ACS APPLIED MATERIALS & INTERFACES

Research Article

www.acsami.org

Facile Method for Modification of the Silicon Nanowires and Its Application in Fabrication of pH-Sensitive Chips

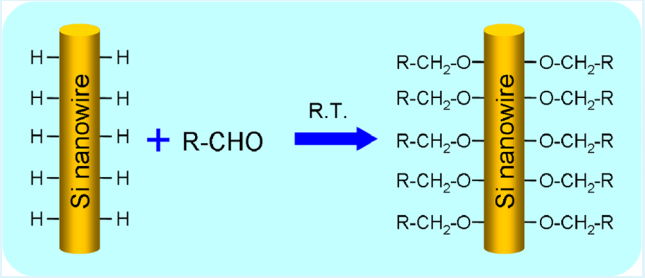
Rong Miao,[†,‡] Lixuan Mu,*[,†] Hongyan Zhang,[†] Haitao Xu,[†] Bingjiang Zhou,[†,‡] Guangwei She,[†] Pengfei Wang,[†] and Wensheng Shi*[,†]

[†]Key Laboratory of Photochemical Conversion and Optoelectronic Materials, Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing, 100190 China

[‡]Graduate School of Chinese Academy of Sciences, Beijing, 100039 China

Supporting Information

ABSTRACT: A novel, facile, and effective method for modification of SiNWs or SiNW arrays has been developed. In this method, reaction between reductive Si−H bonds on the surface of SiNWs and the aldehyde group containing in organic molecules has been used for immobilization of organic molecules onto the surface of SiNW arrays. The method is time saving and can be operated at room temperature without any other complex reaction requirement. Fluorescence images, XPS, fluorescence spectra, and IR spectra were used for characterization of the modification. Through this method, a SiNW array-based pH sensitive chip was realized by covalently immobilizing 5-aminofluorescein molecules onto the surface of SiNW arrays with glutaraldehyde as linker molecules. Fluorescence intensity of the chip increased with increasing of pH value and a linear relationship between fluorescence intensity and pH values was acquired. In addition, the chip has been successfully used for real-time and in situ monitoring of extracellular pH changes for live HeLa cells and the result exhibited fine resolution of time and space.



KEYWORDS: *SiNWs, SiNW array, modification, Si−H bonds, aldehyde group, pH sensitive chips*

1. INTRODUCTION

Silicon nanowires (SiNWs) as well as SiNW arrays are promising building blocks for future nanoelectronics, optoelectronics, and nanosensors.[1−3] Because of their nontoxicity and fine biocompatibility, SiNWs or SiNW arrays modified by specific functional groups have been successfully used in solid-state electronic devices and biomedical nanosensors.[4−7] The method for surface modification of SiNWs is crucial not only to the fabrication but also the subsequent application of the SiNW-based nanodevices.[8−12] It is known that the surface of the SiNWs is very easy to be oxidized.[13] Such silicon oxide layer is usually employed to immobilize specific molecules onto the surface of the SiNWs by hydrolysis reaction between Si−OH and Si-methoxide or Si-ethoxide groups.[14−16] However, such modification approach would bring about the inhomogeneity and variability in the number of Si−O−Si and Si−OH linkages, which could affect the consistency of the SiNWs-based devices.[8] In order to improve the controllability of the SiNWs-based devices, two-step amine-promoted reaction procedure has been used to passivate most of the SiO_2/SiNW surface trap states by appropriate monolayers.[9] An alternative way is to remove the native oxide layer by hydrofluoric acid (HF) and the resultant Si−H bonds dominating the surface of the SiNWs could be utilized to functionalize the SiNWs. Based on these abundant surficial Si−H bonds, the two-step chlorination/alkylation route and photochemical hydrosilation reaction are employed to modify the SiNWs.[8,17−22] SiNW-based devices acquired through such approaches exhibit improved performances.[23,24] However, for the purpose of bioapplication, it would be more suitable if the preparing procedure is facile and can be operated at room temperature especially when the SiNWs are already integrated in a device platform. The reaction between Si−H on silicon wafer and aldehyde has been reported and it needs UV irradiation.[25] Reaction between C═O (in carboxyl group) and Si−H has also been used for modification of silicon nanoparticles[26,27] under blue light irradiation or microwave induced heating. Despite these attractive advances, substantial effort is still needed to develop new method for SiNWs that is easily realized. It has been found that the Si−H bonds on the surface of the oxide layer-removed SiNWs own high reducibility and they have been used to reduce some metal ions (Au^{3+}, Ag^{+}, Pt^{2+}, etc.) in solution to form metal particles on the surface of SiNWs.[28,29] Meanwhile, the C═O in aldehyde group (−CHO) is much more reactive than the C═O in carboxyl group and it can be reduced easily in many cases.[30] Considering the unique reactivities of the Si−H on SiNWs surface and −CHO, the

Received: December 3, 2012
Accepted: February 20, 2013
Published: February 20, 2013

reaction between Si−H and −CHO has been used for modification of SiNW arrays in this study. Both UV irradiation and microwave induced heating can be avoided. 7-diethylaminocoumarin-3-aldehyde (COAL) and several other kinds of −CHO containing molecules have been respectively decorated onto the surface of SiNW arrays and the results demonstrate that this method is facile and effective. The reaction can be operated at room temperature under mild conditions. Furthermore, using this method, a pH sensitive chip was achieved by immobilizing 5-aminofluorescein (5-AFLU) onto the surface of SiNW arrays with glutaraldhyde as linker. The chip was successfully used for real-time and in situ monitoring of extracellular pH changes for live HeLa cells with high time and space resolutions.

2. EXPERIMENTAL SECTION

2.1. Materials. 5-AFLU was purchased from Alfa Aesar. Other reagents were purchased from Beijing Chemical Regent Co. All reagents and chemicals were AR grade and used directly without further purifications. Water used for measurement was purified by Millipore filtration system.

2.2. Instruments. Fluorescence spectra were obtained with F-4600 spectrophotometers. SEM images were recorded by a Hitachi S-4300FEG. Fluorescence images were taken with Olympus BX51TRF microscope.

2.3. Synthesis of COAL Molecules. COAL was synthesized according to a reported literature.[31] 4-Diethylaminosalicylaldehyde (4.33 g, 21 mmol), diethylmalonate (7.5 g, 47 mmol) and piperidine (4 mL) were added into absolute ethanol (100 mL). After stirring for 6 h under reflux conditions, ethanol was evaporated under reduced pressure. Then 40 mL concentrated HCl and 40 mL glacial acetic acid was added to hydrolyze the above residue. With another 7 h stirring, the solution was cooled to room temperature and poured into 300 mL ice water. Then NaOH solution (50%) was added dropwise to modulate pH of the solution to about 7, and a pale precipitate was formed immediately. After stirring for 30 min, the mixture was filtered, washed with water, dried, and then recrystallized with toluene to obtain 7-diethylaminocoumarin (1).

Fresh distilled DMF (5 mL) was added dropwise to $POCl_3$ (6 mL) at 45 °C under N_2 atm and stirred for 30 min to yield a red solution. This solution was mixed with a portion of 1 (4.25 g, 19.5 mmol, dissolved in 20 mL DMF) to yield a scarlet suspension. The mixture was stirred for 20 h at 65 °C and then poured into 300 mL of ice water. NaOH solution (40%) was added to adjust the pH of the mixture to yield large amount of precipitate. The crude product was filtered, thoroughly washed with water, dried, and recrystallized in absolute ethanol to obtain COAL (3.46 g, 14.1 mmol).

2.4. Fabrication of Substrate with SiNW Arrays. Silicon wafer (n-type, ⟨100⟩) was cut into 2 cm × 2 cm rectangular strips. In order to remove organic contaminants, the strips were ultrasonicated in acetone, ethanol and deionized water at room temperature for 20, 15, and 10 min, respectively. The cleared strips were then immersed into 4% hydrofluoric acid (HF) solution to remove the oxide layers and bring Si−H bonds onto the surfaces of the strips. Then the Si−H terminated silicon strips were soaked in a 5 mM silver nitrate and 4.6 M HF solution for 4 min to deposit appropriate Ag particles onto their surfaces, which would act as metal catalyst in the following etching process. Afterward, the strips attached with Ag particles were soaked in the etching solution consisting of 4.6 M HF and 0.2 M H_2O_2 at 50 °C for 30 min and then immersed into a mixture of nitric acid and sulfuric acid (V:V = 3:1) for 1 h to dissolve Ag and finally rinsed with deionized water three times. High-quality substrates with SiNW arrays were characterized by SEM (Figure 1a,b). The diameters of the SiNWs are in the range of 100−250 nm, whereas the wire length is around 30 μm.

2.5. Modification of SiNW Arrays with Molecules Containing Aldehyde Group. First the SiNW arrays were soaked into a 4% HF aqueous solution for 1 h to obtain highly reactive SiNW arrays with abundant Si−H bonds on their surface. Then the H-terminated SiNW arrays were immersed in 10 mM COAL (dichloromethane solution) for 1 h. Afterward, the SiNW arrays were repeatedly rinsed with dichloromethane and unreacted COAL molecules were removed completely by brief ultrasonication and monitoring the fluorescence of the washing liquid.

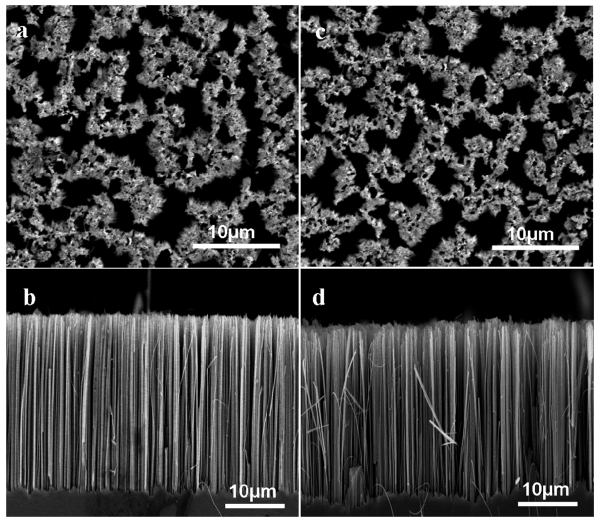


Figure 1. Morphologies of SiNW arrays before and after immersing in HF. SEM (a) top and (b) side view images of SiNW arrays before and (c) top, (d) side after immersing in 4% HF aqueous solution for 1 h.

Modification procedures of SiNW arrays with *p*-nitrobenzaldehyde and 1,4-phthalaldehyde were the same as above. The SiNW array substrates were soaked into a 4% HF solution for 1 h. Then the H-terminated SiNW arrays were immersed in a solution (dichloromethane) of 10 mM p-nitrobenzaldehyde or 1,4-phthalaldehyde for 2 h. Afterward, the SiNW arrays were repeatedly rinsed with dichloromethane and unreacted *p*-nitrobenzaldehyde or 1, 4-phthalaldehyde were removed completely by brief ultrasonication and monitoring the UV-absorbance of the washing liquid.

2.6. Modification of SiNW Arrays with 5-AFLU. After being immersed in a 4% HF aqueous solution for 1 h, the SiNW arrays were soaked into 5 mL of 50% glutaraldehyde (ethanol solution) for 1.5 h and obtained the aldehyde functionalized SiNW arrays (CHO-SiNW arrays). Then the CHO-SiNW arrays were repeatedly rinsed with ethanol after brief ultrasonication. Next, the cleaned CHO-SiNW arrays were immersed in 5 mmol 5-AFLU (ethanol solution) for 1.5 h. The SiNW arrays were repeatedly washed with ethanol and unreacted 5-AFLU molecules were removed completely by brief ultrasonication and monitoring the fluorescence of the washing liquid. Then, the arrays were soaked into a round bottomed flask containing 6 mL of 0.024 mmol/mL sodium triacetoxyborohydride (ethanol solution). After stirring for 4 h at 50 °C, the chips defined as 5-AFLU-SiNW arrays were acquired by repeatedly washed with ethanol and then dried under vacuum for 12 h.

2.7. Cell Culture, Cell Capture Assay and In situ Monitoring of pH Changes for live Cells. The HeLa cell line was obtained from Beijing Xiehe Hospital. The cell lines were maintained in Dulbecco's modified Eagle's medium containing 10% heat-inactivated FBS.

The chip was placed into a 24-well plate (Costar), and then 1 mL of a cell suspension (10^6 cells/mL) was loaded. After incubating for 24 h at 37 °C and 5% CO_2, the chip was rinsed with sterile PBS (pH 7.4) for at least five times. In order to identify the cell nuclei, the chip was incubated in 1 mL medium containing 2 μL 4′, 6-diamidino-2-phenylindole solution (DAPI: 2 μg/mL in deionized H_2O) for 20 min and followed by five sterile PBS (pH 7.4) washes. After that, the chip was placed upside down in a specific dish with 1.5 mL sterile PBS (pH 7.4) for detection by laser scanning confocal microscope (LSCM) and imaged with LSCM (Nikon- Ti + UltraVIEW VoX).

For real-time and in situ monitoring of pH changes for live cells, the PBS (pH 7.4) was drawn off carefully and a pH 5.0 citric acid-disodium hydrogen phosphate buffer was added into the dish. After 60 s, the pH 5.0 citric acid-disodium hydrogen phosphate buffer solution was drawn off and a pH 3.0 citric acid-disodium hydrogen phosphate buffer was added. The fluorescence was monitored continuously in the whole process under excitation at 405 and 488 nm simultaneously.

3. RESULTS AND DISCUSSION

3.1. Characterization of Modification. To observe the influence of the HF aqueous solution to the morphologies of the SiNW arrays, the morphologies of SiNW arrays before and after immersing into 4% HF aqueous solution have been characterized by SEM. It is found that morphologies of the SiNW arrays have little change after one hour's immersing in 4% HF aqueous solution (Figure 1).

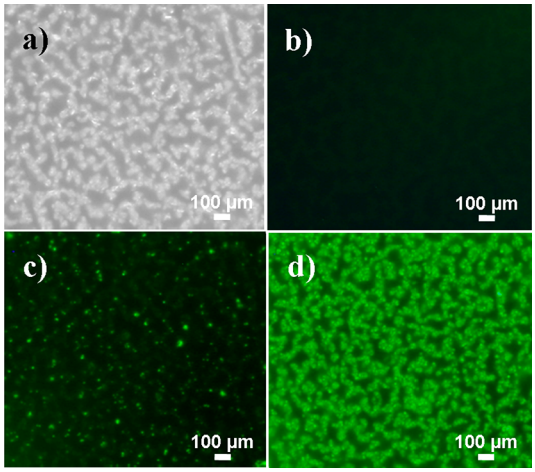


Figure 2. Fluorescence images of COAL modified SiNW arrays through different modification procedures. (a) bright-field image of SiNW arrays; (b) fluorescence image of SiNW arrays without immersing in 4% HF aqueous solution before soaking into COAL solution; (c) Fluorescence image of SiNW arrays immersing in 4% HF aqueous solution for 1 h and washed with deionized water for three times before soaking into COAL solution; (d) fluorescence image of SiNW arrays immersing in 4% HF aqueous solution for 1 h and then soaked into COAL solution immediately.

The fluorescent molecule COAL was selected as reactive agent to clarify the reaction between SiNW arrays and organic molecules. Figure 2a shows the bright-field image of the SiNW arrays. Figure 2b–d exhibits the fluorescence images of SiNW arrays after different modification procedures. As is shown in Figure 2b, SiNW arrays soaked into COAL solution without a previous immersing in 4% HF aqueous solution shows little fluorescence. Figure 2c is the fluorescence image of SiNW arrays that were immersed in 4% HF aqueous solution for 1 h and then washed with deionized water three times before soaking into COAL solution. While Figure 2d shows the fluorescence image of SiNW arrays that were immersed in 4% HF aqueous solution for 1 h and then soaked into COAL solution immediately without any water wash. It is not difficult to observe that the order of the fluorescence intensity is Figure 2d ≫ Figure 2c > Figure 2b. As the Si–H bonds on the surface of the SiNWs can be oxidized easily during the conservation.[13] Such oxide layer (e.g., native SiO_2) would arrest further bonding of the COAL onto the surface of SiNWs since few Si–H bonds are preserved. As a result, little fluorescence can be observed from HF-untreated SiNWs (Figure 2b). Even though the native SiO_2 was removed by the HF aqueous solution, most of the Si–H bonds were still oxidized during the subsequent water washes and only a few Si–H bonds could be conserved. As a result, a small number of COAL molecules could be bonded onto the surface through the reaction between remnant Si–H bonds and the –CHO containing in COAL. This is why only a weak fluorescence was observed from water washed SiNWs (Figure 2c). When SiNW arrays were immersed in HF aqueous solution for a while and then soaked into COAL solution immediately, there were abundant Si–H bonds on the surface of the SiNWs and they could react with COAL molecules. So plentiful COAL molecules can be covalently bonded onto the SiNWs surface and a strong fluorescence was observed (Figure 2d). From these results, it can be demonstrated that the Si–H bonds on SiNWs play a crucial role during the modification.

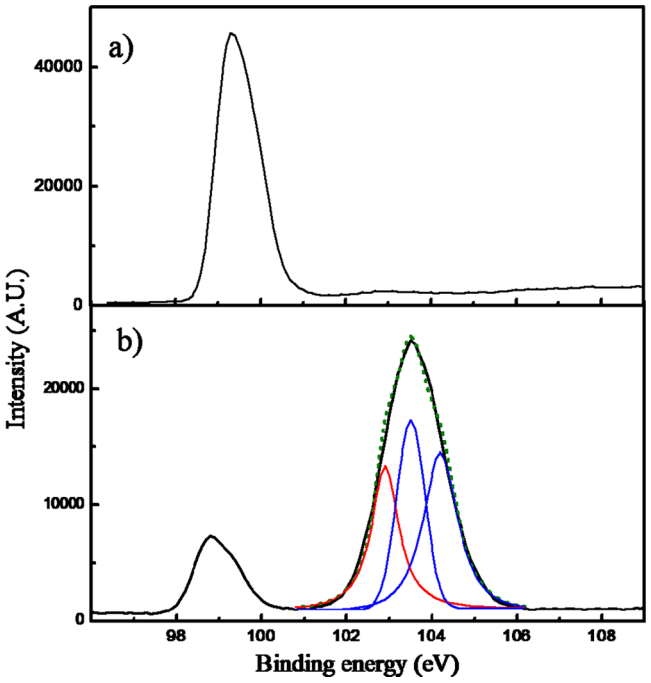


Figure 3. High-resolution XPS spectra of the Si (2p) region of (a) H-terminated SiNW arrays and (b) COAL modified SiNW arrays. The black solid lines are the data, the colored solid lines (blue and red) are the deconvolutions, and the green dashed line is the resulting fits to the spectrum.

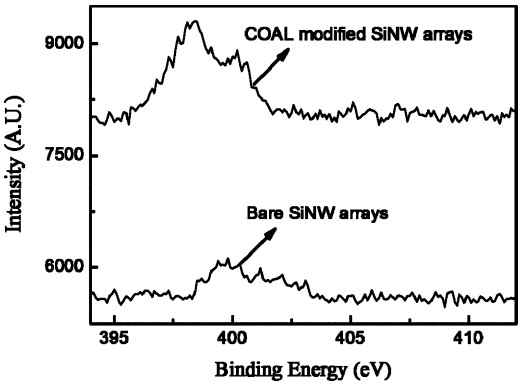
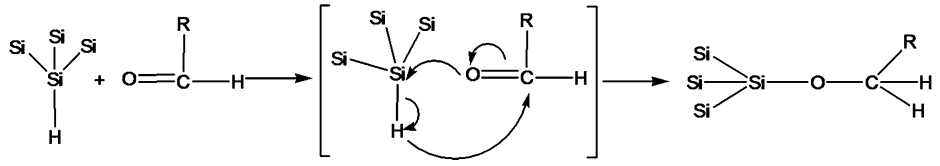


Figure 4. N1 XPS spectra of the bare SiNW arrays and COAL modified SiNW arrays.

dx.doi.org/10.1021/am302953f | ACS Appl. Mater. Interfaces 2013, 5, 1741–1746

Scheme 1. Proposed Mechanism of Reaction between Reductive Si−H Bonds and −CHO



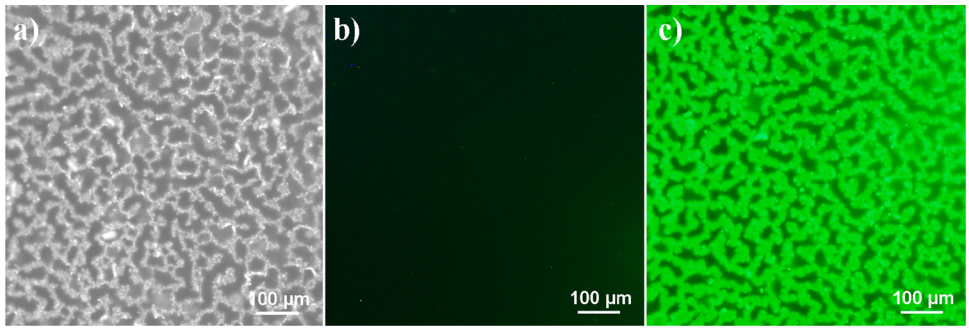


Figure 5. Fluorescence images of SiNW arrays (b) before and (c) after modification with 5-AFLU. (a) bright-field image of SiNW arrays.

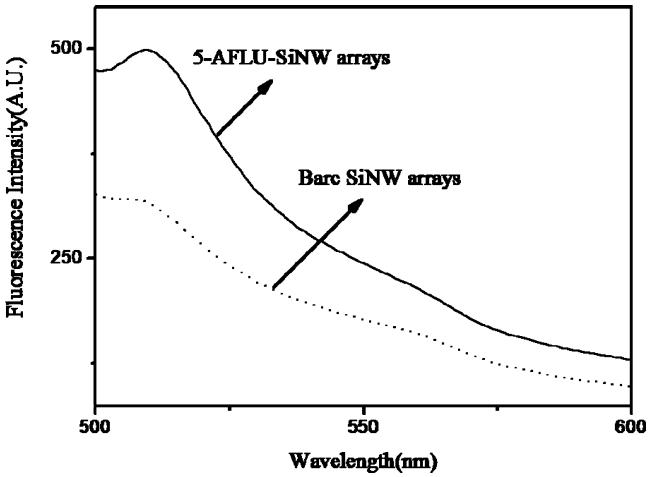


Figure 6. Fluorescence spectra of SiNW arrays (dashed line) and 5-AFLU-SiNW arrays (solid line), λ_{ex} = 450 nm.

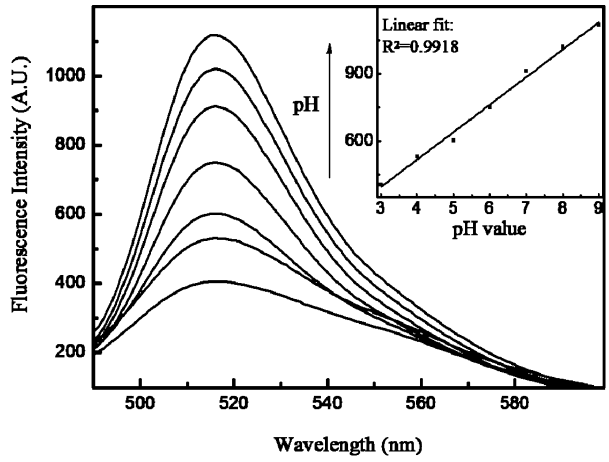


Figure 7. Fluorescence spectra of 20 μg/mL 5-AFLU-SiNWs solution in pH 3−9 buffered system (10 mM citric acid-disodium hydrogen phosphate with different pH values). The inset plot shows the linear relationship between the fluorescence intensity and the pH values, λ_{ex} =450 nm; λ_{em} = 516 nm. Measurements of the fluorescence intensity in solutions with different pH values have been repeated for five times with a RSD of 1.1%.

For further confirming the modification, XPS spectra of the bare SiNW arrays and COAL modified SiNW arrays were analyzed. The Si2p signal of H-terminated SiNW arrays (Figure 3a) only shows a peak at around 99 eV, which could be assigned to silicon from the SiNW arrays.[32] After modification, a broad peak was observed in the higher binding energy (Figure 3b) in Si2p region and it can be deconvoluted into three peaks as follow. The 104.2 and 103.5 eV were attributed to SiO_2 on Si substrate; the peak at 102.9 eV was in accordance with the Si−O−C bonds.[33] Furthermore, the contents of nitrogen on the surface of bare SiNW arrays and COAL-modified SiNW arrays can be analyzed by N1s signal. From Figure 4, it can be observed that there was little nitrogen atom on the surface of bare SiNW arrays but more nitrogen on COAL modified arrays. These observations demonstrate that the COAL molecules have been connected to the SiNW arrays. Combining the results from the fluorescence images, it could be further confirmed that the COAL molecules were covalently bound onto the surface of the SiNWs via the reaction between Si−H bonds and −CHO. Scheme 1 provides a reaction profile between reductive Si−H bonds and −CHO.[34,35] On the basis of such a method, other −CHO containing organic molecules, such as *p*-nitrobenzaldehyde and 1, 4-phthalaldehyde can also be immobilized onto the surface of SiNW arrays (see Figure S1 in the Supporting Information).

Further more, stability of the as prepared COAL modified SiNW arrays have been investigated (see the Supporting Information, Figure S2). The result showed that the COAL modified SiNW arrays own satisfactory stability after being kept in dark for a month.

3.2. pH Sensitive Chip and Its Application. On the basis of the above approach, we fabricated a SiNW array-based pH sensitive chip for real-time and in situ monitoring of pH changes for live HeLa cells. Using glutaraldehyde as linker molecules, the water-soluble, nontoxic, and pH sensitive molecule 5-AFLU was covalently immobilized onto the surface of SiNW arrays. The fluorescence images of 5-AFLU-modified SiNW arrays (5-AFLU-SiNW arrays) are shown in Figure 5

dx.doi.org/10.1021/am302953f | ACS Appl. Mater. Interfaces 2013, 5, 1741−1746

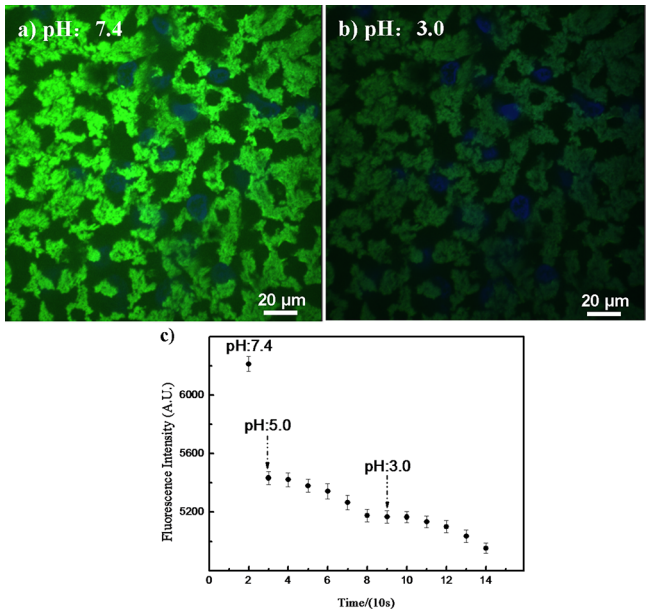


Figure 8. Fluorescence images of the substrate for in situ monitoring of pH changes for live cells. The fluorescence images of the substrate under (a) pH 7.4 and (b) pH 3.0 respectively. (c) Fluorescence intensity of the substrate after citric acid-disodium hydrogen phosphate buffer solution (10 mM) with different pH values (pH 5.0 and 3.0) was added into the system. Error bar was the mean ± SD from three independent measurements.

(Figure 5a is the bright-field image of the SiNW arrays.). The bare SiNW arrays were nonfluorescent (Figure 5b), whereas the SiNW arrays modified by 5-AFLU exhibited high fluorescence (Figure 5c). Meanwhile, the fluorescence spectra of 5-AFLU-SiNW arrays exhibited an additional emission at 516 nm when excited at 450 nm (Figure 6). These results show that 5-AFLU molecules have been successfully decorated onto the surface of SiNW arrays.

To investigate the response of the 5-AFLU-SiNW arrays to pH, we dispersed 1.5 mg of 5-AFLU-SiNWs scraped from the chip in 1 mL of absolute ethanol. After ultrasonicating for 15 min, a stock solution was formed ([5-AFLU-SiNWs] = 1.5 mg/mL). 5-AFLU-SiNWs (from stock solution) were dispersed in citric acid-disodium hydrogen phosphate buffer solutions with different pH values (pH 3–9). The fluorescence spectra of 5-AFLU-SiNWs under different pH values were recorded and the results are shown in Figure 7. It was found that the fluorescence intensity of the 5-AFLU-SiNWs increased gradually with pH increase and there is a good linear relationship between the fluorescence intensity of 5-AFLU-SiNWs and pH values from 3 to 9 (inset plot in Figure 7).

To verify its cellular application, the as-prepared 5-AFLU-SiNW arrays were utilized as a chip for monitoring extracellular pH changes for live HeLa cells (Figure 8). The HeLa cells (blue dots in Figure 8a and Figure 8b) were captured by the 5-AFLU-SiNW arrays and the fluorescence of the cell-captured 5-AFLU-SiNW arrays under different pH values was monitored. It was found that the substrate exhibited strong fluorescence under pH 7.4, but the fluorescence intensity of the substrate decreased obviously when the buffer was changed into pH 5.0 and dropped to the lowest point at pH 3.0 (Figure 8c). However, the cells showed little change during the process, which should be attributed to the acid resistance of the cancer cells.[36,37] Though the substrate that the modified SiNWs stand on contributes little to pH sensing, it is the carrier of the sensor and facilitate its modification and help its further bioapplication.

4. CONCLUSIONS

In summary, a new method for covalently immobilizing organic molecules onto the surface of SiNW arrays by reaction between reductive Si–H bonds and aldehyde group was reported. This facile and effective method is of universality to aldehyde group containing molecules, such as COAL, p-nitrobenzaldehyde and 1, 4-phthalaldehyde. On the basis of this method, a pH sensitive chip was achieved by covalent immobilization of 5-AFLU molecules onto the surface of SiNW arrays by using glutaraldehyde as linker molecules. The chip performed satisfactorily in pH sensing. Fluorescence intensities of the chip sensitively increased with pH value increasing and there is a good linear relationship between fluorescence intensity and pH values (from 3 to 9). When used for real-time and in situ monitoring of extracellular pH changes (from 7.4 to 3) for live HeLa cells, the chip exhibited fine resolution of time and space. The fluorescence of the cell-captured chip decreased gradually when the pH of the cell culture was changed from 7.4 to 5.0 and then to 3.0. It is envisioned that the facile and effective method described here for modification of SiNW arrays holds potential use for further developing more powerful SiNWs and SiNW array-based devices.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figure S1 is the IR spectra of *p*-nitrobenzaldehyde and 1,4-phthalaldehyde modified SiNW arrays. Stability of the as prepared COAL modified SiNW arrays is shown in Figure S2. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: shiws@mail.ipc.ac.cn (W.S.S.); mulixuan@mail.ipc.ac.cn (L.X.M.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by the Chinese Academy of Sciences, NSFC (Grants 51272302, 61025003, 50902134, 21103211, 51272258, and 61204128), National Basic Research Program of China (973 Program) (Grants 2010CB934103 and 2012CB932400) and Beijing Natural Science Foundation (Grant 2102043).

■ REFERENCES

(1) Cui, Y.; Lieber, C. M. *Science* **2001**, *291*, 851–853.
(2) Michael, T. K.; Jonathan, K. M. C.; Andrew, B. B. *Nature* **1996**, *382*, 214–215.
(3) Shao, M. W.; Shan, Y. Y.; Wong, N. B.; Lee, S. T. *Adv. Funct. Mater.* **2005**, *15*, 1478–1482.
(4) Gao, Z. Q.; Ajay, A.; Alastair, D. T.; Navab, S.; Fang, C.; Tung, C. H.; Fan, Y.; Kavitha, D. B.; Kong, J.-M. *Anal. Chem.* **2007**, *79*, 3291–3297.
(5) Li, Z.; Chen, Y.; Li, X.; Kamins, T. I.; Nauka, K.; Williams, R. S. *Nano Lett.* **2004**, *4*, 245–247.
(6) Hahm, J.; Lieber, C. M. *Nano Lett.* **2004**, *4*, 51–54.
(7) Masood, M. N.; Chen, S.; Carlen, E. T.; Berg, A. V. D. *ACS Appl. Mater. Interfaces* **2010**, *2*, 3422–3428.

(8) Assad, O.; Puniredd, S. R.; Stelzner, T.; Christiansen, S.; Haick, H. *J. Am. Chem. Soc.* **2008**, *130*, 17670−17671.
(9) Paska, Y.; Haick, H. *ACS Appl. Mater. Inter.* **2012**, *4*, 2604−2617.
(10) Rabah, B.; Danial, D. M. W. *J. Am. Chem. Soc.* **1999**, *121*, 11513−11515.
(11) Yang, M.-L.; Rosalie, L. M. T.; Marcel, G.; Jacob, B.; Ahmed, A.; Frits, A. W.; Jan, C. M. H.; Han, Z. *Langmuir* **2008**, *24*, 7931−7938.
(12) Aswal, D. K.; Lenfant, S.; Guerin, D.; Yakhmi, J. V.; Vuillaume, D. *Anal. Chim. Acta* **2006**, *568*, 84−108.
(13) Jillian, M. B. *Chem. Rev.* **2002**, *102*, 1272−1306.
(14) Fan, H. Y.; Lu, Y. F.; Stump, A.; Reed, S. T.; Baer, T.; Schunk, R.; Pérez-Luna, V.; Lopez, G. P.; Brinker, C. J. *Nature* **2000**, *405*, 56−60.
(15) Miao, R.; Mu, L. X.; Zhang, H. Y.; Xu, H. T.; She, G. W.; Wang, P. F.; Shi, W. S. *J. Mater. Chem.* **2012**, *22*, 3348−3353.
(16) Nesrine, A.; Latifa, B.; Jessem, L.; Jean-Franc-ois, L.; Souhir, B. *Langmuir* **2012**, *28*, 656−665.
(17) Yang, C. S.; Richard, A. B.; Susan, M. K.; Howard, W. H. L.; Gildardo, R. D. *J. Am. Chem. Soc.* **1999**, *121*, 5191−5195.
(18) Christian, S.; Susann, N.; Roland, F.; Bart, J. R. *Small* **2012**, *8*, 569−577.
(19) Matthew, R. L.; Paul, F.; Peter, M. E.; Christopher, E. D. C. *J. Am. Chem. Soc.* **1995**, *117*, 3145−3155.
(20) Rabah, B.; Danial, D. M. W. *J. Am. Chem. Soc.* **1999**, *121*, 11513−11515.
(21) Su, Y. Y.; Wei, X. P.; Peng, F.; Zhong, Y. L.; Lu, Y. M.; Su, S.; Xu, T. T; Lee, S. T.; He, Y. *Nano Lett.* **2012**, *12*, 1845−1850.
(22) Puniredd, S. R.; Assad, O.; Stelzner, T.; Christiansen, S.; Haick, H. *Langmuir* **2011**, *27*, 4764−4771.
(23) Paska, Y.; Stelzner, T.; Christiansen, S.; Haick, H. *ACS Nano* **2011**, *5*, 5620−5626.
(24) Bashouti, M. Y.; Tung, R. T.; Haick, H. *Small* **2009**, *5*, 2761−2769.
(25) Hacker, C. A.; Anderson, K. A.; Richter, L. J.; Richter, C. A. *Langmuir* **2005**, *21*, 882−889.
(26) He, Y.; Kang, Z. H.; Li, Q. S.; Tsang, C. H. A.; Fan, C. H.; Lee, S. T. *Angew. Chem.* **2009**, *121*, 134−138.
(27) He, Y.; Zhong, Y. L.; Peng, F.; Wei, X. P.; Su, Y. Y.; Su, S.; Gu, W.; Liao, L. S.; Lee, S. T. *Angew. Chem.* **2011**, *123*, 3136−3139.
(28) Elisabeth, G.; Jacques, B.; Yannick, C.; Sabine, Szunerits.; Gilles, P.; Rabah, B. *ACS Appl. Mater. Inter.* **2009**, *1*, 1396−1403.
(29) Peng, K. Q.; Wang, X.; Wu, X. L.; Lee, S. T. *Nano Lett.* **2009**, *9*, 3704−3709.
(30) Ingrid, K. H.; Arie, C. B.; Jan, M. J.; Johan, W. T.; Ted, M. S. *Starch* **2006**, *58*, 616−622.
(31) Wu, J. S.; Liu, W. M.; Zhuang, X. Q.; Wang, F.; Wang, P. F.; Tao, S. L.; Zhang, X. H.; Wu, S. K.; Lee, S. T. *Org. Lett.* **2007**, *9*, 33−36.
(32) George, J. C.; Gottlieb, S. O. *Appl. Phys. Lett.* **1985**, *47*, 604−606.
(33) Wagner, C. D.; Passoja, D. E.; Hillery, H. F.; Kinisky, T. G.; Six, H. A.; Jansen, W. T.; Taylor, J. A. *J. Vac. Sci. Technol.* **1982**, *21*, 933−944.
(34) Han, Z. Y.; Chen, D. F.; Wang, Y. Y.; Guo, R.; Wang, P. S.; Wang, C.; Gong, L. Z. *J. Am. Chem. Soc.* **2012**, *134*, 6532−6535.
(35) Vikram, P. D.; Satyabrata, S.; David, M. J.; Ian, R. H.; Jason, L. *ACS Appl. Mater. Interfaces* **2011**, *3*, 2830−2837.
(36) Izumi, H.; Torigoe, T.; Ishiguchi, H.; Uramoto, H.; Yoshida, Y.; Tanabe, M.; Ise, T.; Murakami, T.; Yoshida, T.; Nomoto, M.; Kohno, K. *Cancer Treatment Rev.* **2003**, *29*, 541−549.
(37) Xu, T.; Su, H.; Suthakar, G.; Yuan, Z. M. *Landes Biosci.* **2011**, *11*, 1316−1322.