

## Enhanced amperometric detection of glucose using Si<sub>29</sub> particles

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The 1 nm Si<sub>29</sub> particle is used as the sensing element for an enzyme-free amperometric electrochemical glucose sensor. The sensor shows selective glucose detection against interfering substances at physiological concentrations with long-term stability, reusability, and the absence of electrode poisoning. The Si<sub>29</sub> particle is significantly more efficient in generating signal current compared to both dissolved and immobilized enzyme. This observation suggests that the particle can be used to replace enzyme in making glucose sensors and that the particle is a suitable material for the realization of nanoscale devices that generate signals sufficiently high for use. © 2006 American Institute of Physics. [DOI: 10.1063/1.2405384]

Direct electrochemical detection has been explored for three decades for making stable and miniature sensors for biomedical applications. This sensing approach is adopted to replace enzyme-based sensors due to enzymes' intrinsic instability under physiological conditions. To date, enzyme-free sensors have been made using noble metals,<sup>1,2</sup> alloys of these metals,<sup>3</sup> conducting polymers,<sup>4</sup> and carbon nanotubes.<sup>5</sup> These sensors, while rendering device stability, still suffer from issues related to material selectivity and/or electrode poisoning due to adsorption of reaction intermediates. Presently, the enzyme, glucose oxidase (GOx), is used as the sensing element for glucose sensors.

Here, we demonstrate direct electrochemical amperometric detection of glucose using the ultrasmall Si<sub>29</sub> particles<sup>6</sup> that are deposited on a silicon wafer. The particle-covered (Si<sub>29</sub>-Si) electrode showed exclusive detection of glucose in the presence of interfering species within the physiological concentration ranges of these substances. The electrode also showed detection stability over a 14 week period of repeated use and the absence of electrode poisoning. A comparison between the glucose detection characteristics of the Si<sub>29</sub>-Si electrode and a GOx-immobilized electrode shows an enhanced amperometric response of the particle electrode. Our results reveal several advantages of using the Si<sub>29</sub> particle in bioelectronics.

The 1 nm Si<sub>29</sub> particle was prepared as a water-based colloid as described previously.<sup>6</sup> Monte Carlo simulation suggests a filled fullerene structure of Si<sub>29</sub>H<sub>24</sub>, in which a central core silicon atom and four other silicon atoms are arranged in a tetrahedral coordination and the 24 remaining silicon atoms undergo a H-terminated bulklike (2 × 1) reconstruction of dimer pairs on (001) facets (six reconstructed surface dimers).<sup>7</sup> The particle exhibits interesting optical properties such as laser oscillation<sup>8</sup> and second harmonic generation<sup>9</sup> in the visible part of the spectrum. Figure 1(a) shows a schematic model of the Si<sub>29</sub>H<sub>24</sub> structure. Heavily doped ( $\rho < 0.005 \Omega \text{ cm}$ ) *n*-type silicon wafers were used to

support the Si<sub>29</sub> particles as sensing elements for electrochemical detection. The wafer with its surface containing the native oxide was cleaned with ethanol, isopropanol, and deionized water. The wafer surface was covered with a mask to achieve a working area of about 1 × 1 mm<sup>2</sup>. A drop of 0.1 ml of the Si<sub>29</sub> colloid was spread on the wafer surface, and the sample was incubated for 10 h and then rinsed with deionized water. The particle-covered wafer was used as the working electrode in a typical three-electrode electrochemical cell for cyclic voltammetry measurements. A Ag/AgCl electrode was used as the reference electrode. Glucose was dissolved in a phosphate buffer solution (PBS), which was introduced into the cell for measurements. Note that the bare silicon wafer showed no electrochemical response to the substances used in this work up to a potential as high as 1.6 V.

Figure 1(b) shows the Si<sub>29</sub>-Si electrode's response to glucose at pH 7. The curves are the cyclic voltammograms (CVs) of the electrode. The increase of the anodic current due to the presence of glucose (curve *b*) above the background (curve *a*) is clearly shown. The calibration curve of the electrode at pH 7 as shown in the inset is linear over a range of 0–50 mM of glucose, which covers the physiological level of 3–8 mM.<sup>10</sup> The absence of electrode poisoning is reflected in the electrode's reversible response to varying the glucose concentration as indicated by the arrows. Curve *b* in Fig 1(b) indicates that glucose is oxidized at the electrode. As mentioned above, the bare silicon wafer shows no response to glucose. Thus, the Si<sub>29</sub> particle exhibits a catalytic character in the detection of glucose. A study on the effect of sweeping speed of the potential indicates that the current of curve *b* in excess of curve *a* is mainly due to glucose and charging current is negligible.

The electrode's time domain response to glucose is shown in Fig. 1(c). Figure 1(c) also shows that the presence of three interference agents, ascorbic acid (AA), uric acid (UA), and 4-acetamidophenol (AP), at the physiological levels does not leave any measurable trace on the electrode's response. The inset of Fig. 1(c) shows the electrode's response to glucose under identical conditions over a period of

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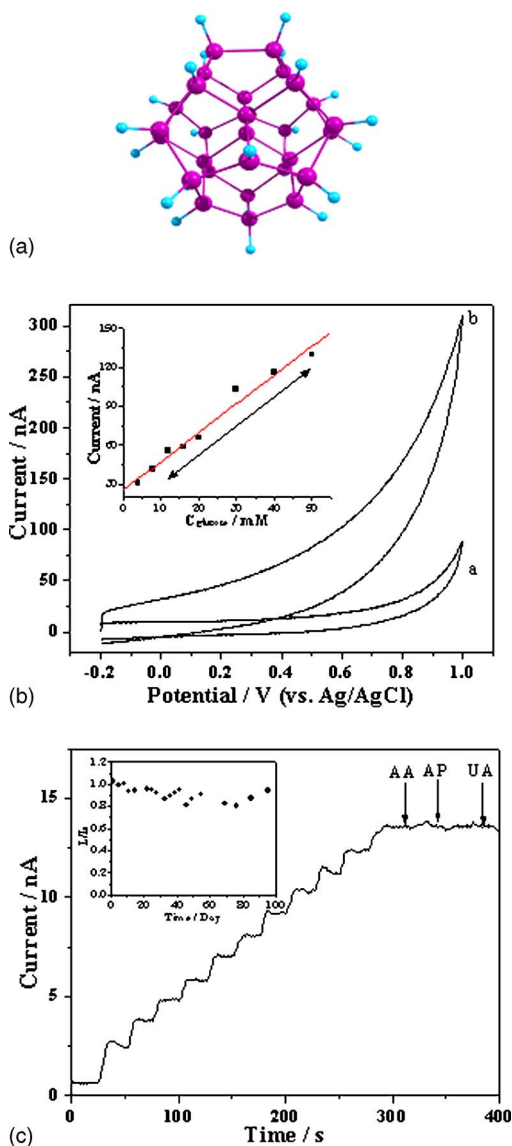


FIG. 1. (a)  $\text{Si}_{29}$  particle. The purple (larger) and blue (smaller) spheres represent the silicon atom and the hydrogen atom, respectively. (b) CVs of the  $\text{Si}_{29}$ -Si electrode obtained at 50 mV/s in 5 mM nitrogen-purged PBS at pH of 7 (curve a) and in the presence of 50 mM glucose in the PBS (curve b). The inset shows the electrode's calibration curve obtained at 0.7 V. The arrows indicate the reversibility of the response to the glucose concentrations. (c) Current-time response of the  $\text{Si}_{29}$ -Si electrode to successive additions of equal amount of 5 mM of glucose. The solution was purged with nitrogen and stirred magnetically during data acquisition. The addition of 4 mM of AA, 4 mM of AP, and 4 mM of UA to the solution does not cause changes in the electrode's response. The inset shows the electrode's stability.  $I_0$  and  $I_t$  are the initial electrode current and the subsequent electrode current, respectively.

14 weeks, during which the electrode was repeatedly used every other day and ten times per day on the average and was stored under ambient conditions. As indicated, the electrode's response has reduced by only 10% of its initial value on the average.

To gain insight into the  $\text{Si}_{29}$  particle's performance in glucose detection, we compare the glucose response of the  $\text{Si}_{29}$ -Si electrode to that of the GOx electrode, which was prepared by immobilizing GOx on the same kind of silicon wafer used to make the  $\text{Si}_{29}$ -Si electrode.<sup>11</sup> Figure 2(a) is an atomic force microscopy (AFM) image of the  $\text{Si}_{29}$ -Si electrode, showing a typical particle distribution on the silicon surface, which is only partly covered with the particles. Fig-

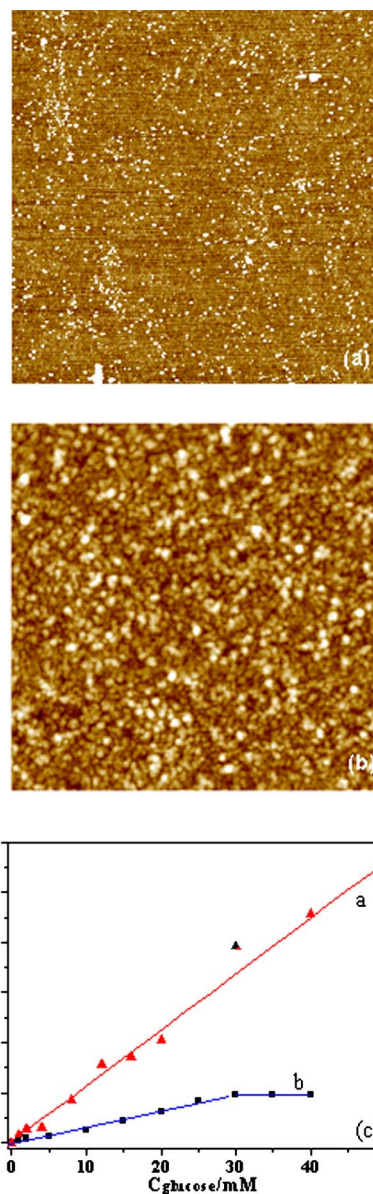


FIG. 2. (a) AFM image ( $2 \times 2 \mu\text{m}^2$ ) of the  $\text{Si}_{29}$ -Si electrode. The 1 nm particles appear as individual bright spots. (b) AFM image ( $1 \times 1 \mu\text{m}^2$ ) of the GOx electrode, showing a complete monolayer of GOx with scattered molecules forming the second layer. In both images, the particles and molecules appear to be larger than their actual sizes due to tip-induced convolution. (c) Amperometric responses of the  $\text{Si}_{29}$ -Si electrode and the GOx electrode to glucose. The current values were measured at a potential of 0.7 V for both electrodes.

ure 2(b) is an AFM image showing the GOx electrode, where the entire electrode surface is covered with a monolayer of the enzyme. Estimation based on Figs. 2(a) and 2(b) shows that typically there are 4000 GOx molecules or 8000 flavin adenine dinucleotide (FAD) centers within an electrode surface area of  $1 \times 1 \mu\text{m}^2$ , while there are only 1000  $\text{Si}_{29}$  particles within the same area. Figure 2(c) shows the amperometric responses of both kinds of electrode having the same size as the glucose concentration is varied. The response of the  $\text{Si}_{29}$ -Si electrode is at least four-fold larger than that of the GOx electrode. Characteristic rate constants for the conversion of glucose to glucose-lactone have been calculated using the results of Figs. 2(a)–2(c) as listed in Table I. The turnover rate constant ( $1/\text{s}$ ) measures the number of electrons generated by one GOx molecule per second as a result

TABLE I. Characteristic rate constants of glucose oxidation by the GOx–Si electrode and the Si<sub>29</sub>–Si electrode.

Electrode	Turnover rate constant (s <sup>-1</sup> )	Rate constant of biocatalytic process $k_{\text{red}}$ (M <sup>-1</sup> s <sup>-1</sup> )	Electrochemical rate constant (cm s <sup>-1</sup> )
GOx–Si	4	$1.07 \times 10^3$	$9.0 \times 10^{-7}$
Si <sub>29</sub> –Si	842	$1.55 \times 10^5$	$6.0 \times 10^{-3}$
GOx in solution <sup>a</sup>	750	$1.10 \times 10^4$	

<sup>a</sup>Reference 16.

of the conversion process,<sup>12,13</sup> while  $k_{\text{red}}$  is the rate constant describing the entire substance conversion process (M<sup>-1</sup> s<sup>-1</sup>).<sup>14,15</sup> The rate of the reaction between glucose and the catalytic interface GOx/Si<sub>29</sub> particle) is described by the electrochemical rate constant (cm/s).<sup>13</sup>

The above results suggest that the Si<sub>29</sub> particle is more efficient than GOx in performing the oxidation of glucose and in transducing the detected electrical signal to the silicon electrode. This enhanced detection is likely to be the result of two effects. First, the particle is accessible to glucose, allowing oxidation to take place. In the case of GOx, glucose needs to enter a small opening on the enzyme in order to reach the FAD center. Moreover, when GOx is immobilized on an electrode, random molecular orientation may reduce the possibility for glucose to reach the FAD centers. Second, if the signal transduction process involves electron tunneling across the particle to the silicon electrode, the 1 nm tunnel distance is less than that for GOx, whose shortest tunnel distance is about 2 nm.<sup>11</sup> The above consideration of the number of sensing elements causing the responses of Fig. 2(c) suggests an additional advantage of using the Si<sub>29</sub> particle in making miniature devices. The size of the particle is 1 nm<sup>3</sup>, while the size of GOx is  $6 \times 5.2 \times 7.7$  nm<sup>3</sup>. Thus, assuming that each material forms a monolayer, the surface density of active sites is higher for the particle electrode than that for the GOx electrode. Within the two-dimensional extent of a GOx molecule, about 30 Si<sub>29</sub> particles can be accommodated. Figure 3 illustrates this situation schematically.

The experimental work was performed at Hunter College of City University of New York.

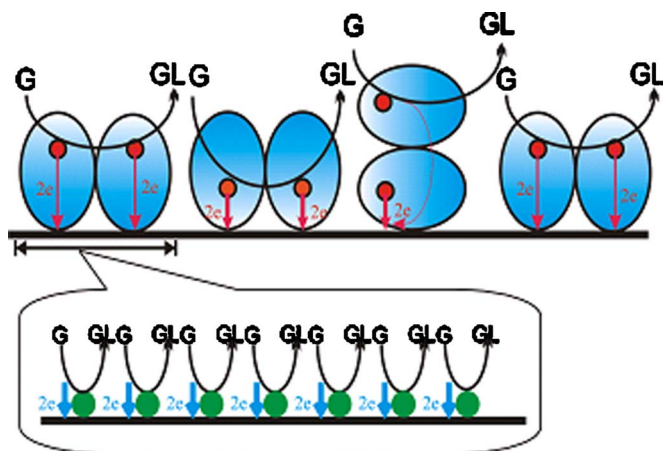


FIG. 3. Schematic illustration of the advantages of using the Si<sub>29</sub> particle compared to GOx in detecting glucose. Each “double-egg” shaped structure represents a GOx molecule, in which two FAD centers (smaller circles) reside. GOx molecules may assume different orientations when immobilized on an electrode. The arrowed lines with different widths indicate electron transfer with different strengths. The Si<sub>29</sub> particles are represented by green circles (larger circles). G and GL denote glucose and gluconolactone, respectively.

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