Covalently-Functionalized Single-Walled Carbon Nanotube Probe Tips for Chemical Force Microscopy

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Herein, we report the first covalent modification of single-walled carbon nanotubes[1] (SWNTs) to create high-resolution, chemically sensitive probe microscopy tips. Carboxylic acid groups at the open ends of SWNTs were coupled to amines to create additional probes with basic or hydrophobic functionality. Force titrations recorded between the ends of the SWNT tips and hydroxy-terminated self-assembled monolayers (SAMs) confirmed the chemical sensitivity and robustness of these SWNT tips. In addition, images recorded on patterned SAM and partial bilayer surfaces have demonstrated chemically sensitive imaging with nanometer-scale resolution. These studies show that well-defined covalent chemistry can be exploited to create functionalized SWNT probes that have the potential for true molecular-resolution, chemically sensitive imaging.

Recent atomic force microscopy (AFM) studies of amyloid fibrils showed[2] that multiwalled carbon nanotube (MWNT)[3] tips and especially SWNT tips provide significantly better lateral resolution compared with commercial Si and Si_3N_4 AFM tips. Indeed, the ca. 0.5-nm radii of individual SWNTs indicate that such tips could enable true molecular-resolution imaging.[2] Sharp tips offer advantages for structural imaging but do not necessarily provide information about the functionality central to binding and reactivity in chemical and biological systems. Such chemical information can be obtained by using functionalized probes in chemical force microscopy (CFM). In the past, we[4−6] and others[7,8] have used SAMs to functionalize conventional tips and have used CFM to measure intermolecular forces and map chemical functionality. We have also recently shown that the ends of MWNT tips can be covalently modified to present chemically and biologically active functionality.[6] However, covalent functionalization of the ends of SWNTs, which offer the highest spatial resolution possible in force microscopy, has not been demonstrated before, nor is it known whether the ends of SWNTs can be opened to present functionality similar to MWNTs.

Our modification strategy follows the approach we developed for MWNTs,[6] that is selective reaction with the carboxyl groups[9] (-COOH) believed to exist at the open ends of oxidatively processed nanotubes. Studies of oxidized bulk MWNT and graphite samples have shown the presence of -COOH.[10,11] We have demonstrated the existence of -COOH at the opened ends of MWNTs[6] and thus believe it is reasonable to expect -COOH at SWNT ends opened in a similar manner. We illustrate the elaboration of -COOH here by selective coupling with amines to form amide-linked groups (Figure 1a).[12] The functionality at the SWNT tip ends was determined by measuring the adhesion force between the tip ends and hydroxyl (-OH)-terminated SAM surfaces.[13] Previous studies of adhesion vs pH (force titrations) for functionalized tips and substrates have shown that the fraction of proton dissociation can be readily monitored in this way.[4c,d,7c,g,14]

Force titrations made with SWNT tips on -OH-terminated SAMs exhibit well-defined drops in adhesion at ca. pH 4.5 (Figure 1b). In our experiments, the applied loads were less than the nanotube buckling force to ensure that only the nanotube end contacted the surface.[2,3] The drop in adhesion with increasing pH was observed reproducibly with this tip and other tips prepared in the same way[13] and is characteristic of -COOH deprotonation. The absolute value of the adhesion force at low pH can vary between tips, and such differences are believed to reflect variations in the number of -COOH groups at the ends of different tips.[15] Finally, the similarity of the pK_a determined from the SWNT force titrations (4.5) to the bulk solution value for benzoic acid (4.2) indicates that the -COOH groups at the SWNT ends are well-solvated and hence accessible for reactions.[4d,6]

SWNT tips were covalently modified by coupling amines (RNH_2), using carbodiimide chemistry to selectively form amide linkages with carboxyl groups (Figure 1a).[6,12,16,17] Tips reacted with benzylamine, which expose nonionizable, hydrophobic functionality, yield the expected pH-independent adhesion forces on -OH-terminated SAMs (Figure 1b). This covalent modification clearly eliminates the pH-dependent adhesion observed with the unmodified tips. The absolute values of the adhesion forces obtained in aqueous solutions using these phenyl-terminated tips

(1) Thess, A.; Lee, R.; Nikolaev, P.; Dai, H.; Petit, P.; Robert, J.; Xu, C.; Lee, Y. H.; Kim, S. G.; Rinzler, A. G.; Colbert, D. T.; Scuseria, G. E.; Tomanek, D.; Fischer, J. E.; Smalley, R. E. *Science* **1996**, *273*, 483.

(2) Wong, S. S.; Harper, J. D.; Lansbury, P. T.; Lieber, C. M. *J. Am. Chem. Soc.* **1998**, *120*, 603.

(3) Dai, H.; Hafner, J. H.; Rinzler, A. G.; Colbert, D. T.; Smalley, R. E. *Nature* **1996**, *384*, 147.

(4) (a)Frisbie, C. D.; Rozsnyai, L. F.; Noy, A.; Wrighton, M. S.; Lieber, C. M. *Science* **1994**, *265*, 2071. (b) Noy, A.; Frisbie, C. D.; Rosznyai, L. F.; Wrighton, M. S.; Lieber, C. M. *J. Am. Chem. Soc.* **1995**, *117*, 7943. (c) Vezenov, D. V.; Noy, A.; Rozsnyai, L. F.; Lieber, C. M. *J. Am. Chem. Soc.* **1997**, *119*, 2006. (d) Noy, A.; Vezenov, D. V.; Lieber, C. M. *Annu. Rev. Mater. Sci.* **1997**, *27*, 381.

(5) Noy, A.; Sanders, C. H.; Vezenov, D. V.; Wong, S. S.; Lieber, C. M. *Langmuir* **1998**, *14*, 1508.

(6) Wong, S. S.; Joselevich, E.; Woolley, A. T.; Cheung, C.; Lieber, C. M. *Nature* **1998**, *394*, 52.

(7) (a) Green, J.-B.; McDermott, M. T.; Porter, M. D.; Siperko, L. M. *J. Phys. Chem.* **1995**, *99*, 10960. (b) Thomas, R. C.; Houston, J. E.; Crooks, R. M.; Kim, T.; Michalske, T. A. *J. Am. Chem. Soc.* **1995**, *117*, 3830. (c) Marti, A.; Hahner, G.; Spencer, N. D. *Langmuir* **1995**, *11*, 4632. (d) Akari, S.; Horn, D.; Keller, H.; Schrepp, W. *Adv. Mater.* **1995**, *7*, 549. (e) Sinniah, S. K.; Steel, A. B.; Miller, C. J.; Reutt-Robey, J. E. *J. Am. Chem. Soc.* **1996**, *118*, 8925. (f) Williams, J. M.; Han, T.; Beebe, T. P. *Langmuir* **1996**, *12*, 1291. (g) van der Vegte, E. W.; Hadziioannou, G. *J. Phys. Chem.* **1997**, *101*, 9563. (h) McKendry, R.; Theoclitou, M.-E.; Rayment, T.; Abell, C. *Nature* **1998**, *391*, 566.

(8) Finot, M. O.; McDermott, M. T. *J. Am. Chem. Soc.* **1997**, *119*, 8564.

(9) March, J. *Advanced Organic Chemistry*; John Wiley and Sons: New York, 1992.

(10) Hiura, H.; Ebbesen, T. W.; Tanigaki, K. *Adv. Mater.* **1995**, *7*, 275.

(11) (a)Evans, J. F.; Kuwana, T. *J. Electroanal. Chem.* **1977**, *80*, 409. (b) Wandass, J. H.; Gardella, J. A.; Weinberg, N. L.; Bolster, M. E.; Salvati, L. *J. Electrochem. Soc.* **1987**, *134*, 2734.

(12) Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*, 2nd ed. Springer-Verlag: New York, 1994.

(13) Ropes of SWNTs were prepared in-house by laser vaporization[1] and were attached to gold-coated Si cantilevers (k = 0.5−5 N/m, Digital Instruments, Inc.) using an acrylic adhesive.[2,6] The as-made SWNT tips were shortened and opened by applying a bias voltage between the tip and a Nb surface in oxygen. The mounting and sharpening procedures are described in greater detail in the Supporting Information. The adhesion forces between SWNT tips functionalized with different groups and hydroxy-terminated SAMs were determined from force vs distance curves.[4c,d] Each data point corresponds to the mean of 50−100 adhesion measurements, and the error bars represent one standard deviation. The -OH terminated SAMs were prepared by immersing Au-coated Si samples into a 2−3 mM ethanolic solution of 11-mercaptoundecanol for at least 12 h. All SAMs were rinsed in ethanol and dried in a stream of N_2 prior to use.

(14) (a) Hu, K.; Bard, A. J. *Langmuir* **1997**, *13*, 5114. (b) Senden, T. J.; Drummond, C. J. *Colloids Surf., A* **1995**, *94*, 29.

(15) This SWNT tip had approximately 5 active -COOH groups, based on an adhesion force of 0.1 nN for a single interacting pair.[4d]

(16) Giles, M. A.; Hudson, A. Q.; Borders, C. L., Jr. *Anal. Biochem.* **1990**, *184*, 244.

(17) SWNT ends were modified by placing a cantilever-tip assembly in 0.1 M MES (2-[N-morpholino]ethanesulfonic acid) (Sigma) pH 6.0 buffer containing 50 mM 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (Pierce) and 5 mM of either benzylamine or ethylenediamine for 2 h. The tips were then successively washed in 0.1 M MES buffer pH 6.0, 0.1 M NaCl (Fisher), and deionized water.

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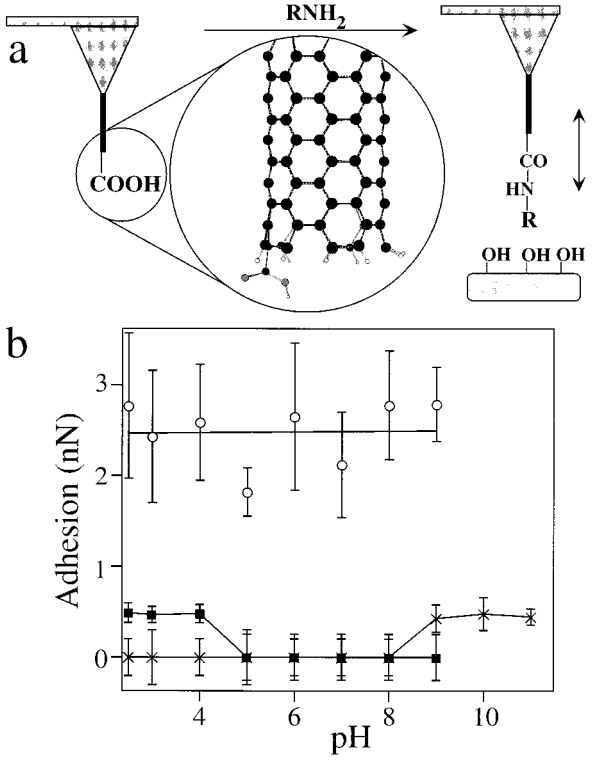

Figure 1. (a) Schematic illustrating the modification of a SWNT tip by coupling an amine (RNH_2) to a terminal -COOH, and the application of this probe to sense specific interactions between the functional group (R) and surface -OH groups. (b) Adhesion force as a function of pH between SWNT tips and an -OH-terminated SAM: -COOH/filled squares (unmodified); phenyl/open circles (modified with benzylamine); and amine/crosses (modified with ethylenediamine).

are generally larger than for the -COOH-terminated nanotubes and are consistent with the hydrophobic nature of the tips.[4c,d,5] Furthermore, force titrations with ethylenediamine-modified (amine-terminated) SWNT tips show no measurable adhesion at low pH and finite adhesion above pH 8. This pH-dependent behavior correlates with our expectations for exposed amine groups that are neutral at high pH and protonated and charged at low pH.[18] As a control, titrations using SWNT tips, reacted with ethylenediamine in the absence of the carbodiimide coupling reagent, yielded the same pH-dependent adhesion as unmodified -COOH-terminated tips. We believe these data clearly show that there are exposed -COOH groups at the ends of SWNT tips and that these -COOH groups can be covalently modified to produce probes with very distinct chemical properties.

Functionalized SWNTs have also been used for chemically sensitive imaging (Figure 2). Intermittent contact (tapping mode) images recorded in ethanol with carboxyl-terminated SWNT tips on patterned substrates[19,20] exhibit greater phase lag in tip-COOH/sample-COOH vs tip-COOH/sample-CH_3 regions (Figure 2a). Recent tapping mode experiments using functionalized Si_3N_4 tips have shown that phase lag images can be interpreted as maps of chemical functionality.[5,6] Because the SWNT tip-COOH/sample-COOH adhesion force is greater than that for tip-COOH/sample-CH_3, these results are consistent with chemically sensitive

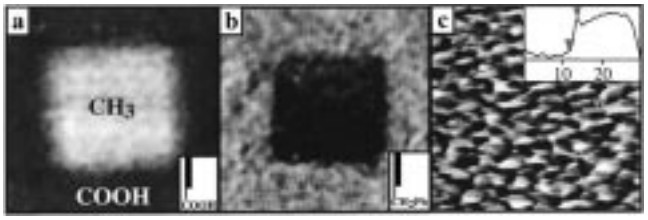

Figure 2. (a) Tapping mode phase image of a patterned sample in ethanol recorded with an unmodified SWNT tip (-COOH-terminated). (b) Analogous image of a patterned sample with a benzylamine-functionalized SWNT tip. Darker regions indicate greater phase lag; the contrast in (a) and (b) corresponds to phase variations of 1.3° and 1.1°, respectively. The images are 16 μm × 16 μm. (c) Tapping mode phase image recorded on a partial bilayer structure. The image is 100 nm × 100 nm. (inset) Variation of the phase vs position along the line in (c); the numbers correspond to the distance in nanometers. Inverted triangles indicate the distance (3.3 nm) separating adjacent chemically distinct regions.

imaging. In addition, benzylamine-modified SWNT tips, which interact more strongly with the CH_3 vs COOH sample regions, yield images with the opposite phase contrast (Figure 2b). This inversion in contrast demonstrates clearly that chemically sensitive imaging is possible with functionalized SWNT tips.

These new tips also provide very significant improvements in lateral chemical resolution compared with modified Si and Si_3N_4 tips. Qualitatively, the improved resolution manifests itself as the 50−150 nm granular structure in images of the patterned SAMs (Figure 2a and b). This structure is consistent with the grain size of the Au substrates but is not typically observed with the use of functionalized Si, Si_3N_4, or MWNT tips. To characterize the lateral chemical resolution of the SWNT tips, we have imaged partial bilayer structures consisting of a COOH-terminated SAM capped by a partial layer of stearic acid that presents elevated CH_3-terminated domains;[7a,8,21] the resolution corresponds to the broadening between the COOH-terminated surface and CH_3-terminated islands.[7a,8] Notably, images recorded on these samples (e.g., Figure 2c) show a lateral chemical resolution of ca. 3 nm that is significantly better than those obtained with the use of Si and Si_3N_4 tips (15 nm)[8] or MWNT tips (8 nm).[22]

In summary, these studies demonstrate that SWNT tips present -COOH groups that can be selectively modified using well-defined covalent chemistry to yield a wide range of terminal functionality. These modified SWNT tips have been used to produce chemically sensitive images with the highest lateral resolution to date and can be used to study binding in biological and chemical systems.[6] Because individual SWNTs have radii on the order of 0.5 nm, these studies demonstrate that functionalized SWNT tips now offer the possibility of creating single-molecule probes capable not only of mapping functional groups with true molecular resolution but also of modifying or creating structures at the molecular scale.

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Supporting Information Available: Figures and experimental details (4 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(18) The nanotube-bound amine pK_a (8.5) is lower than that of the homogeneous solution (9−10) although similar behavior was observed in studies of functionalized Si_3N_4 tips[4c,d] and MWNT tips.[6]

(19) Kumar, A.; Biebuyck, H.; Whitesides, G. M. *Langmuir* **1994**, *10*, 1498.

(20) Patterned samples were prepared by microcontact printing[19] on gold, and consisted of 10-μm squares of a hexadecanethiol SAM region surrounded by a 16-mercaptohexadecanoic acid SAM background. Images and force curves were acquired with a Nanoscope III (Digital Instruments, Inc.).[4c,d] Typical parameters used for imaging in ethanol (air) were (i) resonant frequencies, 28−33 (50−75) kHz; (ii) free RMS oscillation amplitude, 30−90 (30−80) nm; (iii) setpoint, 1−3 (0.8−2) V.; and (iv) scan rate, 1−1.2 (0.5 to 2.0) Hz.

(21) Partial bilayer samples were prepared by immersing flat Au (111)-coated mica substrates in ethanolic solutions of 0.1 mM mercaptohexadecanoic acid and 1 mM stearic acid for 5 to 25 h. The resolution was assigned as the distance separating two regions of different phase.[8] The flat Au(111) substrates were prepared by deposition on mica at 300 °C.

(22) The lateral resolution of functionalized MWNT tips[6] was determined in the same way on partial bilayer samples.