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Switchable redox activity by proton fuelled DNA nano-machines†

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The switching electrochemical property of an SWNT/DNA hybrid can be produced through reversible conformational changes between the closed and open state originating from the pH-responding i-motif DNA which significantly improves its molecular switching and stability by hydrophobic interactions with SWNTs.

A DNA nanomachine is considered a versatile building block for nano-electronics devices because of its well defined structure and controllable intermolecular interactions to external signals.[1–3] A key challenge of DNA nanomachines will require molecular-sized electro-active materials that can work efficiently in generating motion and electric/electrochemical activity.[4] Interestingly, single-walled carbon nanotubes (SWNTs) effectively lower the junction resistance due to the tunneling effect arising from π–π interactions between the DNA and the walls of the nanotubes.[5,6] These properties of the SWNT are considered to be suitable to overcome the lack of electrical property underlying the DNA nanomachines. Here, we show that conjugating SWNT to a DNA motif significantly improves its molecular strand strength and the stability of this pH driven enthalpic molecular machine. In addition, the switching electrochemical properties of the SWNT/DNA hybrid have been investigated for use in nano-bioelectronic devices.

To construct nanomachines possessing switchable and controllable redox properties, we synthesized a SWNT/DNA hybrid based on i-motif DNA (21 mer single strand) that was formed from the covalent bonding between the carboxyl groups on the SWNT surface and the amine groups on the i-motif DNA (Fig. 1(a)). The i-motif DNA is a four-folded DNA strand structure due to intramolecular noncanonical base-pair interactions between protonated and unprotonated cytosine residues (*i.e.*, a C^+:C base-pair) under acid conditions.[7] The protonated cytosines are deprotonated with increased pH and the DNA strand then adopts a random coil structure. The SWNT/DNA hybrid gave a transparent, blackish and homogeneous suspension in aqueous solution

and showed improved dispersion of SWNTs by chemically attached DNA compared with a carboxyl functionalized SWNT (f-SWNT) dispersed solution (Fig. 1(b)). Fig. 1(c) shows both small bundles and individually dispersed SWNTs by attachment to DNA at pH 8, which is further direct evidence for the soluble sample containing carbon nanotubes. The absorption peaks of the SWNTs were broader than the reported van Hove singularity (vHs) transitions of well-dispersed HiPCO SWNT in solution because of the presence of the small bundles and surface modification of SWNTs (Fig. 1(d)), but the peak positions were in good agreement.[8] The SWNT/DNA hybrid showed vHs transitions of metallic (E^M_{11}) and semiconducting SWNTs (E^S_{11}, E^S_{11}) in the expected spectral ranges. We thus hypothesized that the electronic properties of SWNTs were retained in the hybrids.[9] The absorption peak occurring at 268 nm was shifted to shorter wavelength with increasing pH (inset in Fig. 1(d)).[10] This result indicates that the i-motif DNA on the SWNT underwent a conformational change to a random coil structure.

The conformational changes in the DNA were also confirmed by circular dichroism (CD) spectroscopy either in the absence or in the presence of SWNTs (Fig. 2(a)). Positive and negative bands near 287 and 256 nm, respectively, are observed in Fig. 2(a), indicating that the SWNT/DNA hybrid adopted a typical i-motif conformation at pH 5.[11] As the pH
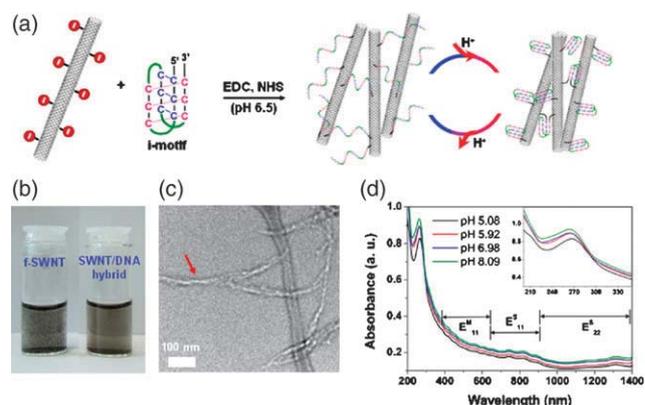
Fig. 1 (a) Schematic diagram showing f-SWNT (SWNT-COOH) combining with i-motif DNA modified by amine linkers by covalent bonding and the working cycle between random coil (pH > 7) and i-motif (pH < 5) structures. (b) Photographs of well dispersed SWNT/DNA hybrid solution compared with an f-SWNT dispersion solution (c = 0.1 mg ml^{-1}). (c) Cryo-TEM images of SWNT/DNA hybrids at pH 8. Arrow indicates the SWNT/DNA hybrids. (d) UV–Vis absorption spectrum of the SWNT/DNA hybrids as a function of pH. The inset shows a close-up in the i-motif DNA absorption region.

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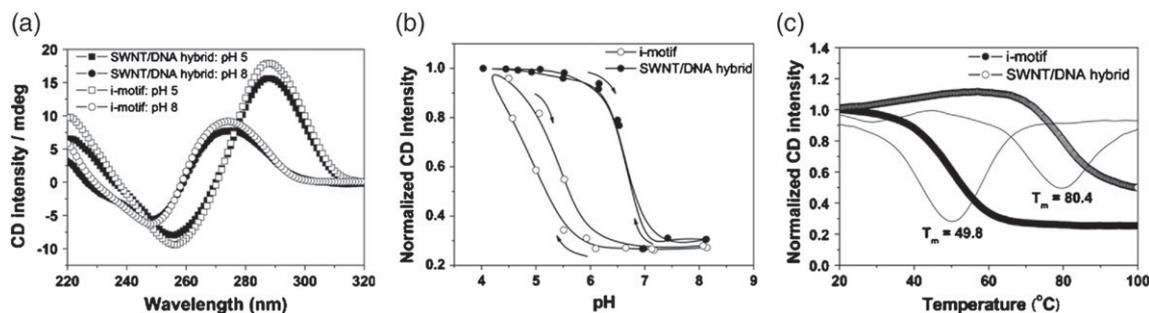
Fig. 2 (a) CD spectra of the i-motif DNA and the SWNT/DNA hybrid in 0.15 M PBS at pH 5 and 8. (b) Normalized CD intensity at 287 nm (the maximum positive band wavelength of the closed state) of the i-motif DNA and the SWNT/DNA hybrid when the pH was gradually increased to pH 8 and then decreased to pH 4. The change in pH was produced by the addition of 1 M HCl and or 1 M NaOH in 0.15 M PBS. (c) CD melting spectral changes of i-motif DNA and the SWNT/DNA hybrids in 0.15 M PBS at pH 5. Normalized absorption changes at 287 nm were plotted against temperature. The derivative of the curve is in arbitrary units.

gradually increased, the DNA strands on the SWNTs adopted a random coil conformation as the cytosine was deprotonated. This structural change was followed by a sharp decrease the ellipticity at 287 nm. During a pH change cycle (pH 4 to pH 8, followed by pH 8 to pH 4), the open conformation transition point in the SWNT/DNA hybrid occurred under more basic conditions (pH $\approx$ 6.5) than did that of the i-motif DNA (pH $\approx$ 4.5) as shown in Fig. 2(b). Because the SWNTs can easily induce the i-motif structure of DNA this facilitates protonation of cytosine as the SWNT can promote protonation of conjugated polymers by lowering their pK_a values.[12] Additionally, the SWNTs might interact hydrophobically with exposed bases of the TAA loop in the four-folded structure of i-motif DNA (all cytosines form hydrogen bonds) at pH 5. When increasing the pH to 8, the all exposed bases on unfolded i-motif DNA generated hydrophobic interaction with SWNTs surface, and then the DNA strands might be coating SWNTs. Therefore, the stability of the i-motif structure was improved by increased stacking of loop structure and so promoting protonation of C$^+$:C.

It was elucidated experimentally for SWNT/DNA hybrids with a closed structure at pH 5, that they had an increased melting point of ~80 °C compared with i-motif DNA (T_m = 49.8 °C) (Fig. 2(c)). The free energy as derived by a van't Hoff analysis[13] of the melting profiles for the intramolecular structures is related to the closing energy of the i-motif structure in the presence or absence of SWNT. Table S1 in ESI† summarizes the thermodynamic parameters calculated from the melting profiles. The ΔG values for the conversion of the random coil to the i-motif structure at 25 °C are −11.1 and −41.3 kJ mol^{-1} for the i-motif DNA and the SWNT/DNA hybrids, respectively. In addition, the average cycling efficiency (η) of the conformational change, estimated from the change in CD ellipticity at 287 nm, was approximately 100% for the hybrid, indicating no loss over 10 cycles (ESI,† Fig. S3). Although these results suggest that the SWNT may affect the transformations of the i-motif structure, the pH-induced changes in the DNA strand with the SWNTs attached appears to be preserved.

To assess the switchable redox electroactivity, cyclic voltammograms (CVs) of a SWNT/DNA hybrid modified glassy carbon electrode were measured in the presence of various pH electrolytes. The rectangular shape of the CVs shown in Fig. 3(a)
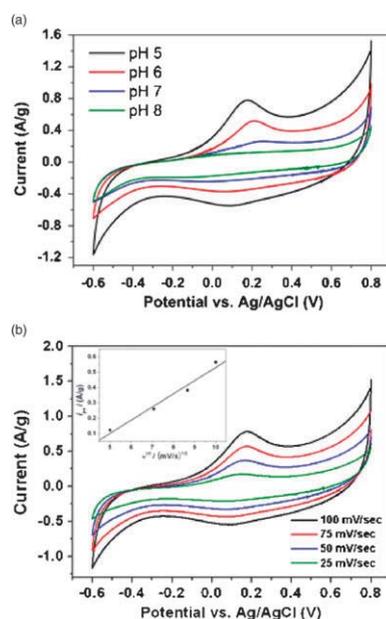
Fig. 3 (a) CVs of the SWNT/DNA hybrid obtained as a function of pH. The change in pH of 0.15 M PBS was produced by the addition of 1 M HCl and 1 M NaOH (scan rate = 100 mV s^{-1}). (b) CVs for the different potential scan rates. Inset: Potential scan rate dependence of peak anodic current, i_{pa}, for the SWNT/DNA hybrid at pH 5.

indicates that a favorable electrical conductivity is maintained in the wet state. While a pair of redox peaks (E_{pa}: 0.15 V, E_{pc}: 0.07 V, 25 mV s^{-1}) associated with the bonding of the C$^+$:C base-pair or TAA loops through π stacking charges along the nanotubes is apparent, the CV is dominated by the double layer capacitance at the SWNT/DNA–electrolyte interface. In our previous study, the redox peaks of a SWNT/DNA (double strand, salmon sperm) hybrid fiber show more negative potential (E_{pa}: −0.01 V E_{pc}: −0.11 V, scan rate: 25 mV s^{-1}).[14] The redox peaks show a positive potential shift and which is diminished with increasing pH values due to the i-motif structure forming random coils with deprotonation of the C$^+$:C base-pair. Typically, π-stacked hydrogen bonding on double strand DNA base pairs provides a medium to facilitate charge transport compared with single strand DNA.[15] Therefore, the stacked hydrogen bonds of C$^+$:C base-pairs in the i-motif structure may increase the charge transfer to a higher degree than the
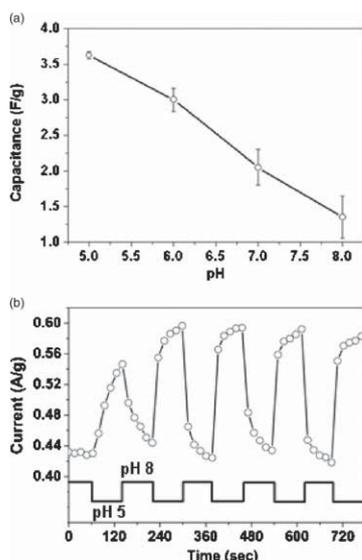
Fig. 4 (a) Specific capacitance of the SWNT/DNA hybrid as a function of pH. (b) Reversible switching of the SWNT/DNA hybrid modified electrode activity when the environmental pH value was oscillated as a step function between pH 5 and 8 by measuring the current at 0.17 V (oxidation peak potential). (scan rate = 100 mV s^{-1}).

random coil structure (single strand DNA). In a previously reported study, the electrochemical response of natural DNA was greatly enhanced at the SWNT-modified electrode due to electrocatalytic action of SWNT and interfacial accumulation. The facile electron transfer reaction of natural DNA can be attributed to the unique properties of SWNTs (*e.g.*, the excellent electrical conductivity, the enhanced surface area arising from the high aspect ratio, and the amenability of SWNTs for the attachment of biomolecules).[16]

Additionally, the anodic current peak is proportional to the square-root of the potential scan rate as predicted by the Randles–Sevcik equation for a diffusion-controlled electro-chemical process.[17] This result indicated that DNA is strongly bound to the SWNT surface. A linear relationship shows that there is no transition in the mass transfer regime on the explored timescale. In the case of electron hopping between redox sites homogeneously distributed in an isotropic medium, a proportionality of the peak current with the square root of scan rate is expected, since hopping can be assimilated to a diffusion process. Therefore, stacked hydrogen bonding of i-motif DNA provides a medium to facilitate electron transfer between SWNTs. The redox potential, $E_{1/2}$ derived from the CV of the SWNT/DNA hybrid modified electrode is positively shifted with increasing pH, having a slope of approximately 43 mV pH^{-1}, which is slightly smaller than the Nernstian value of 59 mV pH^{-1} for a 1e$^-$/1H$^+$ redox reaction.[17]

The measured electrochemical capacitance ($\sim$3.5 F g^{-1} in pH 5 PBS, where g is the combined weight of i-motif DNA and the SWNT) was similar to that of previous heat-treated SWNT fibers spun from DNA-stabilized dispersions ($\sim$5 F g^{-1})

(Fig. 4(b)).[18] The specific capacitances also decreased from pH 5 to 8. Stepwise electrochemical experiments from pH 5 to 8 (Fig. 4(a)) showed reversible and reproducible switching between the inactive and the active states of the SWNT/DNA hybrid modified electrode. It should be noted that the pH-controlled change of the electrochemical activity is a novel observation of conformational changes in DNA nanomachines. This simple demonstration illustrates the potential application of switchable pH-controlled electrodes with a switchable redox function.

In summary, we have conjugated SWNTs to an i-motif DNA nanomachine and evaluated in detail the pH induced conforma-tional changes. The SWNT attachments significantly affect the thermodynamic properties of the DNA strand by improving the stability of the i-motif structure through hydrophobic inter-actions. Furthermore, the electrochemical activity was con-trolled by changing the charge transport upon stacking or unstacking of DNA. As a result, the SWNT/DNA hybrid showed controllable/switchable electrochemical activity and capacitor behavior. Overall, the controllable electrochemical properties will form the basis for new intelligent electrode materials for nano-bio devices, such as biosensor or actuator.

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