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Research paper



Silicon dioxide based Nano sensor to measure glucose level in blood

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Abstract

Diabetes is a growing problem affecting many people in the world. Diabetes leads to various complications like lower limb amputations, blindness, cardiovascular disease etc. Diabetes has many complexity that is reduced by individual monitoring and control of glucose level. Glucose level monitoring occur with recent development in Nanotechnology. Nanotechnology develops nanosensors which measure glucose level. Nanosensors fabricated by silicon dioxide in mass production reduces the cost of the nanosensors. Nanosensors made of silicon dioxide read the blood samples of a person without diabetes and a diabetic person with the help of SIGVIEW and analyzed using MATLAB. Statistical analysis is made with comparison of spectrogram, magnitude response, probability distribution, time domain and the autocorrelation of normal blood signals and diabetic signals. Comparison results in separation of a normal and diabetic person with an excellent performance of nanosensors in mass production.

Keywords: *Diabetes; Nano Sensors; Nanotechnology; Silicon Dioxide; Surface to Volume Ratio.*

1. Introduction

Nanotechnology has many applications in various fields. Nanotechnology play a major role in nanopowder nanomedicine especially for disease diagnosis. Nanotechnology uses nanosensors for disease diagnosis in nanomedicine. Nanomedicine aim to reduce side effects and increase the cure rate. Nanomedicine intent for early detection of many diseases with nano sensors [1] [2]. Nanosensors fabricate with various nanopowders. Nanopowders commonly used in nanosensors namely Cu_2O, ZnO, Feo Ag, Au, SiO_2. Cu_2O nano powder has great potential in disease diagnosis. Cu_2o nanopowder limits the application because of toxic preparation method. Toxic preparation method of Cu_2o leads to next nanopowder.Nano powder ZnO has high surface to volume ratio preferred in nanosensor.Nanopowders ZnO, Ag and Au materials not preferred due to the cost in mass production of nanosensors[3]. Nanopowder Iron oxide increase the content of enzymes in blood. Increase of enzymes in blood raise the quantity of uric acid and creatinine. Creatinine increase affect the kidney and liver. Damaged kidney spills the enzymes into blood that causes toxicity in blood [4]. Toxicity of iron oxide give preference to silicon dioxide nanopowder[5]. Silicon dioxide nanopowder with no toxic nature implant inside the body. Implantation of nanosensor inside the body fabricate with the help of silicon dioxide

2. Survey

Nanotechnology develop a biosensor namely nanobiosensor. Nanobiosensors are widely used for the detection of disease [6] Nanobiosensors detect biological agents such as antibodies, nucleic acid, proteins,lipids which cause disease. Nanobiosensors detects disease like diabetes, tumor,HIV and many other diseases. Nanobiosensors uses nanomaterials for the detection of disease [7]. Nanobiosensors namely Single-Walled Carbon Nanotube (SWCNT) has high sensitivity for early detection of tumors [8].Tumor cells have large refractive index than normal cells. Nanocavity Photonic Crystal Waveguide can also detect tumor cells. Nanocavity Photonic Crystal Waveguide has high sensitivity and selectivity for detection of tumor cells. Tumor cells can also be detected by Nano Abnormality Detection Scheme (NADS). Nano Abnormality Detection Scheme consists of Sensor Nanomachine for the abnormal detection of cancerous cells [9]. Proteins or gene expression detects cancerous cells behaviour. Gene expression detection is by Nanowire which help in the development of nanosensors.Nanosensors has high surface to volume ratio which bind the tumor cells [10]. Nanosensors are implanted inside human body to monitor the health and disease diagnosis of heart attack [11]. Nanosensors uses molecular communication to identify the location and the pattern of the disease. [12] [13].Nanosensors also uses gold nanoparticles for the detection of a DNA sequence which helps in disease diagnosis [14]. Nanosensors with large film thickness create a good conductivity path for an efficient disease diagnosis. Nano sensors with silicon Nanowire have an advantage of faster, smaller, rapid detection of disease. Nanosensors with silicon Nanowire have good biocompatibility, surface to volume ratio that attach easily to various functional groups [15]. SiNW sensors has good chemical and biological sensing elements for detection of DNA, protein detection and electrical properties measurement. SiNW electrical properties measurement are used for glucose detection, viral detection and DNA hybridization detection [16]. SiNW ohmic properties measurement make the device readable and portable for Point of care diagnosis.

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3. Methodology

Nanowire sensors fabricated by two approaches namely top-down approach and bottom-up approach. In the bottom-up approach, sensor fabrication has poor controllability due to many statistical variations in electrical properties resulting in the minimal interconnection between nanowires. The interconnection between nanowires improves in the top-down approach which enables uniformity and sensitivity. High sensitivity results because of increase in surface to volume ratio. Higher surface to volume ratio attains by taking silicon with the diameter less than 100nm. [17]

Fabrication of nanowire sensor in the top-down approach makes an excellent choice of Silicon on account of optimum control of nanowire potential by gate potential. In sensor fabrication silicon wafer used as substrate in a crystalline consistency

Silicon wafer in sensor fabrication undergoes a multistep process as shown in Fig.1. Silicon wafer washing in water removes dirt , invisible organic residue of the wafer and ions in water. Ions in water alter the electrical property of silicon wafer. Wafer's electrical property namely resistance increases with a decrease in width of the wafer. Silicon wafer experience a reduction in breadth by a process namely patterning. Patterning of a silicon wafer at consistent distance leads to uniformity of the sensor.

Patterning of a silicon wafer by photolithography, assures good features on the wafer surface. The patterned silicon wafer coated by a thin film of photoresist through spin coating act as a mask layer. Mask layer namely photoresist with a thickness of 1-10 µm applied at the centre of the wafer. The coated wafer immersed in a chemical solution removes the thin film not surfaced with photoresist. The flimsy removal by etching leaves the photoresist. The photoresists in silicon wafer scale down the device to 10nm after etching. This process ensures in non-perfect geometry with the requirement of advanced lithography in sensor fabrication which leaves holes in wafer occupy by SiO_2.

4. Block diagram

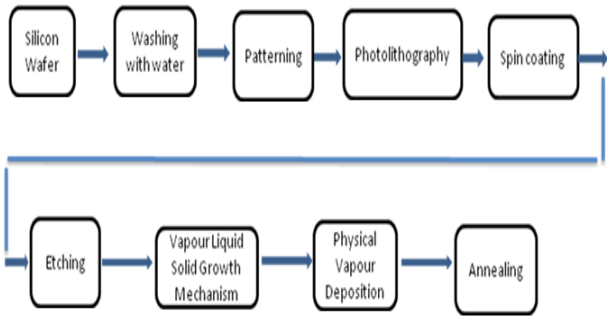


Fig. 1: Block Diagram of Silicon Dioxide Nanosensor Fabrication.

Sio_2 created by oxidation of silicon wafer at high temperature 900°c in a quartz tube. Sio_2 oxidation in sensor fabrication synthesises silicon nanowire through VLS(Vapour Liquid Solid) growth mechanism. In sensor fabrication process, a thin film of Au deposits in Au-Si catalyst by a method namely Physical Vapour Deposition. After Physical Vapour Deposition, silicon wafer undergoes a process of annealing with hydrogen at 450°c for 300 seconds. The annealing alters electrical and mechanical characteristics of the sensor [18].

The sensor fabricated has many applications in the field of Health and Medicine. Nanosensors are more sensitive and more flexible. Nanosensors are widely for the diagnosis of diseases like diabetics and cancer. Nanosensor with the high surface area is necessary for early detection of disease. Nanosensors with a increase in surface area result in high sensitivity. [19]

5. Sensitivity

Nanosensors are more suitable for sensing biomolecules detection in disease diagnosis. Nanosensors have many advantages like high sensitivity and real-time detection. Silicon On Insulator wafer can maximize the sensitivity of biosensor with better electron mobility and lower current leakage[20]. A more number of Sio_2 allows high surface to volume ratio which increase the sensitivity. Greater surface to volume ratio results by taking silicon with a diameter less than 100 nm. Device with small nanowire is more sensitive than large nanowire because of high surface to volume ratio. Electrical measurement determines the sensitivity of nanosensor. Electrical measurement includes resistivity and conductivity. Resistance is inversely proportional to the width of the nanowire. A decrease in R improve the ohmic characteristics that enhance the sensitivity of the device.

6. Nano particle interaction with blood

Blood is a high fluid comprise with protein and cells. Nano articles exposed to blood interact with blood components namely blood cells, proteins and lipoproteins. Nanoparticle exposure to blood attracts many different proteins to their surface to form a protein corona. Protein corona formation depends on nanoparticle physicochemical properties. Nanoparticle properties change the function of cellular and acellular elements in blood. Earlier component contains RBC, WBC for body protection and platelets. Acellular elements composed of water and biomolecules. Interaction of nanoparticle with blood depends on particle size which damages RBC[21]. Nanoparticle interaction with blood should not induce platelet aggregation that produce unwanted side effects. Hemolysis determine the size of the nanoparticle. Hemolysis guarantees the absence of nanoparticle interaction with blood resulting in side effects. Haemocompatibility of nanoparticle takes care of deformation, a property in blood flow. Interaction of nanoparticle with blood depends on surface derivatives [22].Nanoparticle interaction with RBC's is minimum which regulates blood circulation.

7. Results and discussion

Collection of non-diabetic and diabetic blood samples considered as the case (i) and the case (ii). Samples are read using SIGVIEW and statistically analyzed using MATLAB. Statistical analysis of non-diabetic blood signals and diabetic signals like spectrogram, magnitude response, probability distribution, time domain, the autocorrelation function takes place. For non-diabetic patient the blood sample acquire before and after food intake. The glycemic index with glucometer was found to be 90 and 140 respectively. Similarly, the diabetic patient glycemic index before and after food intake was 110 and 220 respectively. The below results shows the glycemic index analysis for non diabetic and diabetic patient with silicon dioxide nano sensor after food intake.

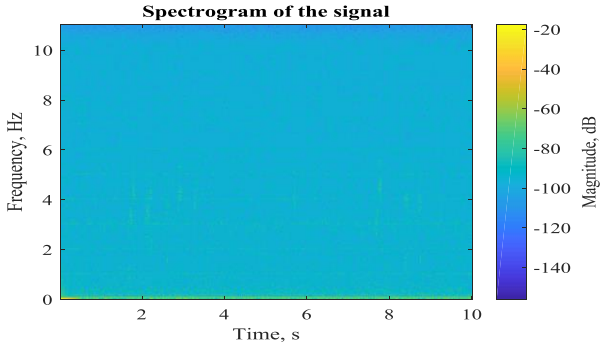


Fig. 2: A) Spectrogram of Non-Diabetic Blood Signal.

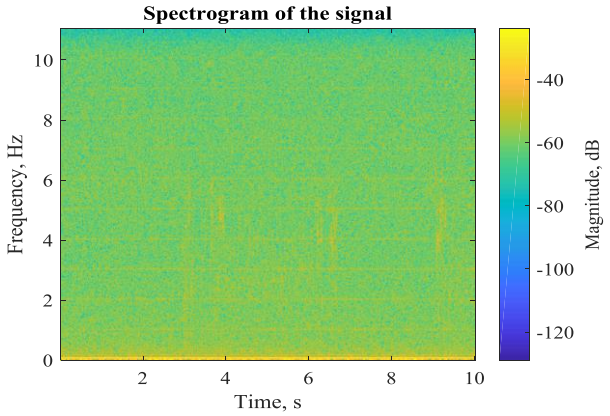


Fig. 2: B) Spectrogram of Diabetic Blood Signal.

Spectrogram analysis is carried from nanosensor signal as shown in Fig.2 (a) and Fig.2 (b). Spectrogram is a visual representation of the spectrum of frequencies of sound or other signals as they vary with time. Spectrum analysis involve Fast Fourier Transform which separates frequencies and amplitude of signal component. Hanning window is used because it removes any discontinuity in the signal. Hanning window with a size of 1.7 sec with 512 samples points is used. Spectrogram is not pre-processed by Band Pass Filter to know the original characteristics of the signal. From Fig.2(b) and Fig.2(a) the color bar indicates the power in dB with yellow representing high power and blue indicating low power.

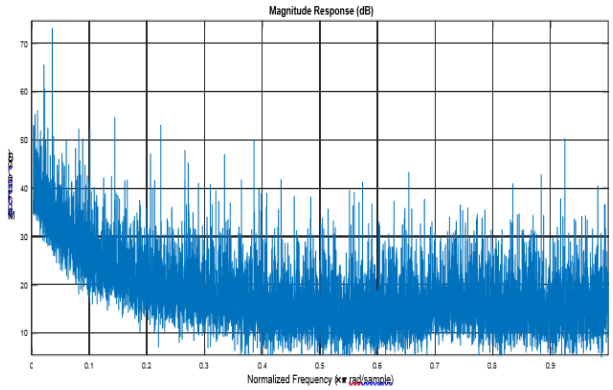


Fig. 3: A) Magnitude Response of Non- Diabetic Blood Signal.

The magnitude of filter varies with frequency and response is obtained for the normal blood sample as shown in Fig.3(a). The amplitude of signal reaches to zero at a normalized frequency value of 0.4 from Fig.3 (a). Power spectral analysis describes power as a function of the frequency component. Magnitude response is a quantitative measure of output of spectrum which characterises the dynamics of the system.

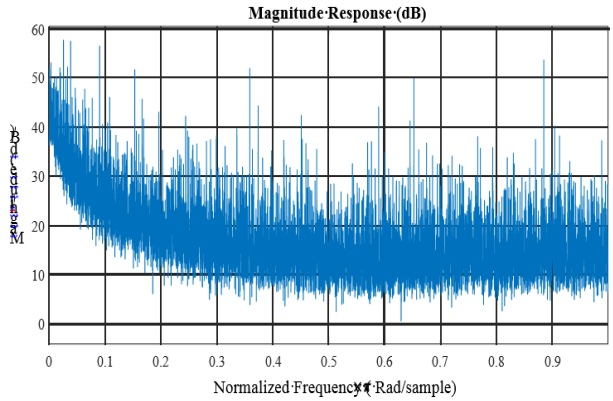


Fig. 3: B) Magnitude Response of Diabetic Blood Signal.

Magnitude of filter varies with frequency and response is obtained for diabetic blood sample as shown in Fig.3 (b). From Fig.3 (b), the magnitude of signal not reaches to zero at normalized frequency. Power spectral analysis describes power in signal as a function of frequency component. Magnitude response is a quantitative measure of output of spectrum which characterise the dynamics of the system

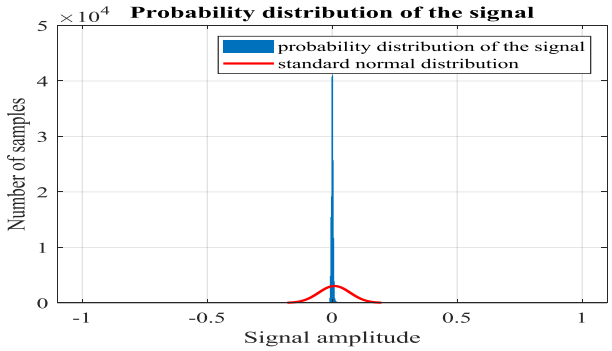


Fig. 4: A) The Probability of Normal Blood Signal.

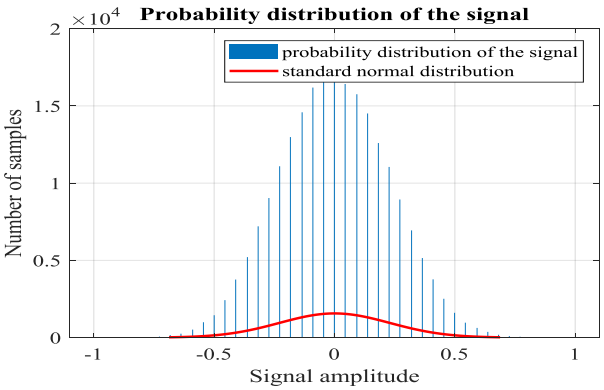


Fig.4: B) Signal The Probability of Diabetic Blood Signal

The probability distribution of signal has cumulative distribution function, which is continuous. This distribution is typically a stochastic process. The distribution function also called the cumulative distribution function describes the probability that a variant takes on a value less than or equal to a number. The probability distribution of the signal reaches the maximum strength at $5x10^4$ and the standard normal distribution of the non-diabetic signal;the value will be low and near to zero as shown in Fig.4(a). The probability distribution of the signal reaches the maximum strength at $2x10^4$ and the standard normal distribution of the diabetic signal; the value will be -0.5 to 0.5 as shown in Fig.4(b)

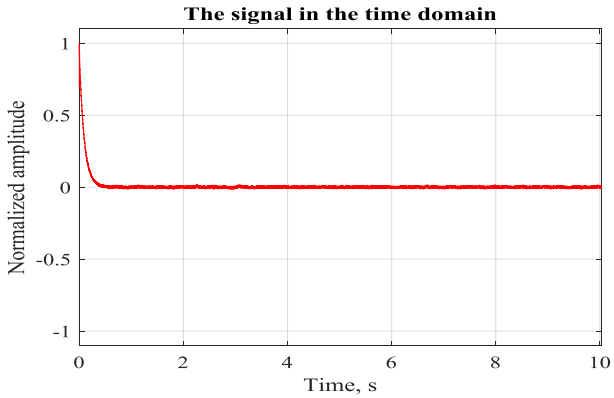


Fig. 5: A) Time Domain of Normal Blood Signal.

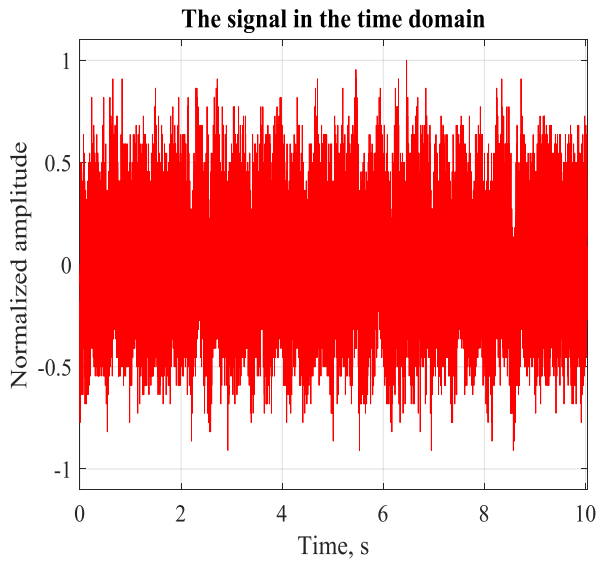


Fig. 5: B) Time Domain of Diabetic Blood Signal.

Time domain is the analysis of mathematical functions, physical signals concerning time as shown in Fig.5 (a) and Fig.5 (b).The function value is knew for all real numbers in continuous time domain , or at various separate instants in the case of discrete time. Time domain refers to the variation of amplitude with time. The signals can be in time domain or frequency domain. The traditional way of detecting signals is in the time domain. The time domain is a record of what happens to an amplitude of the system versus time. Here the graph is plotted between normalized amplitude. From Fig.5 (a), the signal lies constantly from 1 to remaining values. From Fig 5(b) The wave spread between the range of -0.5 and above to 0.5 and above with a multiple variations for 10 seconds of the signal recorded.

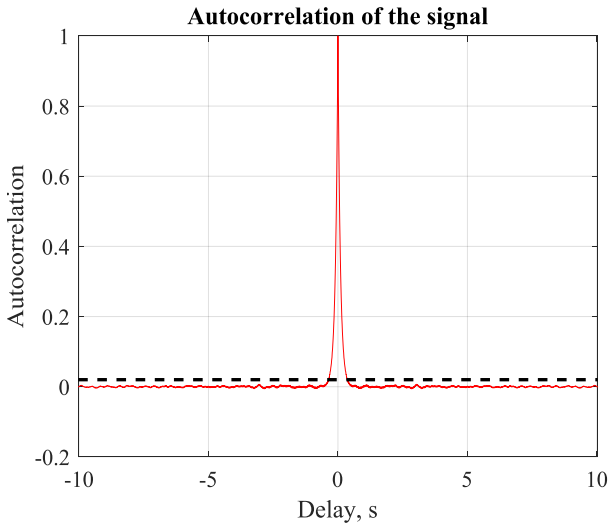


Fig. 6: A) Autocorrelation of Normal Blood Signal.

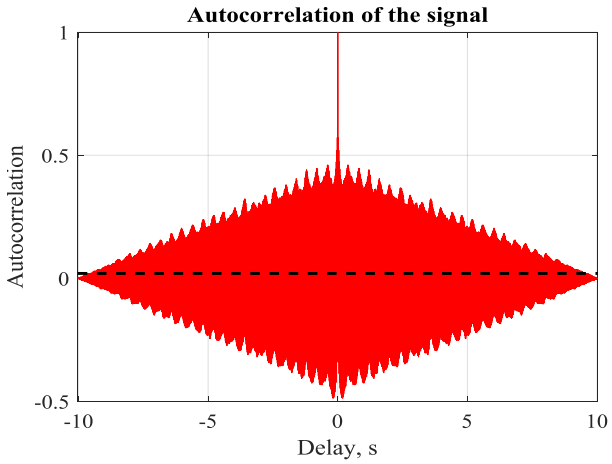


Fig. 6: B) Autocorrelation of Diabetic Blood Signal.

Autocorrelation is a function to measure the similarity between its original signals versus time-lag applied on same the signal as shown in Fig.6 (a) and Fig.6 (b). This function can search repetitive pattern that suppressed with another signal. Autocorrelation commonly appliy on statistical signals. The analysis of autocorrelation function is a tool to find the presence of a periodic signal obscured by noise, or identifying the missing fundamental frequency in a signal implied by its harmonic frequencies. It has an application in signal processing for analyzing functions or series of values, such as time domain signals. For the normal signal with the delay, the statistical value will be equal to zero maximum as shown in Fig.6 (a). For the abnormal signal without the delay, the statistical value vary like dynamic shape as shown in Fig.6 (b).

Pearson correlation coefficient analysis

The pearson correlation coefficient help correlate glucometer values with proposed silicon dioxide sensor values is shown in figure 7. The pearson correlation coefficient R value obtain by equation

$$r = \sum\left(\left((X - My)(Y - Mx)\right)/\left(\sqrt{\left((SSx)(SSy)\right)}\right)\right)$$

Where,
Mx - mean values of x
My- mean values of y
SSx - $\sum(X - Mx)^2$
SSy - $\sum(Y - My)^2$

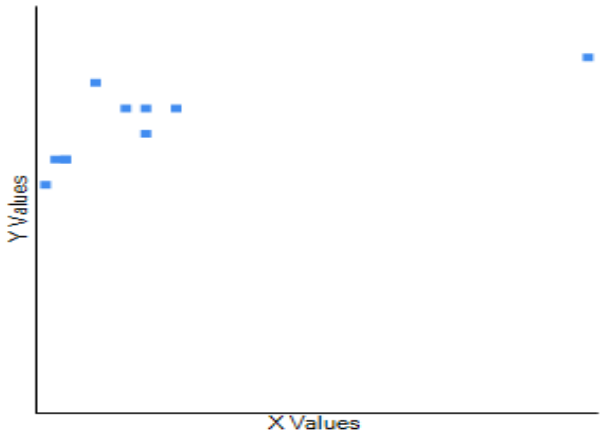


Fig. 7: Pearson Correlation Coefficient for Glucometer and Silicon Dioxide Values.

x values- Glucometer values
Y values - Silicon dioxide nano sensor values.
The R value is found to be 0.7417, which shows correlation between glucometer values and silicon dixoide sensor values.

8. Conclusion

Nanosensors development for glucose level measurement become a siginificant area of research nowadays. Nanosensors fabricated by silicon dioxide reduces the cost of the nanosensors in mass production. Nanosensors with various nanomaterials comparison is with silicon dioxide nanosensors. Nanosensors overcome the drawback of existing glucose sensor through direct oxidation which undergoes a sampling method. Nanosensors detect non-diabetic blood sample signal and diabetic blood sample signal. The blood samples acquire for 20 patients and their glucometer glycemic level compare with silicon dioxide nanosensor processed signal. The analysis shows silicon dioxide nanosensor detects increased glycemic level with 92% accuracy. Both sample signals are read with SIGVIEW and statistically analyzed using MATLAB. Analysis of signals helps in detection of diabetes with the improvement in the response of signals.

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