Detection of pH and Enzyme-Free $\text{H}_2\text{O}_2$ Sensing Mechanism by Using GdO$_x$ Membrane in Electrolyte-Insulator-Semiconductor Structure

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Abstract

A 15-nm-thick GdO$_x$ membrane in an electrolyte-insulator-semiconductor (EIS) structure shows a higher pH sensitivity of 54.2 mV/pH and enzyme-free hydrogen peroxide ($\text{H}_2\text{O}_2$) detection than those of the bare SiO$_2$ and 3-nm-thick GdO$_x$ membranes for the first time. Polycrystalline grain and higher Gd content of the thicker GdO$_x$ films are confirmed by transmission electron microscopy (TEM) and X-ray photo-electron spectroscopy (XPS), respectively. In a thicker GdO$_x$ membrane, polycrystalline grain has lower energy gap and Gd$^{2+}$ oxidation states lead to change Gd$^{3+}$ states in the presence of $\text{H}_2\text{O}_2$, which are confirmed by electron energy loss spectroscopy (EELS). The oxidation/reduction (redox) properties of thicker GdO$_x$ membrane with higher Gd content are responsible for detecting $\text{H}_2\text{O}_2$ whereas both bare SiO$_2$ and thinner GdO$_x$ membranes do not show sensing. A low detection limit of 1 $\mu$M is obtained due to strong catalytic activity of Gd. The reference voltage shift increases with increase of the $\text{H}_2\text{O}_2$ concentration from 1 to 200 $\mu$M owing to more generation of Gd$^{3+}$ ions, and the $\text{H}_2\text{O}_2$ sensing mechanism has been explained as well.

Keywords: Enzyme-free $\text{H}_2\text{O}_2$, pH detection, GdO$_x$, Sensing mechanism, Catalytic, EIS structure

Background

Recently, hydrogen peroxide ($\text{H}_2\text{O}_2$) is a major intermediate of biological cycles which has been used as a potential biomarker for oxidative stress diagnosis as well as a major catalyst for immune sensing [1, 2]. On the other hand, it is also an essential compound of bleach industries and waste water treatment. $\text{H}_2\text{O}_2$ has a major role in modulating mitochondrial function by inhibiting activities of the mitochondrial enzyme in a fully reversible fashion [3, 4]. The $\text{H}_2\text{O}_2$ sensing assay relies on the use of the enzyme horse radish peroxidase (HRP) to oxidize its substrates and detection using spectrophotometer [5]. $\text{H}_2\text{O}_2$ sensing in a simple way, with a short time detection with high specificity, is demanded for future disease diagnosis of the human body, and enzyme-free electro-catalytic methods have gained the attention for $\text{H}_2\text{O}_2$ sensing. Therefore, various catalysts such as metal, metal oxides, and redox polymers have been reported to detect $\text{H}_2\text{O}_2$ [6–12]. Huang et al. [13] have used the glassy carbon electrode modified by Si nanowire-dispersed CuO nanoparticle. Maji et al. [14] have demonstrated an amperometric $\text{H}_2\text{O}_2$ sensor based on reduced graphene oxide-coated silica modified with Au nanoparticles. Wang et al. [15] have developed a $\text{H}_2\text{O}_2$ sensor by using MoS$_2$ nanoparticles. Sun et al. [16] have reported a dumbbell-like Pt-Pd-Fe$_3$O$_4$ nanoparticle-modified glassy carbon electrode which shows electro-catalytic reduction. Liu et al. [17] have reported an amperometric $\text{H}_2\text{O}_2$ sensor based on a Si substrate modified with carbon nanotube microelectrode coated by Pd nanoparticles. Kong et al. [18] have reported a non-enzymatic $\text{H}_2\text{O}_2$ sensor based on a Co$_3$O$_4$ nanowire.
grown over a reduced graphene oxide sheet. Hao et al. [19] have developed an amperometric \( \text{H}_2\text{O}_2 \) sensor based on \( \text{Fe}_2\text{O}_3 \) nanoparticles. Bai et al. [20] have reported a sensor based on carbon dot-decorated multi-walled carbon nano-composites. Silver (Ag) nanowire [21] and nanoparticle-decorated graphene [22] have been also reported for \( \text{H}_2\text{O}_2 \) sensing. Most of the above groups have used different materials using cyclic voltammetry/amperometric methods to sense \( \text{H}_2\text{O}_2 \) (ranging from few nanomolars to millimolars) due to different oxidation states in the presence of \( \text{H}_2\text{O}_2 \). On the other hand, high-k materials such as \( \text{Al}_2\text{O}_3 \) [23], \( \text{Ta}_2\text{O}_5 \) [24], and \( \text{HfO}_2 \) [25] in an electrolyte-insulator-semiconductor (EIS) structure have been reported for pH sensing only; however, the \( \text{Gd}_2\text{O}_3 \) materials that have been reported are few [26, 27], and even then, there is no report for enzyme-free \( \text{H}_2\text{O}_2 \) sensing by using a \( \text{GdO}_x \) \((x < 1.5) \) material in a simple EIS structure. In this paper, detection of a pH and enzyme-free \( \text{H}_2\text{O}_2 \) sensing mechanism has been investigated by using a \( \text{GdO}_x \) membrane in a simple EIS structure for the first time. Polycrystalline grain, Gd content, and oxidation states (\( \text{Gd}^{2+}/\text{Gd}^{3+} \)) have been confirmed by transmission electron microscope (TEM), X-ray photo-electron spectroscopy (XPS), and electron energy loss spectroscopy (EELS) on grain and boundary regions. The 15-nm-thick \( \text{GdO}_x \) membrane detects \( \text{H}_2\text{O}_2 \) whereas both 3-nm-thick \( \text{GdO}_x \) and bare \( \text{SiO}_2 \) membranes do not sense \( \text{H}_2\text{O}_2 \). Due to the strong catalytic activity of Gd, a low detection limit of 1 \( \mu \text{M} \) is obtained. Both time- and concentration-dependent \( \text{H}_2\text{O}_2 \) sensing and its mechanism have been investigated.

**Methods**

p-type 4-in. Si (100) wafer was cleaned by the Radio Corporation of America (RCA) process. Prior to thermal growth of \( \text{SiO}_2 \), HF dip was used to remove native oxide from the surface. After the cleaning process, a 40-nm-thick \( \text{SiO}_2 \) layer was grown as an insulating layer by dry oxidation process at 950 °C. Then, the back-side-grown \( \text{SiO}_2 \) layer was removed by using a buffer oxide etching (BOE) solution. To fabricate the EIS chip, a 300-nm-thick Al film was deposited on the back side of the Si wafer. The sensing membrane area was defined by standard photolithography process using a negative photoresist-SU8. Then, EIS devices were attached on a printed circuit board having copper lines. An epoxy layer was used to encapsulate the EIS structure and the copper line. Therefore, a sensor (S1) using \( \text{SiO}_2 \) membrane was fabricated. Our fabrication process of EIS structure can be found elsewhere [28]. This \( \text{SiO}_2 \) sensing membrane was modified by deposition of 3-nm- \((S2)\) and 15-nm-thick \((S3)\) \( \text{GdO}_x \) films. The \( \text{GdO}_x \) film was deposited by electron beam evaporation. The \( \text{Gd}_2\text{O}_3 \) granules were used during deposition, and the deposition rate was 6 nm/min. A schematic view of the \( \text{Gd}_2\text{O}_3 \)– (or \( \text{GdO}_x \) \((x < 1.5)\)) modified \( \text{SiO}_2 \) sensor is shown in Fig. 1. To probe the thickness and microstructure of \( \text{GdO}_x \) films, low-voltage spherical aberration corrected field emission TEM (Cs-corrected FE-TEM) was performed. The model number is JEOL JEM-ARM200F with accelerating voltages of 60, 120, and 200 kV. In addition, a Cs-corrected FE-TEM Oxford energy spectrometer (energy-dispersive spectroscopy, EDS) and electron loss EDS (EELS, Model 965 QuantumER\textsuperscript{TM}) were used to observe the elemental composition on polycrystalline grain and boundaries. The ambient temperature of our laboratory was \( 21 \pm 3 \) °C and relative humidity was \( 50 \pm 10 \) %. The elemental composition was investigated by XPS analyzing chamber. The vacuum of the XPS chamber was \( 1 \times 10^{-9} \) Torr. The spectra were recorded by using an Al K\( \alpha \) monochrome X-ray at an energy of 1486.6 eV. The scanning energy range from 0 to 1350 eV was used. All spectra were calibrated by C1s spectrum at a centered peak energy of 284.6 eV. After depositing the \( \text{GdO}_x \) films on the \( \text{SiO}_2/\text{Si} \) substrates, the samples were transferred immediately to the XPS chamber. The capacitance-voltage (C-V) measurements were performed by using Agilent 4284A LCR meter and an Ag/AgCl reference electrode was used. The measurement frequency was 100 Hz. The sweep voltage was applied on the Ag/AgCl electrode. The reference voltage \((V_r)\) was measured at 50 % of accumulation capacitance.

**Results and Discussion**

Figure 2 shows the cross-sectional TEM images of the S2 and S3 sensors. The thickness of \( \text{SiO}_2 \) is 41.2 nm (Fig. 2a), and the thickness of the \( \text{GdO}_x \) film is 3.3 nm (Fig. 2b). The TEM image of the S3 sensor shows that the thickness of \( \text{SiO}_2 \) is 41.5 nm (Fig. 2c).
However, peak binding energies of Gd $3d_{5/2}$ and Gd $3d_{3/2}$ are reported as 1218 and 1186 eV, respectively.

The ratio of O:Si is 1.84, which signifies the stoichiometric SiO$_2$. An XPS spectrum of GdO$_x$ shows Gd$3d_{3/2}$ and Gd$3d_{5/2}$ doublet with binding energy of 1220.5 and 1188.3 eV, respectively (not shown here).

The strong peaks at 531.5 eV correspond to the oxygen in the Gd$_2$O$_3$ film, whereas lower (O1$s$ A) and higher (O1$s$ B) binding energy peaks centered at 529 and 532.9 eV are attributed to the hydroxyl (OH$^-$) and carbonate groups in Gd$_2$O$_3$ films, respectively [33, 34]. Moreover, the lower binding energy peak corresponds to Gd-O bonding or GdO$_3$ [35]. The area ratios of O1$s$ A and O1$s$ B with respect to O1$s$ are 0.04:1 and 0.48:1 for the S2 samples whereas those values are 0.08:1 and 0.1:1 for the S2 samples, respectively. Therefore, the S2 samples show higher percentage of O1$s$ B owing to higher carbonate groups in the GdO$_x$ films, which is insensitive to H$_2$O$_2$ sensing. On the other hand, the S3 samples have higher percentage of O1$s$A owing to higher OH$^-$ and higher Gd content in Gd$_2$O$_3$ film, i.e., GdO$_x$ film. So, oxygen can be bonded loosely with Gd on a polycrystalline grain boundary as well as a thicker GdO$_x$ film will help to sense H$_2$O$_2$, which will be explained below.

Figure 4a shows the C-V characteristics with pH values from 6 to 10 for the S2 and S3 sensors. The $V_r$ values of the S2 sensors are -0.84, -0.75, and -0.63 V for pH 6, 8, and 10, while those values are 0.01, 0.1, and 0.23 V for the S3 sensors, respectively. The $V_r$ values of the S3 sensor are shifted towards the positive direction and are lower than the $V_r$ values of the S2 sensors. This is due to lower oxide charges for the thicker GdO$_x$ membrane (55 vs. 43 nm [36]) and polycrystalline grains with higher OH$^-$ ions (Fig. 3f). The pH sensitivity values are found to be 51.2 and 54.2 mV/pH for the S2 and S3 sensors, respectively, which are higher than the pH sensitivity of approximately 35 mV/pH from pH 2 to 10 [28, 37] and 42 mV/pH from pH 6 to 10 for the S1 sensors. The pH sensitivity of a 30-nm-thick GdO$_x$ film is approximately 51.7 mV/pH (not shown C-V curves), which is slightly lower than the S3 sensors. The pH sensitivity value of our GdO$_x$ membrane is comparable with other reported values of 48.29 mV/pH by Wang et al. [27], 64.78 mV/pH by Chang et al. [38], and 55 mV/pH by Yang et al. [39]. However, the S3 sensors show the lowest drift rate as compared to the S1 and S2 sensors (2.12 mV/h vs. 3.12 mV/h and 2.16 mV/h), as shown in Fig. 4b. The drift characteristics were measured a long time up to 500 min at pH 7 buffer solution. Considering a
Fig. 3 XPS characteristics of Si2p for a S1, b S2, and c S3 samples. Corresponding O1s spectra of d S1, e S2, and f S3 samples are shown. The S3 film shows higher Gd/Gd$_2$O$_3$ ratio or oxygen deficient and higher OH group which helps to sense H$_2$O$_2$.

Fig. 4 a C-V characteristics of the S1, S2, and S3 sensors are shown. b Drift rate characteristics of the S1, S2, and S3 sensors. c Time-dependent response of H$_2$O$_2$ and d reference voltage shift vs. H$_2$O$_2$ concentration for all sensors.
low drift rate (2.12 mV/h), the pH detection limit of the S3 sensors is 0.039 pH, which is due to high pH sensitivity. It is interesting to note that the GdOₓ membrane will detect H₂O₂. Figure 4c shows the time-dependent response of H₂O₂ for the S3 sensors. A negligible Vᵣ shift is observed for pH 7 buffer solution up to 10 min. By including H₂O₂ with a concentration of 1 μM, a good Vᵣ shift of approximately 40 mV is observed because of Gd¹⁺, Gd²⁺, and Gd³⁺ oxidation states (https://en.wikipedia.org/wiki/Work_function) [40]. On the other hand, both S1 and S2 sensors do not show H₂O₂ sensing. When in contact with H₂O₂, the Gd²⁺ changes to the Gd³⁺ oxidation state and provides electrons for the reduction of H₂O₂. H₂O₂ as a byproduct is observed (Fig. 1). However, the pH value is unchanged by adding H₂O₂ in the buffer solution. A short response time of <2 min is needed without enzyme. After washing out, the sensor does not show any Vᵣ shift owing to the reduction from the Gd³⁺ to Gd²⁺ states. Therefore, this sensor can be used repeatedly for H₂O₂ sensing. Based on our knowledge, this is the first ever report of H₂O₂ detection with a polycrystalline GdOₓ membrane. Basically, the oxidation/reduction of the GdOₓ material in contact with H₂O₂ with buffer solutions is responsible for the Vᵣ shifting, which is shown by chemical reactions below:

\[
\text{Gd}^{2+} \leftrightarrow \text{Gd}^{3+} + 2e^- \tag{1}
\]

\[
\text{H}_2\text{O}_2 + e^- \leftrightarrow \text{OH}^- + \text{OH}^+ \tag{2}
\]

\[
\text{OH}^+ + e^- \leftrightarrow \text{OH}^- \tag{3}
\]

\[
2\text{OH}^- + 2\text{H}^+ \leftrightarrow 2\text{H}_2\text{O} \tag{4}
\]

By following the above Eqs. (1), (2), (3), and (4), the oxidation state of Gd changes from Gd²⁺ to Gd³⁺. The H⁺ ions are supplied by buffer solutions. The Vᵣ shift increases with increasing H₂O₂ concentration from 1 to 200 μM because the generation of Gd³⁺ ions increases (Fig. 4d). A moderate sensitivity of 0.13 mV/μM is obtained from a linear range of 1 to 200 μM whereas it is 82 mV/μM from a linear range of 0.5 to 1 μM. Our detection limit of 1 μM is inferior than the published results [9–12, 15, 16, 41–43], comparable with the published results [44–47], and superior than the published results [13, 17, 18, 20, 48–52] in literature by using different sensing methods, as shown in Table 1. Further study is needed to improve the detection limit in the future. However, our sensing method’s surface potential is changed when in contact with H₂O₂ because of the catalytic activity of Gd. It is known that Gd₂O₃ material is n-type and the energy difference in between the Fermi level and the conduction band (Eᵥ) is 2.71 eV [53]. The electron affinity of Gd₂O₃ is 1.45 eV by considering the conduction band offset of 2.6 eV with Si [54]. The work function of Gd increases from 2.9 eV (https://en.wikipedia.org/wiki/Work_function) to 4.16–4.76 eV [53–55] after oxidation. This suggests that the work function of GdOₓ is modulated by oxidation/reduction or Gd³⁺ concentration as well as the energy band bending of Si is changed. In consequence, the Vᵣ is needed to bring Si energy bands to be flat. On the other hand, the S1 and S2 sensors do not show H₂O₂ detection because they do not have redox properties. The thinner GdOₓ film (S2) has a smaller crystalline grain with less Gd content (Fig. 3), while the S3 sensor has larger crystalline grain (Fig. 5a) with higher Gd content. Figure 5b shows electron energy loss spectroscopy of Gd measured at polycrystalline grain (P₁) and amorphous region or grain boundary (P₂). The regions of P₁ and P₂ are marked on Fig. 5a. The edges of the Gd M-4 and M-5 peaks at the P₁ region are located at 1216.8 and 1187.5 eV, while those values at the P₂ region are 1216.5 and 1187 eV, respectively. Du et al. [56] have reported the M-4 and M-5 peak values of 1217 and 1185 eV for the Gd(OH)₃ nanorods. The edges of the O-K

### Table 1 Comparison of linear range and detection limit of H₂O₂ published in literature [9–13, 15–18, 20, 41–52]

| Sensing materials | pH value | Linear range (μM) | Detection limit (μM) |
|-------------------|----------|------------------|---------------------|
| MoS₂ NP [15]      | 7.4      | 5–100            | 0.002               |
| WS₂ NS [10]       | 7.4      | –                | 0.002               |
| Pt-Pd-Fe₂O₃ [16]  | 7.4      | 0.02–0.1, 2–14,000| 0.005               |
| Pt-Pd/rGO [11]    | 7.0      | 0.1–37.6         | 0.01                |
| Au NP [12]        | 7.0      | 2–5000           | 0.01                |
| Pt NP [9]         | 7.2      | 3–300            | 0.03                |
| rGO [41]          | 7.0      | 0.05–1500        | 0.05                |
| Au/C/Pt [42]      | 7.0      | 9.0–1860, 1860–7110| 0.13               |
| Au NP [43]        | 6.8      | 3–605            | 0.18                |
| Ag NP [44]        | 7.5      | 100–10,000       | 0.88                |
| GS/Co₂O₃–ZnO NP [45]| 7.0  | 2–20,000            | 1.1               |
| Pt-Pd and Pt–Ir [46]| 7.4 | 2.5–125            | 1.2               |
| Pt NP [47]        | 6.9      | 5–2000           | 1.23               |
| CeO₂ NP/N–rGO [48]| 7.0      | 1.8–920.8        | 1.3                |
| CuO [13]          | 7.0      | 10–13,180        | 1.6                |
| Ag NPs/Pt/Fe₂O₃ [49]| 7.2 | 5–11,500          | 1.7                |
| Pd NP [17]        | 7.4      | 2–1300           | 2                  |
| Co₃O₄ NW [18]     | 7.4      | 15–675           | 2.4                |
| Carbon dots [20]  | 7.4      | 3–300            | 3                  |
| Se/Pt [50]        | 7.0      | 10–15,000        | 3.1                |
| Ag NP [51]        | 7.0      | 25–500, 500–5500  | 10                 |
| Co–Mn [52]        | 7.2      | 100–25,000       | 15                 |
| GdOₓ in EIS structure (this work) | 7.0 | 1–200          | 1                  |

NP nanoparticle, NS nanosheet, rGO reduced graphene oxide, GS graphene sheet, NW nanowire
peak at both P1 and P2 regions are located at 538.5 eV, as shown in Fig. 5c, which is close to the reported value of 536.5 eV [56]. It is interesting to note that another peak of crystalline grain (P1) is located at 532.9 eV, which is shifted downwards to 3.9 eV. Egerton has reported the reduced energy gap of SiOx at the SiO2/Si interface with energy shift downwards to 3 eV [57]. In our case, this reduced energy gap is observed in the polycrystalline grain region. Therefore, the crystalline grain is GdOx (or Gd2+) and the amorphous region or grain boundary is Gd2O3 (or Gd3+). When in contact with H2O2, the oxidation state of the S3 sensor changes from Gd2+ to Gd3+ and the crystalline grain takes a major role, which is confirmed by EELS spectra. So, the thicker crystalline GdOx membrane can sense H2O2 repeatedly which will be useful to detect human disease in the near future.

Conclusions
Higher pH sensitivity (54.2 m/pH) and the enzyme-free H2O2 sensing characteristics have been investigated by using 15-nm-thick GdOx membranes for the first time. The polycrystalline grain and thickness of the GdOx/SiO2 film have been observed by TEM image. XPS characteristics of the S3 membrane show higher Gd/Gd2O3
ratio than the S2 membrane (0.69/1 vs. 0.64/1). The S3 membrane shows GdO$_x$ and higher OH content in the crystalline grain, which help to sense H$_2$O$_2$ whereas both S1 and S2 sensors do not show H$_2$O$_2$ detection. Therefore, a larger polycrystalline GdO$_x$ grain has oxidation/reduction properties when in contact with H$_2$O$_2$, which is confirmed by EELS. During oxidation, the Gd$^{3+}$ changes to the Gd$^{4+}$ state and the amount of Gd$^{4+}$ ions increases with increasing H$_2$O$_2$ concentration from 1 to 200 μM. A low deflection limit of 1 μM is obtained owing to the catalytic effect of Gd. The time-dependent response and the sensing mechanism of H$_2$O$_2$ have been explored. Due to the short time detection of H$_2$O$_2$ in the EIS structure, this novel GdO$_x$ sensing membrane paves a way to diagnose other diseases of the human body in the near future.

**Acknowledgements**

This work was supported by the Ministry of Science and Technology (MOST), Taiwan, under contract numbers MOST-104-2221-E-182-075 and MOST-105-2221-E-182-002 and Chang Gung Memorial Hospital (CGMH), Linkou, under contract numbers CMRPD270021 and CMRPD2E0091. The authors are grateful to Mr. S. Chatterjee for the partial support to measure the concentration-dependent hydrogen peroxide sensing.

**Authors’ Contributions**

PK fabricated these sensors and analyzed the data under the instruction of SM. JTQ helped to analyze the sensing mechanism and application of this sensor. SJ and AR helped to measure the pH and H$_2$O$_2$ sensing characteristics and checked the repeatability of these sensors. They review the papers under the instruction of SM. KS helped to check the redox characteristics and review the papers under the instruction of SM. HMC measured the XPS and analyzed the spectra. MTC helped to obtain TEM and EELS. RM helped to analyze the sensing characteristics. HCC helped to deliver the idea for deposition of sensing membrane by using electron beam evaporation. JRY analyzed the EELS spectra for oxidation and reduction. All authors contributed to the revision of the manuscript, and they approved it for publication.

**Competing Interests**

The authors declare that they have no competing interests.

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**Received:** 13 August 2016  **Accepted:** 22 September 2016  **Published online:** 29 September 2016

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