Carbon Nanotubes Grown on Metal Microelectrodes for the Detection of Dopamine

Cheng Yang, † Christopher B. Jacobs, † Michael D. Nguyen, † Mallikarjunarao Ganesana, † Alexander G. Zestos, † Ilia N. Ivanov, ‡ Alexander A. Puretzky, ‡ Christopher M. Rouleau, ‡ David B. Geohegan, ‡ and B. Jill Venton* †

†Department of Chemistry, University of Virginia, McCormick Road, Box 400319, Charlottesville, Virginia 22904-4319, United States
‡Center for Nanophase Materials Sciences, Oak Ridge National Laboratory, 1 Bethel Valley Road, Building 8610, Oak Ridge, Tennessee 37831, United States

Supporting Information

ABSTRACT: Microelectrodes modified with carbon nanotubes (CNTs) are useful for the detection of neurotransmitters because the CNTs enhance sensitivity and have electrocatalytic effects. CNTs can be grown on carbon fiber microelectrodes (CFMEs) but the intrinsic electrochemical activity of carbon fibers makes evaluating the effect of CNT enhancement difficult. Metal wires are highly conductive and many metals have no intrinsic electrochemical activity for dopamine, so we investigated CNTs grown on metal wires as microelectrodes for neurotransmitter detection. In this work, we successfully grew CNTs on niobium substrates for the first time. Instead of planar metal surfaces, metal wires with a diameter of only 25 μm were used as CNT substrates; these have potential in tissue applications due to their minimal tissue damage and high spatial resolution. Scanning electron microscopy shows that aligned CNTs are grown on metal wires after chemical vapor deposition. By use of fast-scan cyclic voltammetry, CNT-coated niobium (CNT-Nb) microelectrodes exhibit higher sensitivity and lower ΔE value compared to CNTs grown on carbon fibers or other metal wires. The limit of detection for dopamine at CNT-Nb microelectrodes is 11 ± 1 nM, which is approximately 2-fold lower than that of bare CFMEs. Adsorption processes were modeled with a Langmuir isotherm, and detection of other neurochemicals was also characterized, including ascorbic acid, 3,4-dihydroxyphenylacetic acid, serotonin, adenosine, and histamine. CNT-Nb microelectrodes were used to monitor stimulated dopamine release in anesthetized rats with high sensitivity. This study demonstrates that CNT-grown metal microelectrodes, especially CNTs grown on Nb microelectrodes, are useful for monitoring neurotransmitters.
and sensitive detection of neurotransmitters by use of fast-scan cyclic voltammetry (FSCV). An alternative strategy is to directly grow CNTs in an aligned manner through chemical vapor deposition (CVD). Recently, Xiang et al.16 used as-synthesized, vertically aligned carbon nanotube sheathed carbon fibers (VACNT-CFs) for the detection of dopamine and ascorbate in vivo. The VACNT-CFs microelectrodes exhibited promising electrochemical performance. However, since the carbon fiber is electrochemically active toward dopamine, the CF substrates limit studies of the properties of CNT coating. In comparison, metal substrates with CNT coating would have several benefits. First, although gold17 and platinum are active to dopamine, many other metals (e.g., Nb, Ta, Mo, W, Pd, Ti, and stainless steel used in this paper) lack electrochemical reactivity to dopamine, which enables the study of interaction of dopamine with CNTs without the convolution of possible substrate reactivity. Second, the inherently low conductivity of CF10 may limit the overall conductivity of sensors, while metals have higher conductivity. Third, the electrochemical properties of the CF core vary with different waveforms and can affect the electrochemical properties.19 Therefore, a metal substrate that lacks reactivity to dopamine and has high intrinsic conductivity and relatively stable electrochemistry may avoid these issues. Although successful growth of CNTs on several metal substrates has been reported,20-28 CNTs have not been grown on niobium (Nb) substrates. In addition, all previous studies of CNT growth on metals have been on flat substrates and not on the cylindrical metal wires that would be needed for implantable electrochemical microsensors.

In this study, we explored the use of CNT-grown metal microelectrodes for enhanced neurotransmitter detection. The CNT-grown metal microelectrodes and CFMEs were fabricated by CVD and characterized by scanning electron microscopy (SEM) and Raman spectroscopy. These are the first studies to grow CNTs on Nb substrates or on small-diameter metal wires, instead of a planar metal surfaces such as foils, which allows them to be implanted in tissue with minimal damage and high spatial resolution.27 CNTs grown on Nb were short and dense, and CNT-Nb microelectrodes exhibited better electrochemical response to dopamine via FSCV compared to CNTs grown on other metals or CFs. Moreover, the CNT-Nb microelectrodes were tested for electrochemical response to ascorbic acid, DOPAC (3,4-dihydroxyphenylacetic acid, a dopamine metabolite), serotonin, adenosine, and histamine. The CNT-Nb microelectrodes were used to detect stimulated dopamine release in anesthetized rats and exhibited high sensitivity with spatial resolution.27 CNTs grown on Nb were short and dense, since the end-caps of the CNTs would be open due to the applied voltage,33 the ends would instead of a planar metal surfaces such as foils, which allows them to be implanted in tissue with minimal damage and high spatial resolution.32 The percent surface coverage, $\Gamma$, can be expressed by the ratio of oxidation current of dopamine to theoretical saturated oxidation current, which is the plateau of the fitting curve. The activity is related to its molar concentration ($C_{DA}$) by eq 2.29

$$\gamma_{DA} = (\gamma_{DA} C_{DA}) (1 \text{ L mol}^{-1})$$

$\gamma_{DA}$ is the activity coefficient of dopamine in bulk solution at the adsorption equilibrium. For a charged adsorbate solution at high concentration, the effect of the activity coefficients must be taken into account because charged adsorbates are governed by ionic interactions.30 According to the Debye–Hückel law:

$$\log \gamma_{DA} = -AZ^2I^{1/2}$$

$\gamma_{DA}$ is a function of ionic strength ($I$) of the solute and charge carried by each solute ($z$), while $A$ is a constant that depends on temperature and is about 0.51 for water at 25°C.31 Thus, $\gamma_{DA}$ for dopamine in phosphate-buffered saline (PBS) is 0.63 at room temperature.32 $b_{DA}$ can be used to calculate the adsorption Gibbs free energy of dopamine (eq 4):

$$\Delta G^a_{DA} = -RT \ln b_{DA}$$

### RESULTS AND DISCUSSION

Characterization of Carbon Nanotubes Grown on Metal Wires and Carbon Fibers. CVD allows direct growth of CNTs on substrates; however, no study had grown CNTs on Nb or on small-diameter cylindrical metal wires. We optimized CNT growth on metal wires for use as microelectrodes. Figure 1 shows SEM images of bare Nb (Figure 1A) and Ta (Figure 1B) wires as well as carbon fiber (Figure 1C) and the same substrates after CNT growth (Figure 1D–F). The CNTs (multiwalled) grown on Nb are short, dense, and aligned, compared to the CNTs grown on Ta and CFs, which are longer and more randomly oriented. Since the end-caps of the CNTs would be open due to the applied voltage, the ends would have more sp$^3$-hybridized, edge plane carbons that can be oxidized to provide functional groups.10 The short, dense CNT bundles on the Nb would have more functionalized edge plane sites exposed compared to the more diffuse CNTs on CFs and Ta, where more sidewalls would be exposed to the analyte.
The variety in CNT morphology grown on different metallic substrates might result from the interaction of Al₂O₃ buffer layer with the substrate or different properties of the metals. Al₂O₃ was used as a catalyst support buffer layer to enhance CNT growth by inhibiting diffusion of the catalyst material into the substrate upon heating. However, the Al₂O₃ buffer layer has a different grain size on different substrates after heating, due to surface energy or wettability, which leads to different CNT nucleation densities. Another possible reason for the varied CNT morphology on different substrates is the amount of hydrogen absorbed in the metal substrates, which could affect the microstructure and mechanical properties of the resulting CNT growth. Among transition metals, group VB metals are good hydrogen storage substrates. The variety in CNT morphology grown on different metallic substrates after heating, due to surface energy or wettability, might be due to hydrogen release that helps maintain the activation of iron catalysts.

To further characterize the CNT surface, Raman spectra of CNTs grown on metal wires and CF substrates were compared (Figure S1). The ratio of D/G peaks (D band originating from defects and G band from graphite) reveals the sp³-hybridized carbon content of the carbon surface can change with application of the triangle waveform. Equilibration with a fast-scan triangle waveform (400 V/s) mildly etches the carbon film. The D/G ratios (n = 5) for CNT-Nb, CNT-Ta, and CNT-CF are 2.2 ± 0.1, 1.8 ± 0.2, and 1.9 ± 0.6, respectively. The ratio of intensities of these peaks is often used as an indicator of the quality of CNTs, and these multiwalled CNTs are defect-rich. The D/G ratio of CNTs grown on Nb is significantly larger than on Ta (unpaired t test, p ≤ 0.05), which demonstrates CNTs on Nb are more defect-rich. The small standard errors observed indicate that the D/G ratio was consistent between electrodes.

Fast-Scan Cyclic Voltammetry of Dopamine at Bare Metal Wire and Carbon Fiber Microelectrodes. To investigate the electrochemical performance of the substrate materials, cylindrical microelectrodes were made of metal wires and carbon fibers. Figure 2A–C shows the background current measured in PBS at bare Nb, Ta, and CF electrodes with similar lengths (∼70–100 μm). The capacitive currents arising from electrical double layer charging are small, around 300 nA for Nb and 100 nA for Ta metal wires. The square shape background for Nb and Ta metal wires reveals good polarizability. In contrast, background currents at CFME can be attributed to surface functional groups as well as capacitive charging.

Figure 2D–F shows the background-subtracted cyclic voltammograms (CVs) of 1 μM dopamine at bare Nb, Ta, and CF microelectrodes. Nb and Ta are not electrochemically active for dopamine and show no Faradaic peaks. Therefore, any dopamine signal at CNT-Nb or CNT-Ta microelectrodes will arise from the CNTs. CFMEs have a robust signal for dopamine (Figure 2F) and are widely used as the standard electrode material in the field of in vivo voltammetry.

Fast-Scan Cyclic Voltammetry of Dopamine at Carbon Nanotube-Grown Metal Wire and Carbon Fiber Microelectrodes. Figure 3 shows the electrochemical response of CNT-grown Nb and Ta microelectrodes and CNT-grown CFMEs. The background charging currents for CNT-Nb and CNT-Ta electrodes (Figure 3A,B) are significantly larger than for the bare metals (Figure 2A,B), indicating substantial CNT growth. For CNTs grown on Nb and Ta wires, background-subtracted CVs for 1 μM dopamine (Figure 3D,E) show Faradaic peaks that were not present for bare wires (Figure 2D,E). Faradaic peaks for dopamine are also observed at CNT-CF microelectrodes, but the contribution of CNTs versus that of CF to the signal is harder to distinguish. Moreover, dopamine oxidation is more reversible at CNT-Nb microelectrodes than at CFMEs, which can be observed in the CVs.
due to abundant defect sites at CNT grown on Nb, which could contrast, CNT-Ta and CNT-CF required a longer equilibration microelectrodes, as the response to dopamine and background 160 min. Equilibration time mattered little for CNT-Nb microelectrodes, the background (Figure 3A) 15 and (---) 160 min of equilibration in PBS solution with a waveform of ~0.4 to 1.3 V and back at 400 V/s, 10 Hz.

**Figure 3.** Comparison of electrochemical response at CNT-grown niobium, tantalum, and carbon fiber microelectrodes: background current at (A) CNT-Nb, (B) CNT-Ta, and (C) CNT-CF and background-subtracted cyclic voltammograms for 1 μM dopamine at (D) CNT-Nb, (E) CNT-Ta, and (F) CNT-CF microelectrodes. Measurements were taken after (—) 15 min and (—) 160 min of equilibration in PBS solution with a waveform of ~0.4 to 1.3 V and back at 400 V/s, 10 Hz.

Table 1. Average ΔEp, Current Density, and Limit of Detection for 1 μM Dopamine at Carbon Nanotube-Grown Microelectrodes and Carbon Fiber Microelectrode

| electrode | ΔEp (V) | current density (pA/μm²) | LOD (nM) |
|-----------|---------|--------------------------|----------|
| CNT-Nb    | 0.73 ± 0.03 | 197 ± 16 | 11 ± 1 |
| CNT-Ta    | 0.87 ± 0.01 | 82 ± 10 | 91 ± 27 |
| CNT-CF    | 0.81 ± 0.03 | 100 ± 25 | 46 ± 10 |
| CFME      | 0.67 ± 0.01 | 135 ± 24 | 19 ± 4 |

*CNT grown on the CF substrate is not as electrochemically active as CF to dopamine. Because of the spaghettilike structure, not all of theCNTs on the CF may be available for electron transfer, but adding CNTs adds to the background current and noise. The limit of detection (LOD) is 11 ± 1 nM (S/N = 3) for dopamine at CNT-Nb microelectrodes, which is significantly lower than those at CNT-Ta, CNT-CF, and CFMEs (one-way ANOVA Bonferroni post-test, p < 0.005, n = 5). Therefore, with higher sensitivity and better LOD than CFMEs, CNT-Nb electrodes show promising electrochemical performance for dopamine detection.

**Characterization of Other Metal Substrates for Carbon Nanotube Growth.** Other metal wires were tested for growing CNTs, including molybdenum (Mo), tungsten (W), palladium (Pd), stainless steel (SS), and titanium (Ti). Figure S4 shows the SEM images of both bare metals and CNT-grown metal wire microelectrodes and CFME. The ΔEp values at CNT-Nb microelectrodes for 1 μM dopamine are 0.73 ± 0.03 V, which is significantly larger than the current density at CNT-Ta, CNT-CF, or CFMEs [one-way analysis of variance (ANOVA) Bonferroni post-test, p < 0.0005, n = 5]. Current density at CFMEs after CNT growth is lower than that for bare CFMEs, indicating that much of the surface and introduces more oxygen-containing functional groups as active adsorption sites for dopamine. For CNT-grown microelectrodes, the background (Figure 3A–C) and response to 1 μM dopamine (Figure 3D–F) were measured at two equilibration time points: waveform application for 15 and 160 min. Equilibration time mattered little for CNT-Nb microelectrodes, as the response to dopamine and background current were similar for both time points (Figure S2A). In contrast, CNT-Ta and CNT-CF required a longer equilibration time (Figure S2B,C). The shorter equilibration time might be due to abundant defect sites at CNT grown on Nb, which could be oxygen-functionalized faster by electrochemical activation.

The ends of CNTs grown on Nb are likely open, especially after continuous scanning with the 1.3 V triangle waveform, while the main sources of adsorption sites at CNT-Ta and CNT-CF are probably defects on sidewalls. The CNT-Nb microelectrode had no significant change in peak oxidative current for dopamine over 4 h, indicating the electrodes are stable over the typical time length of a biological experiment (Figure S3).

To compare the sensitivity of electrodes to dopamine, currents were corrected for surface area (based on their capacitive charging currents), since the metal wires are 25 μm in diameter while the CFME is 7 μm. As shown in Table 1, the current density at CNT-Nb microelectrodes for 1 μM dopamine is 197 ± 16 pA/μm², which is significantly larger than the current density at CNT-Ta, CNT-CF, or CFMEs [one-way analysis of variance (ANOVA) Bonferroni post-test, p < 0.0005, n = 5]. Current density at CFMEs after CNT growth is lower than that for bare CFMEs, indicating that much of the surface and introduces more oxygen-containing functional groups as active adsorption sites for dopamine.
Our studies showed that the size of CNTs and the amount of growth depended on the metal substrate. CNT-Nb microelectrodes are preferred for neurotransmitter detection due to the short, dense, and vertically aligned CNT coating, which leads to high current density, low LOD, fast electron transfer rate, and short equilibration time. Thus, CNT-Nb microelectrodes were used for in vivo characterization studies.

**Langmuir Isotherm Modeling.** The redox reaction of dopamine at the surface of carbon-based sensors is an adsorption-controlled process. Using a model for FSCV data developed by the Wightman group, we previously determined that the adsorption/desorption kinetics of dopamine are different for CNT yarn electrodes than for CFMEs. Here, we used a Langmuir adsorption isotherm to model the adsorption and desorption kinetics of dopamine at CNT-grown electrodes. The percent surface coverage is calculated from eq 1 and then the coverage versus concentration is fit with the Langmuir isotherm. The anodic peak (Figure 4) and the cathodic peak (Figure S7) give information about dopamine and dopamine-quinone (DOQ) adsorption, respectively.

**Figure 4.** Plot of normalized anodic current to corresponding dopamine concentration. The fitting curve is modeled on the basis of eq 3, where $C_{DA}$ is the x-axis and fractional surface coverage is the y-axis. An equilibrium value, $\beta_{DA}$, is fit for each curve. (A) CNT-coated Nb microelectrode; (B) CNT-coated Ta microelectrode; (C) CNT-coated CFME; (D) CFME ($n = 5$ per electrode material; error bar is standard error of mean and sometimes is so small as to be less than the size of the point).

Table 2 gives average adsorption rate constants for CNT-Nb, CNT-Ta, and CNT-CF microelectrodes as well as bare CFME. The $\beta$ value is used to calculate the Gibbs free energy for dopamine and DOQ adsorption.

The adsorption equilibria for both dopamine ($\beta_{DA}$) and DOQ ($\beta_{DOQ}$) at CNT-Nb and CNT-Ta microelectrodes are smaller than those at CF and CNT-CF microelectrodes. This indicates dopamine and DOQ adsorb more strongly to CF and CNT-CF microelectrodes than to CNT-Nb and CNT-Ta microelectrodes. However, at the CNT-Ta and CNT-Nb microelectrodes, $\beta_{DA}$ is similar to $\beta_{DOQ}$ and the ratio of $\beta_{DA} / \beta_{DOQ}$ is about 1 (Table 2). At CFMEs, $\beta_{DA}$ is significantly larger than $\beta_{DOQ}$ (paired t test, $p < 0.005$, $n = 5$), and the $\beta_{DA} / \beta_{DOQ}$ ratio is larger than at CNT-Nb microelectrodes (unpaired t test, $p < 0.05$, $n = 5$). Thus, DOQ is more likely to readorb from the electrode at CNT-Nb, leading to a bigger reduction peak and more reversible reaction. The ratio of equilibrium constants for CNT-CF microelectrodes falls in between that of CFMEs and CNT-grown wires. The overall equilibrium is likely a convolution of the equilibrium at CNT-coated parts of the electrode and bare CFME, which is also partially exposed to solution. These data agree with previous modeling of CNT yarn electrodes, which showed differences in adsorption for dopamine and DOQ compared to CFMEs.

**Fast-Scan Cyclic Voltammetry of Other Neurochemicals.** We tested the electrochemical performance of CNT-Nb microelectrodes toward the detection of other neurochemicals including ascorbic acid (AA), DOPAC (3,4-dihydroxyphenylacetic acid), serotonin, adenosine, and histamine. Since the detection of adenosine and histamine requires scanning to higher potentials, we used a waveform of $-0.4$ V to $1.45$ V at $400$ V/s. Figure 5 shows sample CVs for each neurochemical (black solid line) compared to dopamine (red dashed line) at the same CNT-Nb electrode. The bar graphs compare the ratio of oxidation currents of the different neurotransmitters to dopamine at CNT-Nb microelectrodes and CFMEs.

| Material | $\beta_{DA}$ (×10^1) | $\beta_{DOQ}$ (×10^1) | $\beta_{DA} / \beta_{DOQ}$ | $\Delta G_{DA}$ (kJ/mol) | $\Delta G_{DOQ}$ (kJ/mol) | $\Delta G_{DA} / \Delta G_{DOQ}$ |
|-----------|----------------------|----------------------|-----------------------------|--------------------------|--------------------------|-------------------------------|
| CNT-Nb    | 21 ± 1               | 20 ± 1               | 1.03 ± 0.04                 | $-24.1 ± 0.1$           | $-24.0 ± 0.1$           | 1.003 ± 0.004                 |
| CNT-Ta    | 23 ± 3               | 23 ± 5               | 1.05 ± 0.09                 | $-24.4 ± 0.3$           | $-24.3 ± 0.4$           | 1.003 ± 0.009                 |
| CNT-CF    | 37 ± 4               | 31 ± 2               | 1.10 ± 0.02                 | $-25.6 ± 0.2$           | $-25.1 ± 0.1$           | 1.014 ± 0.005                 |
| CFME      | 39 ± 1               | 32 ± 1               | 1.23 ± 0.04                 | $-25.9 ± 0.1$           | $-25.2 ± 0.1$           | 1.019 ± 0.003                 |

*All $n = 5$. Errors are standard error of the mean.
DOPAC compared to $-0.22 \pm 0.01$ V for dopamine; paired $t$ test, $p < 0.001$, $n = 5$), similar to previous CNT electrode studies. Serotonin is a cationic indolamine neurotransmitter. The ratio of currents for serotonin to dopamine is similar for CNT-Nb microelectrodes and CFMEs (Figure 5F, paired $t$ test, $p = 0.7476$, $n = 5$). The oxidation peak for serotonin is similar to that for dopamine as well, but the reduction peak is shifted by 200 mV (Figure 6E, paired $t$ test, $p < 0.0001$, $n = 5$), which can be used to discriminate the serotonin from dopamine. Adenosine is an important neuroprotective modulator in the brain that regulates neurotransmission and blood flow. Adenosine is identified by its two oxidation peaks in the CV (a primary oxidation peak at 1.4 V and a secondary peak at 1.0 V; Figure 5G). The selectivity for adenosine compared to dopamine at CNT-Nb microelectrodes is similar to that at CFMEs (Figure 5H, paired $t$ test, $p = 0.7476$, $n = 5$). Histamine is a neurotransmitter that regulates sleep. CNT-Nb electrodes have an oxidation peak near the switching potential (Figure 5I) and show significantly higher histamine to dopamine current ratios than CFMEs (Figure 5J, paired $t$ test, $p < 0.05$, $n = 5$), which might be due to the better antifouling properties of the CNT surface toward histamine than CFMEs. Overall, CNT-Nb microelectrodes are useful for detecting a variety of neurochemicals.

**In Vivo Detection of Dopamine at Carbon Nanotube-Grown Niobium Microelectrodes.** To determine the applicability of the CNT-Nb microelectrode as a novel in vivo sensor, stimulated dopamine release was measured in anesthetized male Sprague-Dawley rats. Stimulation pulse trains were applied (300 μA, 12–120 pulses, 60 Hz) to the dopamine cell bodies, and the dopamine response was recorded in the caudate putamen near the terminals. Figure 6A,B show sample CVs and current versus time plots of dopamine detection at a CNT-Nb microelectrode with different stimulation pulses. Current increased as dopamine was released during the stimulation and decreased after the stimulation due to uptake. Figure 6C gives the average dopamine concentration evoked in vivo; released dopamine is still detectable with as low as 12 stimulation pulses. The current density of the stimulated dopamine at CNT-Nb microelectrode in vivo [0.15 ± 0.02 pA/ (nM·μm$^2$)] is slightly lower than that in vitro [0.20 ± 0.02 pA/ (nM·μm$^2$)] but not significantly different (unpaired $t$ test, $p > 0.05$), which indicates CNT-Nb microelectrodes maintained relatively high sensitivity for in vivo dopamine detection. The CV of dopamine in vivo has a larger $\Delta E_p$ than that in vitro, likely due to adsorption of lipids, proteins, and peptides present in the extracellular fluid that slow electron transfer. While the larger $\Delta E_p$ is not ideal, the sensitivity is maintained and the CV could be matched to in vivo spontaneous release. However,
future studies could focus on in vivo studies of protein fouling and adopt strategies that have been implemented for gold\(^6\) and carbon fiber microelectrodes\(^6\) to tune the surface adsorption of dopamine.

**CONCLUSIONS**

In summary, we successfully grew CNTs on Nb and used CNTs on cylindrical wires as microelectrodes for the first time. Small wire microelectrodes should minimize tissue damage and improve spatial resolution, which are needed for in vivo applications. This work is the first to compare CNT growth on various metal wires as well as carbon fibers, and the comparison is useful in choosing appropriate substrates for future CNT studies. CNTs forest-grown on Nb wires are shorter, denser, and more aligned than CNTs grown on other substrates, which led to enhanced current density and better LOD for dopamine. In addition, CNT-Nb microelectrodes are stable over 4 h of continuous measurement and are able to measure stimulated dopamine release in anesthetized rats. CNT-Nb microelectrodes have potential applications for the detection of neurotransmitters in vivo or metal electrode arrays in electrophysiology studies.

**ASSOCIATED CONTENT**

* Supporting Information
  The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.analchem.5b01257.

  Additional text describing solutions and microelectrode preparation, surface characterization, electrochemistry, in vivo measurements, and statistics; seven figures showing Raman spectra of CNTs grown on Nb, Ta, and CF, effect of electrochemical equilibration on CNT-metal microelectrodes, stability test on CNT-Nb microelectrodes, SEM images of bare and CNT-grown metal microwires, electrochemical response of bare metals, comparison of electrochemical response at CNT-grown metals and microelectrodes, and plot of normalized cathodic current to corresponding dopamine concentration fit with Langmuir isotherm (PDF)

**AUTHOR INFORMATION**

**Corresponding Author**
*E-mail jventon@virginia.edu; phone 434-243-2132.

**Notes**
The authors declare no competing financial interest.

**ACKNOWLEDGMENTS**

This research was supported by NIH Grant R21 DA037584. Synthesis and physical characterization of the CNT-metal wires were conducted at the Center for Nanophase Materials Sciences, which is a DOE Office of Science User Facility (User Grant CNMS2014-083).

**REFERENCES**

1. Alwarappan, S.; Liu, G.; Li, C.-Z. Nanomedicine 2010, 6 (1), S2−57.
2. Tsierkezos, N. G.; Ritter, U. J. Solid State Electrochem. 2012, 16 (6), 2217−2226.
3. Salinas-Torres, D.; Huerta, F.; Montilla, F.; Morallón, E. Electrochim. Acta 2011, 56 (5), 2464−2470.
4. Habibi, B.; Jahanbakshi, M.; Pournaghi-Azar, M. H. Electrochem. Acta 2011, 56 (7), 2888−2894.
5. Zestos, A. G.; Jacobs, C. B.; Trikantzopoulos, E.; Ross, A. E.; Venton, B. J. Anal. Chem. 2014, 86, 8568−8575.
6. Swamy, B. E. K.; Venton, B. J. Analyst 2007, 132 (9), 876−884.
7. Jacobs, C. B.; Vickrey, T. L.; Venton, B. J. Analyst 2011, 136 (17), 3557−3565.
8. Zestos, A. G.; Nguyen, M. D.; Poe, B. L.; Jacobs, C. B.; Venton, B. J. Sens. Actuators, B 2013, 182 (2013), 652−658.
9. Pears, M. J.; Ross, A. E.; Venton, B. J. Anal. Methods 2011, 3 (10), 2379.
10. McCreery, R. L. Chem. Rev. 2008, 108 (7), 2646−2687.
11. Jacobs, C. B.; Pears, M. J.; Venton, B. J. Anal. Chem. Acta 2010, 662 (2), 105−127.
12. Liu, J. Science (Washington, DC, U. S.) 1998, 280 (5367), 1253−1256.
13. Yang, C.; Denno, M. E.; Pyakurel, P.; Venton, B. J. Anal. Chem. Acta 2015, 885, 17−37.
14. Álvarez-Martos, I.; Fernández-Gavela, A.; Rodríguez-García, J.; Campos-Álvaraz, N.; García-Delgado, a. B.; Gómez-Plaza, D.; Costa-García, A.; Fernández-Abdel, M. T. Sens. Actuators, B 2014, 192 (2014), 253−260.
15. Xiao, N.; Venton, B. J. Anal. Chem. 2012, 84 (18), 7816−7822.
16. Xiang, L.; Yu, P.; Hao, J.; Zhang, M.; Zhu, L.; Dai, L.; Mao, L. Analyst. Chem. 2014, 86 (8), 3909−3914.
17. Zacheck, M. K.; Hermans, A.; Wightman, R. M.; McCarty, G. S. J. Electroanal. Chem. 2008, 614 (1−2), 113−120.
18. Ciszewski, A.; Milczarek, G. Anal. Chem. 1999, 71 (5), 1055−1061.
19. Swamy, B. E. K.; Venton, B. J. Analyst 2007, 132 (9), 876−884.
20. Delmas, M.; Pinault, M.; Patel, S.; Porterat, D.; Reynaud, C.; Mayne-L’Hermite, M. Nanotechnology 2012, 23 (10), 106504.
21. Attupalli, G.; Eppur, R.; Kumta, P. N.; Yang, M.; Lee, J.-K.; Gray, J. L. J. Phys. Chem. C 2011, 115 (9), 3534−3538.
22. Lepòrò, X.; Lima, M. D.; Baughman, R. H. Carbon 2010, 48 (12), 3621−3627.
23. Gao, L.; Peng, A.; Wang, Z. Y.; Zhang, H.; Shi, Z.; Gu, Z.; Cao, G.; Ding, B. Solid State Commun. 2008, 146 (9−10), 380−383.
24. Hiraoka, T.; Yamada, T.; Hata, K.; Futaba, D. N.; Kurachi, H.; Uemura, S.; Yamura, M.; Iijima, S. J. Am. Chem. Soc. 2006, 128 (41), 13338−13339.
25. Bayer, B. C.; Hofmann, S.; Castellan-Cudia, C.; Blume, R.; Baehtz, C.; Esconauregui, S.; Wirth, C. T.; Oliver, R. A.; Ducati, C.; Knop-Gericke, A.; Schögl, R.; Goldoni, A.; Cepek, C.; Robertson, J. J. Phys. Chem. C 2011, 115 (11), 4359−4369.
26. Zestos, A. G.; Yang, C.; Jacobs, C. B.; Hensley, D.; Venton, B. J. Analyst 2015, 140 (21), 7283−7292.
27. Kozai, T. D. Y.; Jaquins-Gerstl, A. S.; Vasquez, A. L.; Michael, A. C.; Cui, X. T. ACS Chem. Neurosci. 2015, 6 (1), 48−67.
28. Tran, K. Y.; Heinrichs, B.; Colomer, J.-F.; Pirard, J.-P.; Lambert, S. Appl. Catal., A 2007, 318 (2007), 63−69.
29. Graham, D. J. Phys. Chem. 1953, 57 (7), 665−669.
30. Liu, Y. J. Chem. Eng. Data 2009, 54 (7), 1981−1985.
31. Archer, D. G.; Wang, P. J. Phys. Chem. Ref. Data 1990, 19 (2), 371.
32. Mortimer, R. G. Physical Chemistry, 3rd ed.; Academic Press: San Diego, CA, 2008.
33. Holloway, A. F.; Toghill, K.; Wildgoose, G. G.; Compton, R. G.; Ward, M. a H; Tobias, G.; Llewellyn, S. a; Ballesteros, B.; Green, M. L. H.; Crossley, A. J. Phys. Chem. C 2008, 112 (28), 10389−10397.
34. Magrez, A.; Seo, J.; Smajda, R.; Mionić, M.; Forró, L. Materials 2010, 3 (10), 4871−4891.
35. Matthews, K. D.; Lemaître, M. G.; Kim, T.; Chen, H.; Shim, M.; Zuo, J.-M. J. Appl. Phys. 2006, 100 (4), 044309.
36. Delzeit, L.; Nguyen, C. V.; Chen, B.; Stevens, R.; Cassell, A.; Han, J.; Meyyappan, M. J. Phys. Chem. B 2002, 106, 5629−5635.
37. Parthangal, P. M.; Cavcic, R. E.; Zachariah, M. R. Nanotechnology 2007, 18 (18), 185605.
