RNA Functionalized Carbon Nanotube for Chemical Sensing

M. Chen[*], S. S. Datta[**], S. M Khamis[***], J. E. Fischer[****] and A. T. Johnson[*****]

University of Pennsylvania, Philadelphia, PA, USA
[*]Current Address: Simmons College, Boston, MA, USA, michelle.chen@simmons.edu
[**]Current Address: Harvard University, Cambridge, MA, USA, ssdatta@fas.harvard.edu
[***]Current Address: Nanosense, Inc., Redwood City, CA, USA, skhamis@evolvedmachines.com
[****]fischer@seas.upenn.edu
[*****]cjohnson@physics.upnn.edu

ABSTRACT

We demonstrate a versatile class of nanoscale chemical sensors based on single stranded RNAs (ssRNAs) as the chemical recognition sites and single-walled carbon nanotube field effect transistors (SWNT-FETs) as the electronic readout components. The sensor responses differ in sign and magnitude depending on both the type of gaseous analyte and the sequence of ssRNA being used. Such rapid response, sensitivity to large variety of analytes, self-regenerating ability, and reproducibility make ssRNA-functionalized SWNT-FETs promising building blocks in developing large arrays of sensors for electronic olfaction and disease diagnosis.

Keywords: carbon nanotubes, field effect transistors, chemical sensors, RNA functionalization

1 INTRODUCTION

Semiconducting single-walled carbon nanotubes (SWNTs) have electronic states that lie on the one-dimensional carbon cage structure, making them exceedingly sensitive to environmental stimuli. Bare and polymer-coated SWNTs are found to be sensitive to various gases [1-6]. However, SWNT functionalized with biomolecular complexes [7-11] could detect species that otherwise would have only weak interaction with unmodified nanotubes. These derivatized SWNTs and semiconducting nanowires [12-14] are attractive chemical and molecular sensors due to their high sensitivity, fast response time, and compatibility with array fabrication [15].

Recently, bridging the science of SWNTs with biology has evolved into a thriving research initiative [12] Nucleic acid biopolymers' affinity to analytes can be specifically engineered [16,17]. For example, high throughput screening is used to select films of dye-labeled single stranded DNA (ssDNA) for use as gas sensors with fluorescent readout [19,20]. SsDNA, as well as ssRNA, has high affinity to SWNT due to an attractive π–π stacking interaction with the nanotube surface [17]. Even with such interaction the electronic integrity of the SWNT is preserved. These facts motivate the exploration of ssDNA/ssRNA functionalized SWNT hybrid nanostructures as electronic gas sensors.

Nucleic acids (DNA) and ribonucleic acid (RNA) are the genetic materials of all living organisms. RNA, in particular, relays the information stored in DNA to synthesize proteins. Although, the structure of RNA and DNA only slightly differs in their sugar and bases, RNA is much more reactive to chemical and biological species than DNA. In biological research, RNAs have been used as catalysts and mediators for a variety of organic and inorganic reactions [21-26]. Recently, short interfering RNAs have been coupled to carbon nnanotubes as drug delivery systems for RNA interference to silence genes [27]. Long RNA strands have been bound to carbon nanotubes for fluorescent and Raman spectroscopic studies [18]. However, there are still many interesting science and application for RNA-SWNT complex that have yet been explored.

In light of our work on DNA-functionalized carbon nanotube for chemical sensing [16], we aim to improve the sensitivity and specificity of our sensors by functionalization of SWNTs with molecules that interact more strongly with a larger variety of species. Single stranded RNA is a good candidate for such functionalization because it, like DNA, also binds to the nanotubes via π–π stacking interaction. RNA can be a more superior chemical recognition component than DNA due to its higher reactivity to more chemicals. In this report, we discuss the RNA-functionalized SWNT-FETs as chemical sensors

2 EXPERIMENTAL DETAILS

2.1 Device Fabrication

SWNTs are grown on SiO_2/Si substrate (oxide thickness ~ 200-400 nm) by catalytical chemical vapor deposition with $Fe_2(NO_3)_3$ as catalyst. Field effect transistors (FETs) are fabricated by writing source-drain contacts to the nanotubes using electron beam lithography followed by thermal evaporation of chrome and gold. The degenerately doped silicon substrate is used as the

backgate. Source-drain current I_{SD} is measured as a function of gate voltage. Only devices with individual p-type semiconducting SWNT with ON/OFF ratio >1000 are selected for the electrical experiments.

2.2 RNA Functionalization

Two sequences of single stranded RNA (ssRNA) that correspond to prior DNA experiments [16] are used so the data in the two systems can be directly compared:

RNA S1
5' GAG UCU GUG GAG GAG GUA GUC 3'

RNA S2
5' CUU CUG UCU UGA UGU UUG UCA AAC 3'

Single stranded RNA is functionalized onto carbon nanotube surfaces via non-covalent π–π stacking interaction, similar to that of DNA [??]. For both the sequences used, application of single-stranded RNA causes the threshold voltage to decrease by 3-6 volts in the characterization of source-drain current vs. backgate voltage. This corresponds to a hole density decrease of roughly 400/mm, assuming a backgate capacitance (25 aF/mm) that is typical for this device geometry [29]. Furthermore, the functionalization of single stranded RNA typically decrease the ON-state current of SWNT-FET by ~ 10-20%. This suggests weak carrier scattering by the RNA molecular coating.

2.3 Sensing Setup

Five gaseous analytes are measured: methanol, propionic acid, trimethylamine (TMA), dinitrotoluene (DNT; 50 mg/mL in dipropylene glycol), and dimethyl methylphosphonate (DMMP; a simulant to the nerve agent sarin [30]. Saturated vapor of each chemical is stored in a reservoir. Air is pumped through the reservoir and delivers about 3% of the saturated vapor concentration at 0.1 mL/sec to the devices. The air or air/analyte mixture was directed toward the sample through a 2 ± 0.1 mm diameter nozzle positioned 6 ± 1 mm above the sample surface. Valves can be controlled so that diluted analyte and air can be applied to the sample alternately for a set time (~ 50 seconds), after which the flow reverted to plain air. For each sample, source-drain current (I) vs. gate voltage is characterized and air/analyte experiments are done on both the bare and single stranded RNA functionalized SWNT-FETs. The analyte-induced changes in the source-drain current (I) are measured at V_B = 100 mV and V_G = 0V.

3 RESULTS AND DISCUSSIONS

3.1 AFM Analysis

Figure 2 shows the AFM image of a ssRNA (S1) functionalized SWNT. By observing along the length of the nanotube, the ssRNAs appear to "pearl" up on the nanotube, as more brighter/higher structures are seen along the nanotubes. A linescan (data not shown) over the RNA "pearls" along the length of the tube indicates that the height increase due to the RNA is 1.2 ± 0.2 nm. This height increase is in agreement with the value in the DNA case [16].

The pearling of RNA on SWNT is not seen in the case of single stranded DNA. DNA forms a rather uniform thin layer on the nanotube [16]. This can be reasoned by the fact that single stranded RNA is more prone to self-hybridization and formation of secondary structures than DNA, while the single stranded DNA tends to maintain linear structure. Also, note that the pearling of RNA occurs mostly on the nanotube, and not much on the SiO_2 surface. This is different from the pronounced coverage of DNA on the substrate [16]. The elevated structures seen on the sample surface in Figure 2 are residual resist from e-beam lithography process. These residual resists can be removed through an annealing process that is discussed above.

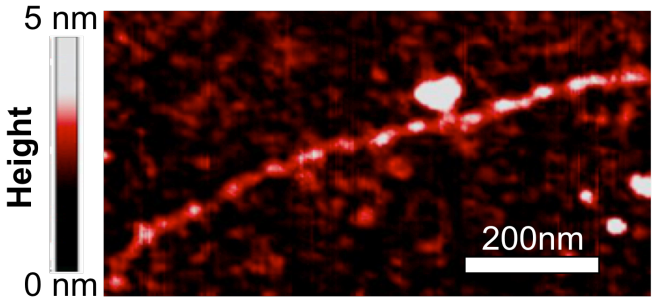

Figure 1: SWNT functionalized with RAN S1 shows pearling along the length of the tube.

3.2 Sensing Response to Chemical Vapors

We electrically detect various chemical vapors by monitoring the current change in the FET device as a function of time when the RNA functionalized carbon nanotube is exposed to the gas/air cycles. Two sequences of RNA and five analytes are tested. The two RNA strands used in this experiments have the same base sequences as the corresponding DNA strands used in the previous experiment [16]. The gases used for evaluating RNA-SWNT sensors are the same as the previous DNA-SWNT experiment, allowing direct comparison of sensing response in the two systems.

Table 1 lists the percent change in the devices' current for all combinations of RNA vs. analytes when the device is exposed to chemical vapors. It is evident from our data that bare SWNTs do not show response to any of the analytes except TMA. However, the response to the analytes is significantly enhanced after the same device is coated with single stranded RNA. Therefore, we conclude that the single stranded RNA enhances the binding affinity of the analytes and increases the sensor's response.

Analyte	Bare SWNT	SWNT + RNA S1	SWNT + RNA S2
PA	0±1	+45±10	+40±5
TMA	-9±2	-40±10	-45±5
Methanol	0±1	+32±5	+20±5
DMMP	0±1	+30±5	-35±10
DNT	0±1	-20±5	-70±10

Table 1. Summary of gas sensing results for ssRNA functionalized SWNT-FETs to five chemical analytes. Each data value (percent current change) is the mean of 5-10 samples, with standard deviation as the uncertainty.

Comparing the responses of SWNTs functionalized with RNA S1 and RNA S2 on the same gas, the two columns cannot be related by a simple multiplicative factor. This suggests that each RNA sequence is a unique chemical recognition component for SWNT-FET sensors.

Different RNA sequence can also have opposite response to the same chemical analyte. In particular, the sign of response to DMMP is opposite for RNA S1 and S2 devices functionalized devices. RNA S1 device shows a 30% current increase with exposure to DMMP (Figure 2), but RNA S2 device shows a 35% decrease in the current with DMMP exposure (Table 1). Although the detailed origin for the difference in the sign of sensing response is not clearly understood, it can be reasonably assumed that the different shapes in secondary structures of RNA S1 and RNA S2 elicit different interactions even with the same chemical analyte.

From the sensing response to DMMP as shown in Figure 2, it is intriguing that the sensor responds very rapidly (< 300 ms) to DMMP, but recovers slower when DMMP is removed. Similar sensing characteristics of fast response and slow recovery are observed when RNA-SWNTs are exposed to TMA and to methanol (data not shown). Such results may suggest that there exist some similarities in the interaction mechanism between RNA and these three chemical analytes: DMMP, TMA, and methanol.

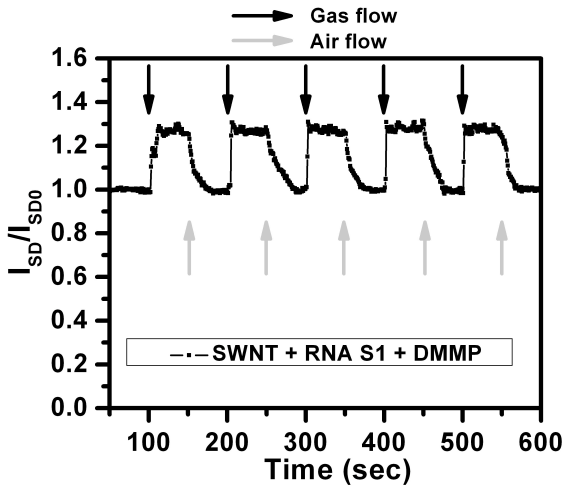

Figure 2. RNA S1 functionalized carbon nanotube shows 30% increase in the current when exposed to DMMP.

The RNA-functionalized SWNT sensors show very rapid response and recovery time to the chemical analytes. Figure 3 shows the nearly rectangular wave-like response characteristics to propionic acid on a RNA (S2) functionalized SWNT. When propionic acid (PA) is introduced (as indicated by the black arrows) the sensor responds rapidly (within 1 second) with 40% increase in the current, indicating that the PA is de-protonated in the residual water near the nanotube, forming a highly negatively charged entity near the nanotube. After flowing air replaces the PA (as shown by the gray arrows), the device current rapidly comes back to baseline, indicating that the device can quickly refresh itself once the analyte is removed.

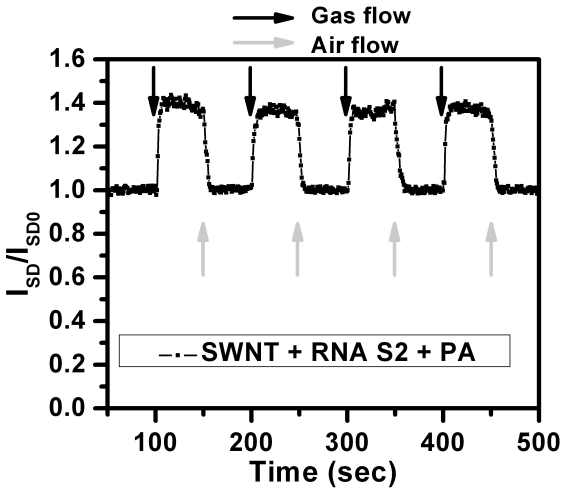

Figure 3. Sensor response to propionic acid (PA) on RNA S2 functionalized SWNT-FET. The sensor responds and recovers very rapidly.

The sign and the magnitude of the sensing response depend on the RNA sequence being functionalized and the chemical analyte being detected (Table 1). The sensor can respond and regenerate very quickly, in the order of seconds (Figure 3). The sensing response is reproducible for more than 50 cycles. Therefore, the RNA-functionalized SWNT-FETs show promise as specific and efficient nano-scaled sensor component for realization of an electronic nose.

An electronic nose is inspired by biological olfactory systems where thousands of different odor receptors, each responsive to many different odorants, perform molecular identification and analysis. The different receptor component in an electronic nose can be achieved by functionalizing SWNT-FETs with different sequences of single stranded RNA. The appropriate RNA sequence, each with distinct response to a collection of chemicals, can be selected by high throughput screening of RNAs' chemical versatility, and nucleic acid engineering. When combined with multiplexed arrays fabrication, a large electronic olfaction array made of single-stranded RNA functionalized SWNT-FETs can be realized.

4 CONCLUSIONS

We demonstrate that single stranded RNA-functionalized SWNT-FETs behave as specific, sensitive, and reproducible gas sensors, with fast response and recovery time. SsRNAs serve as effective chemical recognition sites on SWNT-FET sensors due to their strong interactions with chemical vapors. The sign and magnitude of sensing response for depends on the specific sequence of the ssRNA. Our results suggest that RNA-functionalized SWNT-FETs show great promise for development into a specific and versatile nanosensor for a large variety of gases and molecules.

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