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Sarcosine as prostate cancer biomarker detection through H_2O_2 sensing by using nickel-oxide on Si nanowires

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Abstract

Sarcosine as a prostate cancer biomarker detection by using NiO_x/Si nanowires (NWs) sensing membrane in low cost electrolyte-insulator-semiconductor (EIS) structure is reported for the first time. An 18 µm long length SiNW is processed in chemical etching method. A higher pH sensitivity of 48 mV/pH with good linearity of 99.65% is achieved. By employing a NiO_x thin layer on SiNWs, lower concentration of 1 pM H_2O_2 and 1 nM sarcosine detection have been detected because oxidation-reduction where as pure SiO_2 membrane does not sense H_2O_2.

1. Introduction

Recently, SiNW is in focus due to its potentiality which demands more study using it in different fields like FETs [1], energy resources, memory, bio-sensor [2] etc. Among different techniques of silicon nanowires processing like CVD, VLS, laser abalation, chemical etching method is the lowest cost and easiest route. Detection of multi-analytes by using ISFET, EGFET, LAPS, EIS sensors is drawing much attention now-a-days due to their important applications especially in bio-sensing field. Moreover any kind of cancer detection like breast cancer, lung cancer, lever cancer, prostate cancer detection [3, 4] using different techniques is catching huge attention anywhere. As NiO_x shows novel nature on SiNWs, the NiO_x layer on SiNWs has been employed to investigate its electocatalytic activity on SiNWs.

2. Device fabrication

An n-type Si (100) wafer is cleaned by using RCA process. Then it is immersed in a beaker containing 0.02 mol/L $AgNO_3$ and 5 mol/L aqueous HF solution at room temperature (RT) for 90 minutes. Then a 10 nm-thick SiO_2 layer is grown on Si/SiNWs by thermal oxidation process under 2.5 SLM O_2 flow followed by a 300 nm backside Al contact. The Al layer was deposited by thermal evaporation process after backside cleaning with BOE. Post-metal annealing was performed. Then, a 2 nm-thick NiO_x layer was deposited on it in RF sputter system. The NiO_x layer was formed by using different Ar and O_2 recipes (20:4). After this the sensor region is defined in standard photolithography by using a negative photo-resist SU8 and UV-ray exposure. Finally, an epoxy package is done through attachment into Cu PCB with Ag gel. The SiO_2 on SiNWs (S1), NiO_x on SiO_2/SiNWs (S2), and NiO_x on planar p-Si (S3) were fabricated. Schematic view of the SiNW sensors is shown in Fig. 1.

3. Results and discussions

The XPS spectra of 2 nm-thick NiO_x deposited on SiO_2/p-Si substrate is shown in Fig. 2 & 3. The Ni2$p_{3/2}$ peak (Fig. 2) is de-convoluted into two Gaussian peaks, at 854.5 eV and 856.7 eV, corresponds to NiO_x and Ni_2O_3. The O*1s* peak (Fig. 3) is de-convoluted into three peaks, at 530.5 eV, 532.4 eV and 533.6 eV corresponding to Ni^{3+}, Ni^{2+} and SiO_2. Fig. 4 shows the top and cross-sectional views (inset) of the etched NWs and the SiNWs' height is approximately 18 µm. Figs. 5 & 6 show the capacitance-voltage (C-V) characteristics of the S1 and S2 sensors. The S1 sensor shows a pH sensitivity of 43 mV/pH and linearity of 98.81% whereas the S2 sensors show better pH sensitivity of 48.25 mV/pH and good linearity of 99.65% in the range of pH 6 to pH10. The pH sensitivity of the NiO_x and pure SiO_2 on planar p-Si are 51 mV/pH and 31 mV/pH, while the linearity values are 94.02% and 99.86%, respectively (Fig. 7). Figs. 8 & 9 show hysteresis window and drift rate of the sensors. Low hysteresis windows of the NiO_x membranes with Ar:O_2 of 20:1 and 20:4 are 4.4 mV and 3.4 mV. Among them S3 sensor has the lowest drift rate of 2.4 mV/hr whereas S1 and S2 sensors show 6.6 mV/hr and 8.4 mV/hr. The S2 sensors show H_2O_2 sensing with the range of 1 pM to 0.5 µM (Fig. 10). Reference voltage shift is in negative side owing to reduction of band bending after oxidation of NiO_x and SiO_2 mixture. As difference in energy of conduction band and Fermi level decreases so, band bending also reduces. The S3 sensor shows H_2O_2 sensing and the reference voltage is shifted towards positive direction (Fig. 11). Sarcosine oxidase (SO_x) enzyme units optimization and sarcosine sensing with S3 sensor are shown in Fig. 12. In presence of SO_x ,glycine and H_2O_2 are obtained as products from sarcosine, which is the key point of sarcosine sensing. In our case 10 nM is the minimum detection limit with S3 sensor whereas Lad et al. [3] have reported 0.5 mM and Heger et al. [4] have reported 50 pM as detection limit for sarcosine sensing.

4. Summary

The NiO_x/SiNWs in EIS structure shows a higher sensitivity with a good linearity. Due to low concentration of 1 pM H_2O_2 and 10 nM sarcosine, the prostate cancer biomarker detection is useful for early diagnosis of patient in near future with low cost.

Acknowledgements

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References

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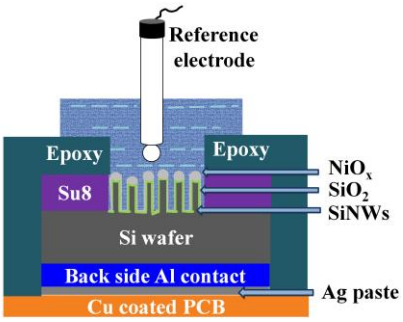

Fig. 1 2D view of NiO_x/SiNWs based EIS (S2) sensor.

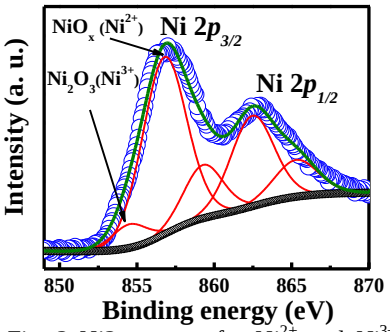

Fig. 2 Ni2*p* spectra for Ni^{2+} and Ni^{3+} oxidation states. In contact of H_2O_2, the Ni^{2+} changes to Ni^{3+} state.

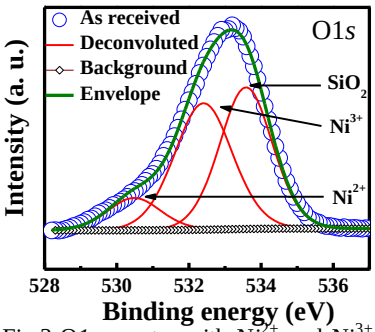

Fig.3 O1*s* spectra with Ni^{2+} and Ni^{3+} oxidation states. The SiO_2 peak is also shown.

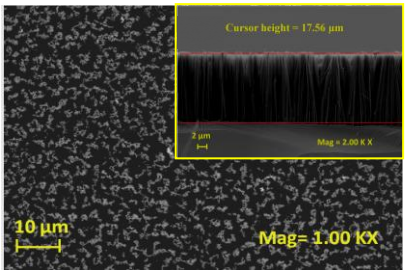

Fig. 4 Top and cross-sectional view of SiNWs etched in chemical etching method for 90 minutes, at RT on RCA cleaned silicon wafer is shown and a highest length of 17.56 µm is obtained.

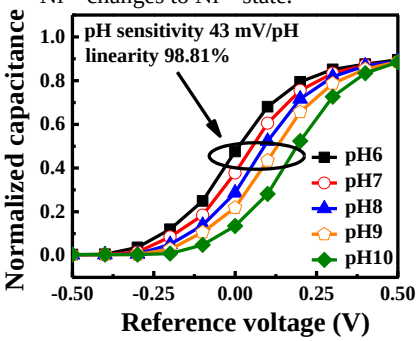

Fig. 5 C-V characteristics of S1 sensor is shown, pH sensitivity is calculated from flat band voltage shift at different pH solutions which is higher than planar SiO_2 due to typical aspect ratio of NWs and roughness factor.

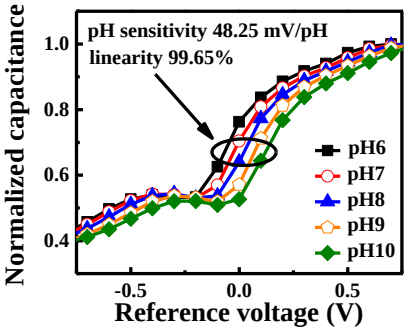

Fig. 6 C-V characteristics of S2 sensor at 100 Hz frequency from pH6 to pH10 solutions is shown. Improvement of pH sensitivity is achieved by implementation of NiO_x layer.

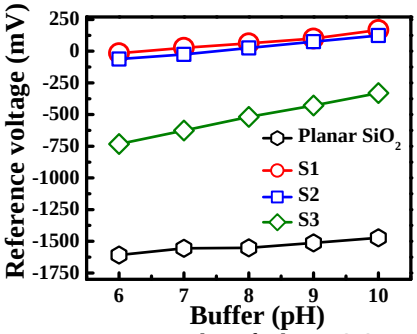

Fig. 7 Linearity plot of planar SiO_2 and S1, S2, S3 sensors are shown.

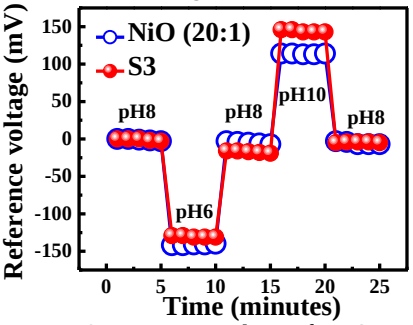

Fig. 8 Hysteresis plots of NiO_x membranes.

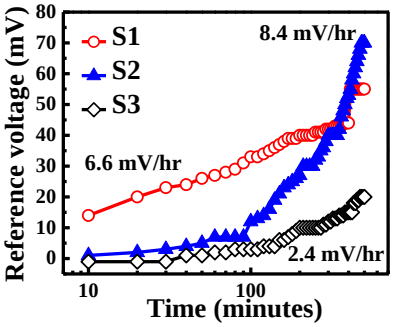

Fig. 9 Comparison of drift characteristics of S1, S2, S3 sensors is obtained.

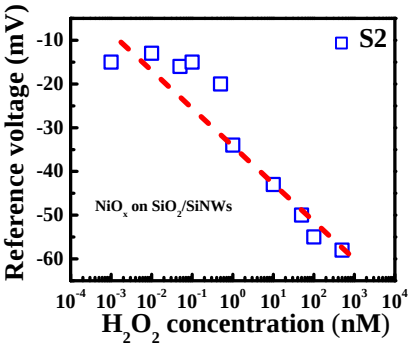

Fig.10 H_2O_2 sensing of S2 sensor in the range from 1 pM to 500 nM is done and a higher shift of 60 mV is achieved. As after oxidation work function of SiO_2 decreases so shift is in negative side. This is reversible with and without H_2O_2 contact on the membrane.

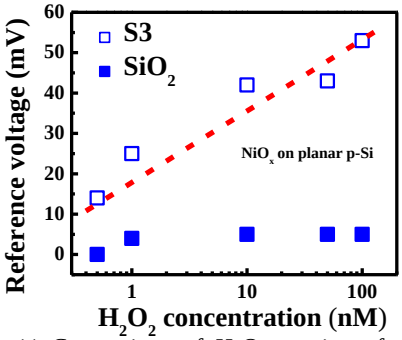

Fig.11 Comparison of H_2O_2 sensing of planar SiO_2 and S3 sensor is shown. A higher shift in voltage value ~55mV in nM range H_2O_2 sensing is obtained by S3 sensor whereas SiO_2 does not sense H_2O_2 due to its higher stoichiometric structure. In presence of H_2O_2 band bending increases and flat band shifts in positive direction.

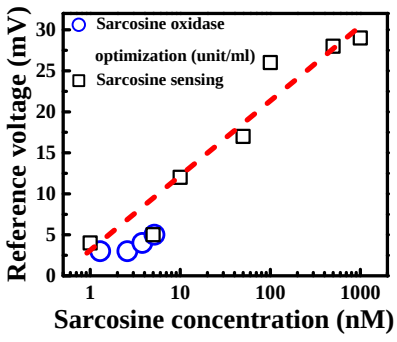

Fig.12 SO_x enzyme concentration-5.18 units is optimized and added in 5 ml, pH 7.4 PBS buffer and sarcosine concentration is varied from 1 nM to 1 µM and it is useful for healthcare unit to early stage prostate cancer diagnosis.