasma. The residence period of ethanol droplets is of the order of 10-1S inside the plasma. In this short span of time ethanol droplets is evaporated and dissociated in plasma, resulting solid particle dust. Finally it is cooled down and filtered and the solid carbon particles are collected. Collected graphene is then send for sonication for 10 minutes. The homogeneous black powder is obtained. The synthesized graphene is shown in the figure 6.

Fig.6: Synthesized grapheme

5. Results & Discussion

The deposition of the synthesized graphene is performed on the silicon wafer for XRD purposes. After cleaning the silicon wafer in sanicator and H2SO4 and HCl (2:3 ratios) solution is made. Graphene is

added in that solution. The spin coater is sued for uniform deposition of the solution is uniformly deposited above the wafer. Then the wafer is dried and prepared for XRD and SEM analysis (given in fig.7). Fig.7 shows the SEM image of synthesized graphene.

Fig.7: Graphene deposited on Silicon wafer

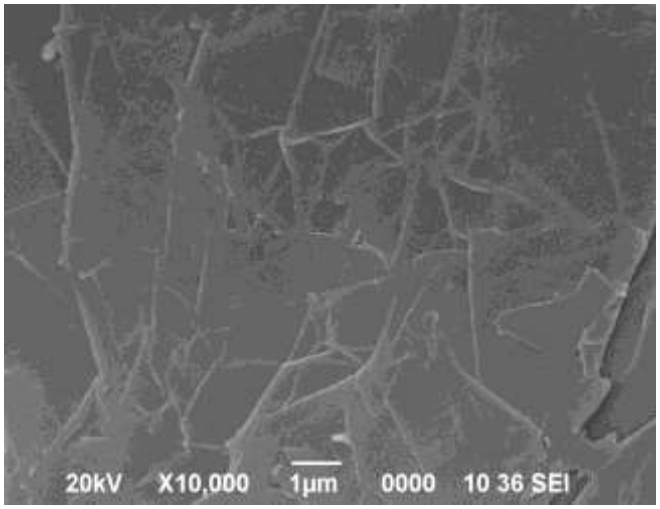
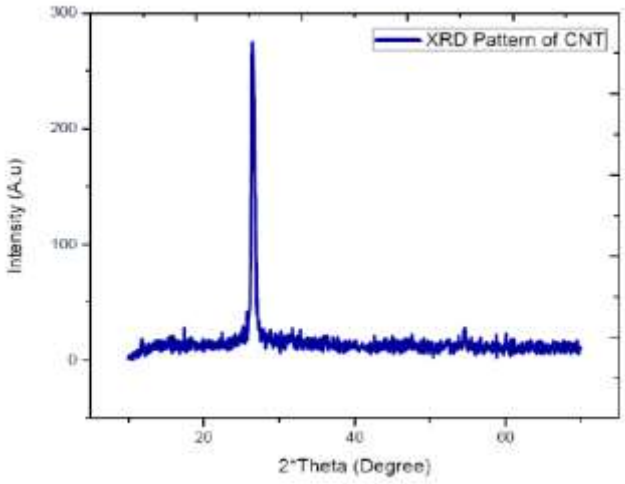


Fig.8: SEM image of graphene

The crystallinity of graphene is analyzed using X-ray which is illustrated in fig.9 (a) and (b). The in-plane diffraction techniques quantifies the scattered diffracted beams which is nearly parallel to the sample surface and hence measured lattice planes that are perpendicular to the lattice surface.

(a)



(b)

Fig. 9 : (a) XRD set up **(b)** XRD plot of Graphene

The diffraction peaks in XRD pattern at ~260 is the reflection from (002). Here the best thing is we have got only one sharp peak which shows the good crystallinity with great level of sensing behavior. The average particle size depends on the peak and can be determined by the Debye-Scherrer formula.

$$D = K\frac{K\lambda}{\beta Cos\theta} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

Where, d = Crystallite size, = Wavelength of the X ray radiation, K is normally 0.89, 2θ is the Bragg angle of a specific peak, is the broadening half at half maximum intensity.

6. Conclusion

Graphene is found to be an appropriate material which can be incorporated as a semiconducting channel in a transistor configuration [16]. The chiral indices are plotted manually on the graphene sheet and structural differences between zig-zag and armchair at the outer end of the sheets are realized and compared with the simulated graphene. E-K diagram for valance bonding, antibonding both bands are discussed. On other hand, the easy and feasible way to synthesis graphene is achieved and good crystal growth at (002) orientation is obtained from the XRD and characterized by SEM. In this paper we have seen different characteristics of graphene as a bio sensing device which will be

usually detection of prostate cancer. Thus prostate cancer can be detected at the curable stage. We are working to develop a device with the help of graphene as a sensing layer.

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