

A Nanometer-Sized Graphite/Boron-Doped Diamond Electrochemical Sensor for Sensitive Detection of Acetaminophen

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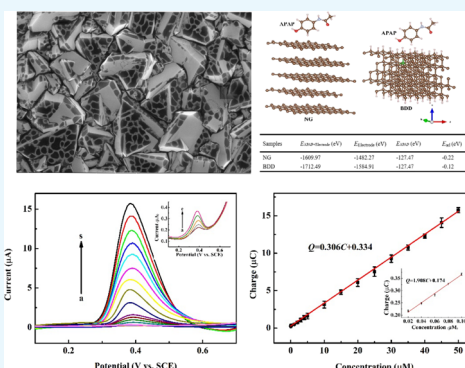


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ABSTRACT: A boron-doped diamond (BDD) has been widely used as an outstanding electrode for constructing high-performance electrochemical biosensors. In this paper, we fabricated a novel electrode combined of nanometer-sized graphite-BDD film (NG-BDD) by chemical vapor deposition. The nanometer-sized graphite (NG) is formed on the (111) facet of BDD via converting an sp^3 diamond structure to an sp^2 graphitic phase at high temperature in boron-rich ambient. The electrode was characterized by means of scanning electron microscopy, Raman spectroscopy, X-ray diffraction, and X-ray photoelectron spectroscopy. This NG-BDD was performed as an electrode of electrochemical biosensor to detect trace acetaminophen (APAP) accurately. Cyclic voltammetry and differential normal pulse voltammetry are used to investigate the overall performance of the electrochemical device. The sensor has a linear electrochemical response to APAP in the concentration range of 0.02–50 μ M, and the detection limit is estimated to be as low as 5 nM. The research has resulted in a solution of constructing a reusable NG-BDD sensor to detect APAP with stability and show potential in extensive application.



1. INTRODUCTION

Carbon-based structures have attracted tremendous attention owing to the outstanding and unique structural characteristics in recent decades.¹ Glassy carbon, carbon nanotubes, graphene, and boron-doped diamond (BDD) are attracting widespread interest in an electroanalysis for inherent natures such as a large specific surface, fast electron transfer, and so on.^{2,3} Among them, innovative hybrid sp^3 -C and sp^2 -C architectures are wonder materials for its high specific surface area, high conductivity, and biocompatibility currently.⁴ Diamond/graphite nanowires were synthesized in 2007 by chemical vapor deposition (CVD) with additionally introducing nitrogen, which consist of a diamond core of 5–6 nm in diameter covered by graphite shells.⁵ Arenal et al. reported diamond nanowires surrounded by graphite sheath adding more than 10% N_2 and revealed that the sp^2 -bonded carbon sheath provides the excellent electrical conductivity.⁶ A low detection limit for Ag^+ could be obtained in the nitrogen-incorporated ultrananocrystalline diamond/multilayer graphene composite films.⁷ Jiang et al. presented diamond/graphite nanoplatelet films grown in CH_4 and H_2 source gases without N_2 addition for the sensitive detection of trace heavy metal ions. They explored the conductive diamond and graphite hybridized configuration as a DNA sensor in biological applications. The hybrid sp^3 -C and sp^2 -C based electrochemical devices fabricated by CVD could operate for a long period of time especially in a harsh environment because of the

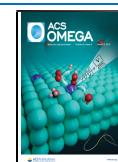
tight interfacial association between graphite and the conductive substrate rather than graphite dispersion on the surface of commercial electrodes. BDD containing almost complete sp^3 carbons throughout the lattice has unique electrochemical properties such as a wide potential window, low background current, and electrochemical stability.^{8,9} The strong interfacial force between graphite and a BDD substrate solved the bottleneck in the manufacturing of stable graphite-diamond electrodes.

In the last several decades, the increasing use of medicine prevented diseases and improved the quality of human health. Acetaminophen (APAP) is widely used as one of most effective painkiller to relieve pain and fever.^{10,11} Due to its increased use, the disposal of APAP and manufacturing wastewater has been found to be increasing in the source water system.¹² APAP exists in concentrations ranging from dozens to hundreds of nanomolar per liter,¹³ thus making it a rapidly emerging worldwide water problem.¹⁴ In addition, increased APAP in drinking water may lead to increased mortality and heart and gastrointestinal diseases.¹⁵ Also, the excessive and

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toxic doses of APAP will not only accumulate toxic metabolites resulting in liver and kidney damage but also contaminate water resources. Thus, monitoring APAP in water is imminently important. Several typical methods, such as spectrophotometry,¹⁶ titrimetry,¹⁷ liquid chromatography,¹⁸ and chemiluminescence,¹⁹ have been used for quantitatively determining APAP in pharmaceutical tablets or biological fluids. However, the classical techniques such as liquid chromatography/tandem mass spectrometry are unsuitable for a routine analysis because of complex pretreatment program and expensive and time-consuming systems.²⁰ Because APAP is electroactive, an electrochemical method is favorable for detecting APAP. Moreover, electroanalytical techniques are highly sensitive, less time-consuming, and inexpensive, as well as a wide dynamic range and quick response can be realized.^{21,22}

In this study, nanometer-sized graphite-BDD (NG-BDD) was synthesized in CH_4/H_2 mixture gas with $\text{B}(\text{OCH}_3)_3$ via CVD. The high temperature will accelerate the process where carbon atoms tend toward the sp^2 state on the (111) facet of BDD, eventually forming nanometer-sized graphite (NG). The fabricated NG-BDD electrode at a higher temperature exhibits a linear electrochemical range of 0.02–50 μM and a low limit of detection of 5 nM for APAP. It reveals that the fabricated sensor shows high selectivity, reproducibility, and stability for monitoring APAP.

2. RESULTS AND DISCUSSION

2.1. NG-BDD Characterization. Figure 1 exhibits the morphological evolution from the BDD to NG-BDD films at

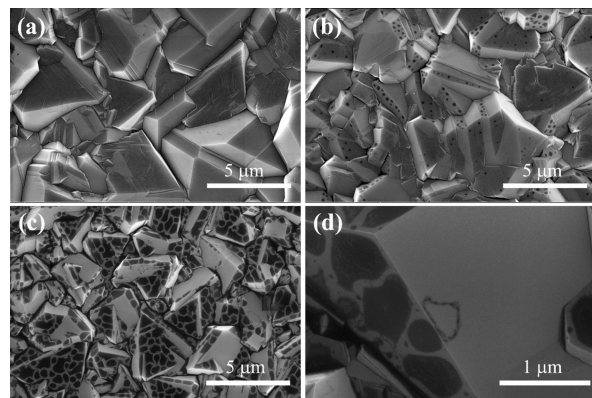


Figure 1. SEM images of (a) polycrystalline BDD films at 850 °C, (b) L-NG-BDD, (c) H-NG-BDD, and (d) is the image obtained at a high magnification of (c).

different temperatures from 850 to 1050 °C with constant $\text{CH}_4/\text{H}_2/\text{B}(\text{OCH}_3)_3$ flow rates (2/150/2 sccm). As can be seen, the temperature plays a vital role in the growth from NG-BDD films at 950 °C (L-NG-BDD) to NG-BDD films at 1050 °C (H-NG-BDD). The polycrystalline BDD films consist of dense grains with an average size of 1–5 μm at the substrate temperature of 850 °C (Figure 1a). When the temperature increases up to 950 °C, the NG uniformly covers a small part of the (111) facets of the BDD substrate, as shown in Figure 1b. With a further increase in temperature to 1050 °C, the area covered by the NG has enlarged (Figure 1c). Figure 1d is the image obtained at a high magnification of Figure 1c. The size of the NG on the (111) facets of BDD is in the region of 70–500 nm, and the thickness of graphite is irregular. Therefore,

the surface characterization of the films presents an obvious structural transformation from diamond crystals ($\text{sp}^3\text{-C}$) to nanometer-sized graphite ($\text{sp}^2\text{-C}$) with increasing the substrate temperature. However, under the same conditions without boron doping, no surface graphitization is found, which shows that the factor of boron doping plays a decisive role. NG grown on the (111) facet of BDD might be caused by the high doping concentration of boron on the (111) facet. The surface characterization of the films presents an obvious structural transformation from diamond crystals ($\text{sp}^3\text{-C}$) to nanometer-sized graphite ($\text{sp}^2\text{-C}$) in Figure 1. As reported in a previous work that the graphene reconstruction favorably occurred on the (111) BDD.²³ In this paper, no surface graphitization is found under the same conditions for the undoped diamond films, meaning that the factor of boron doping plays a crucial role in forming graphite on the BDD surface. At a higher temperature (1050 °C), the formation barrier of transferring diamond to graphite could be easily overcome, and carbon atoms are easier to reconstruct. NG has already grown on the (111) facet of BDD at the temperature of 950 °C, and the area of NG enlarges at the temperature of 1150 °C. It is consistent with the previous work that the graphite-like surface reconstructions on the (111) facet of a diamond are based on the DFT.^{24,25}

Figure 2a displays the characteristics of Raman spectra of the polycrystalline BDD, L-NG-BDD, and H-NG-BDD films. In the Raman spectra, the peak of 1330 cm^{-1} and the broad peaks around at 500 and 1200 cm^{-1} appear on each of the films. The peak around 1330 cm^{-1} corresponds to an sp^3 -bonded carbon, which is the characteristic peak of a diamond. The asymmetry of the diamond peak at 1330 cm^{-1} reveals the high concentration of boron doping. The broad peaks located at 500 and 1200 cm^{-1} are related to the boron doping-induced Fano effect and density of states.^{26,27} However, the L-NG-BDD and H-NG-BDD give an extra band centered at 1594 cm^{-1} (G peak) originating from the radial breathing mode of an sp^2 carbon.^{28,29} The D peak at around 1350 cm^{-1} might be submerged by a diamond peak at 1330 cm^{-1} . Comparing to the diamond peak, the peak at 1350 cm^{-1} submerged, and the weak peak at 1594 cm^{-1} indicated the fact that a small amount of graphite on the (111) facets of BDD is nanometer-sized, while BDD is high-quality microcrystalline, which is consistent with the SEM images in Figure 1.

The X-ray diffraction (XRD) spectra of the BDD, L-NG-BDD, and H-NG-BDD films are presented in Figure 2b. The same characteristic diffraction peaks at 43.9, 75.4, and 91.5° are assigned to (111), (220), and (311) diamond diffraction modes, respectively.³⁰ The sharp peak at 26.0° corresponds to the (002) graphite in the two NG-BDD samples. As revealed by graphite peak intensity at 1050 °C that is larger than that at 950 °C, the graphite grows more on BDD at 1050 °C, consistent with the results of SEM (Figure 1b,c). The XRD spectra at different temperatures demonstrate that the increased temperature will facilitate the growth of NG.

Although the evidence of $\text{sp}^2 \text{C}=\text{C}$ is not obvious in the Raman spectra, the X-ray photoelectron spectrum (XPS) is a more sensitive surface technique. The as-grown films have hydrogen termination and are stored under a vacuum before the XPS measurements. As shown in Figure 3, the strong C 1s spectra peaks located at 284.6 eV in all samples are assigned to the $\text{sp}^3 \text{C}-\text{C}$ present in the diamond bulk.³¹ The spectral feature at 285.3 eV corresponds to the presence of carbon atoms bound to subsurface hydrogen.³² The peak found at

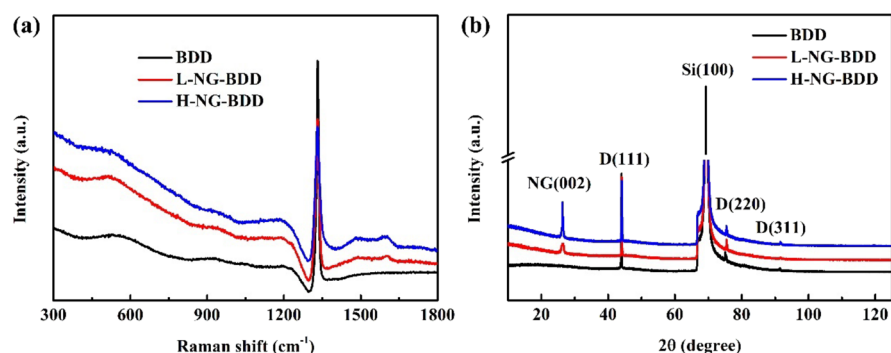


Figure 2. (a) Raman and (b) XRD spectra of BDD, L-NG-BDD, and H-NG-BDD films.

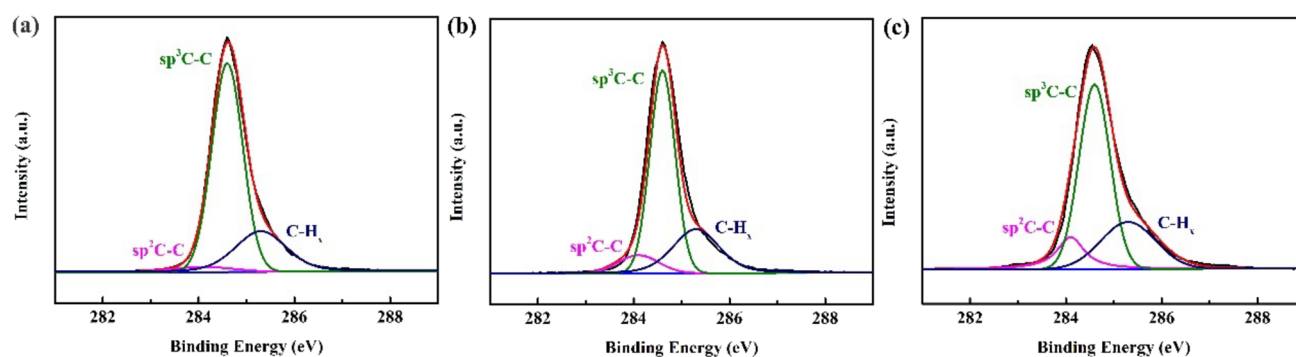


Figure 3. XPS of (a) BDD, (b) L-NG-BDD, and (c) H-NG-BDD films.

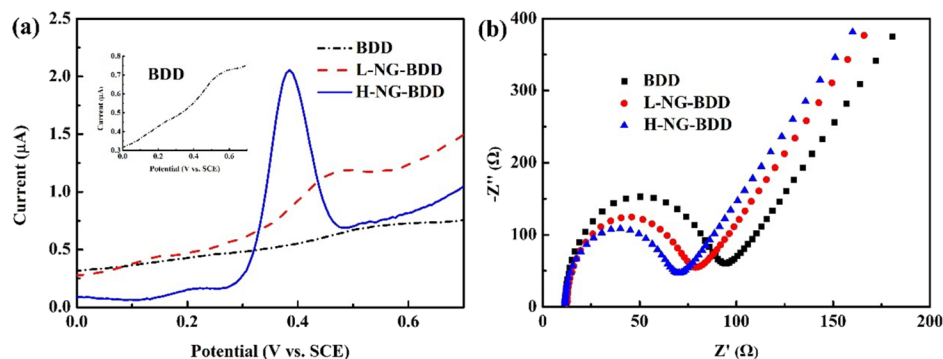


Figure 4. (a) DNPV curves for 6.5 μM APAP obtained on BDD (black short dash dot), L-NG-BDD (red dash), and H-NG-BDD electrodes (blue solid) in 0.1 M PBS with a scan rate of 50 mV s^{-1} . The inset graph is the DNPV curve at a high magnification on BDD. (b) Impedance spectra of BDD, L-NG-BDD, and H-NG-BDD electrodes tested in a 5 mM $\text{Fe}(\text{CN})_6^{3-/4-}$ solution containing 0.1 M KCl.

284.1 eV in Figure 3a can be attributed to $\text{sp}^2 \text{C}=\text{C}$ at the polycrystalline grain boundaries of BDD.³³ The presence of $\text{sp}^2 \text{C}=\text{C}$ (Figure 3b,c) can be assigned to the graphite reconstructed on the BDD surface in the environment with boron.^{23,34} The peak at 284.1 eV, associated with the graphite group, increases significantly after heating. The decrease in the full width at half maximum is attributable to the increase in structural order due to the longer π bonds. The ratio of $\text{sp}^2 \text{C}=\text{C}$ dramatically increased due to the graphitization of the L-NG-BDD films (8.07%) compared to BDD (3.06%). Especially at the elevated temperature of 1050 $^\circ\text{C}$, the ratio of $\text{sp}^2 \text{C}=\text{C}$ increased to 10.46%, which indicates that the graphite component is more than that at the temperature of 950 $^\circ\text{C}$. These results are in good agreement with the SEM measurements that an sp^2 -bonded carbon is present within the films, but its fraction is not very large.

2.2. Electrochemical Characterization for Detecting APAP.

The BDD, L-NG-BDD, and H-NG-BDD electrodes are proposed to detect 6.5 μM APAP solutions by DNPV (Figure 4a). As can be seen, the BDD shows the broad and weak oxidation waves centered at 556 mV. Compared with BDD, it is observed that the oxidation peak potential of APAP shifts negatively by using L-NG-BDD and H-NG-BDD at 476 and 383 mV, respectively. Furthermore, the oxidation peak currents of APAP at L-NG-BDD and H-NG-BDD improved significantly. The peak current at H-NG-BDD is almost sixfold that of BDD, indicating that the NG might enlarge the surface area and reaction sites to obtain a high sensitivity.

Electrochemical impedance spectroscopy (EIS) is an effective way used widely to study the interface characteristics of electrodes. It usually includes a semicircular part and line part at a higher frequency and lower frequency respectively, corresponding to the electron transfer limiting process and the

diffusion process.³⁵ The electron transfer kinetics of BDD, L-NG-BDD, and H-NG-BDD are further explored. Thus, the impedance spectra of BDD, L-NG-BDD, and H-NG-BDD in 5 mM $\text{Fe}(\text{CN})_6^{3-/4-}$ solution are shown in Figure 4b. All the impedance spectra are fitted with a detailed fitting data (Table 1). The charge transfer resistances taking place at the solution

Table 1. $R(Q(RW))$ Circuit Modeling Results of BDD, L-NG-BDD, and H-NG-BDD Electrodes Tested in a 5 mM $\text{Fe}(\text{CN})_6^{3-/4-}$ Solution Containing 0.1 M KCl^a

sample	R_s (Ω)	CPE (mF)	R_{ct} (Ω)	Z_w ($\Omega/\text{cm}^2 \text{ s}^{-1}$)
BDD	11.4	3.48	86.9	243.3×10^{-6}
L-NG-BDD	12.7	4.05	68.7	314.3×10^{-6}
H-NG-BDD	11.6	4.20	57.7	220.6×10^{-6}

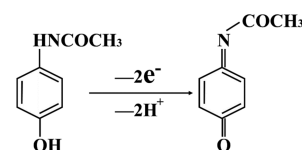
^a R_s is the solution resistance of the electrolyte, CPE is a constant phase element that takes into account the interfacial irregularities, R_{ct} is the charge transfer resistance taking place at the solution interface, and Z_w is the Warburg diffusion impedance element.

interface (R_{ct}) of BDD, L-NG-BDD, and H-NG-BDD are 86.9, 68.7, and 57.7 Ω , respectively. The R_{ct} of L-NG-BDD is smaller than BDD, which means that the graphite promotes electron transfer. It is confirmed that H-NG-BDD has the better electron transfer ability for the lowest R_{ct} .

In order to explore the kinetic reaction of the H-NG-BDD electrode, the various cyclic voltammetry (CV) of 10 μM APAP in 0.1 M NaH_2PO_4 - Na_2HPO_4 buffer solution (PBS) (pH 7.4) with different scan rates is presented in Figure 5a. The scan rates are 10, 20, 30, 40, and 50 mV s^{-1} . The redox peak current linearly increases against the increasing of scan rate with correlation coefficients (R^2) of 0.99 (Figure S1), suggesting an adsorption-controlled process at a low scan rate.³⁶ The redox peak current linearly increases against the increasing square root of scan rates (50, 100, 150, 200, 250, 300, 350, 400, 450, and 500 mV s^{-1}), suggesting a typical diffusion-controlled process at a high scan rate. It can be seen in Figure S2 that the anode peak potential (E_p) is proportional to the natural logarithm of the scan rate with the relationship expressed as: $E_p = 0.015 \ln \nu + 0.358$. Based on Laviron equation,^{37,38} the value of the transfer coefficient (α) and the number of transferred electrons (n) are calculated to be 0.63 and 2.2, in agreement with the previous results.³⁹ The electrochemical redox behavior of APAP is investigated in 10 nM APAP with different pH values ranging from 6.0 to 8.0, and the maximum peak current is obtained at pH 7.4 (Figure

5b). Thus, the 0.1 M PBS buffer solution with pH 7.4 is selected for subsequent experiments. In Figure S3, the peak potential negatively shifting with the increase of pH value indicates that the redox behavior is a process involving protons.⁴⁰ The equation of peak potential depending on the pH is $E_p = 0.055\text{pH} + 0.800$. Based on the slope of 0.055, the proton number (m) is estimated to be about 2. Therefore, the oxidation of APAP involves a two-electron and two-proton process, which is consistent with the previous works.^{41–43} The mechanisms of APAP electrochemical reactions that the molecule loses two electrons and two protons to become N-acetyl-*p*-benzoquinone imine are shown in Scheme 1.

Scheme 1. Mechanisms of APAP Electrochemical Reactions



2.3. Optimization of Accumulation Process. Differential normal pulse voltammetry (DNPV) is a technique that involves applying amplitude potential pulses on a linear ramp potential. In DNPV, a base potential value is chosen at which there is no faradaic reaction and is applied to the electrode. The base potential is increased between pulses with equal increments. The current is immediately measured before the pulse application and at the end of the pulse, and the difference between them is recorded. The parameters that determine the peak current of DNPV include pulse amplitude, first pulse width, and second pulse width on the signal response. The optimization of the parameters of DNPV is an important step to realize the excellent peak current and sensitivity of this pulse technique, including the study of the dependence of the parameters above. The first pulse width varies from 100 to 300 ms, the second pulse width varies from 20 to 60 ms, and pulse amplitude varies from 30 to 60 mV. Experimental details are presented in Figure 6, which gives the experimental data of how the accessible parameters affect the peak current and resolution. From the data in Figure 6 and similar data, optimized parameters for the subsequent analytical work are chosen: first pulse width of 200 ms; second pulse width of 50 ms; and pulse amplitude of 50 mV.

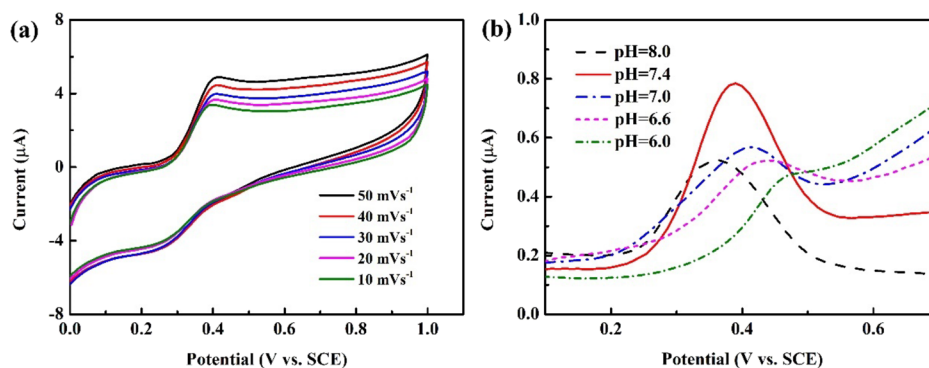


Figure 5. (a) Five CV curves of 10 μM APAP on the H-NG-BDD electrode at different scan rates in 0.1 M PBS (pH = 7.4). The scan rates are 10, 20, 30, 40 and 50 mV s^{-1} . (b) DNPV diagrams of 10 μM APAP on the H-NG-BDD electrode with different pH values. The pH values of 0.1 M PBS are 8.0, 7.4, 7.0, 6.6, and 6.0.

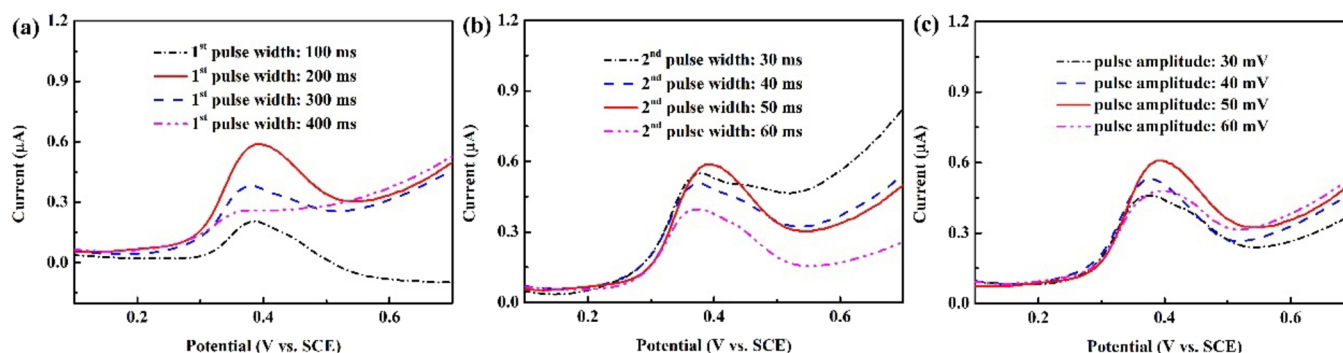


Figure 6. DNPV diagrams on the H-NG-BDD electrode of APAP in phosphate buffer pH 7.4 at different (a) first pulse widths from 100 to 400 ms; (b) second pulse widths from 30 to 60 ms; and (c) pulse amplitudes from 30 to 60 mV. Concentration of APAP for panels (a–c): 2 μ M.

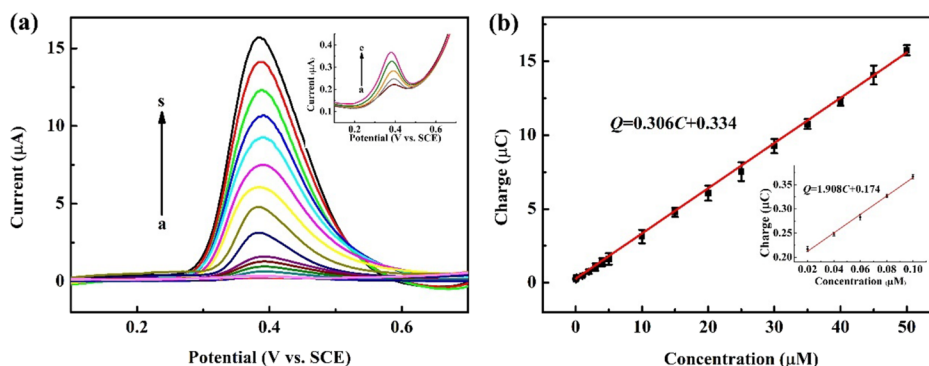


Figure 7. (a) DNPV diagrams of APAP with the concentrations of (a) 0.02, (b) 0.04, (c) 0.06, (d) 0.08, (e) 0.10, (f) 1, (g) 2, (h) 3, (i) 4, (j) 5, (k) 10, (l) 15, (m) 20, (n) 25, (o) 30, (p) 35, (q) 40, (r) 45, and (s) 50 μ M on the H-NG-BDD electrode. Inset graph is the DNPV curves at the high magnification of APAP with the concentrations of 0.02–0.1 μ M (b) Calibration curve of detecting APAP. Inset graph is calibration curve with an APAP concentration of 0.02–0.1 μ M. The buffer is 0.1 M PBS (pH = 7.4).

Table 2. Relevant Published Redox Electrochemical Biosensors for APAP Detection^a

electrodes	techniques	linear range(μ M)	detection limit (μ M)	references
phosphorus-doped graphene/GCE	DPV	1.5–120	0.36	11
electrospun CeBiOx nanofibers/SPE	DPV	2.5–130	0.2	36
MWCNT-polymer/GCE	CV	5–1000	3.5	45
graphite oxide/GCE	DPV	0.2–26.5	0.04	46
BDD	amperometry	0.5–50	0.01	47
Nafion/BDD	DPV	0.05–200	0.017	48
H-NG-BDD	DNPV	0.02–50	0.005	this work

^aGCE: glassy carbon; SPE: screen-printed electrode; and MWCNT: multiwalled carbon nanotube.

2.4. Calibration Curve and Limit of Detection. Under the optimal experimental conditions of DNPV, the electrochemical oxidation of APAP is carried out at the H-NG-BDD electrode with various concentrations of APAP and of detection range from 0.02 to 50 μ M (Figure 7a). We received two linear regression equations: $Q = 0.306C + 0.334$ ($R^2 = 0.99$, 0.02–0.1 μ M) and $Q = 1.908C + 0.174$ ($R^2 = 0.99$, 0.1–50 μ M), a detection limit (DL) of (5 nM) is calculated using the equation $DL = 3 \times SD$ (standard deviation)/slope (Figure 7b). At low APAP levels, the local concentration at the electrode surface is rapidly depleted by the catalysis of NG, resulting in the high sensitivity of the electrode response. At higher APAP concentrations, the surface of the electrode might be fouled by the reaction products resulting in a lower slope.⁴⁴ Also, it attains to the saturation level at a higher concentration. Thus, the sensor showed different linear correlations at different concentration ranges. The performance of the H-NG-BDD electrode exhibits a lower detection limit and wide

detection range comparing to the most previous reports in the literature for the detection of APAP^{11,36,45–48} (Table 2).

2.5. Theoretical Study of APAP Adsorbed on H-NG-BDD and BDD. In order to understand the adsorption of APAP molecules on H-NG-BDD and BDD in detail, the theoretical analysis is carried out by density functional theory (DFT). Because the difference between H-NG-BDD and BDD is the NG grown on the (111) facets of BDD, the theoretical model is simplified to calculate the adsorption energy of APAP and NG (or BDD) to explore the sensitive role of each electrode. The crystal structure of APAP with NG and APAP with BDD are shown in Figure 8. We have considered the hydrogen termination of the BDD when considering the DFT calculation. The result of H-BDD is presented. However, for the case of H-NG, the H-terminated NG is structurally unstable and turns into sp^3 -C. Thus, the NG is calculated without any termination. The adsorption energy (E_{ad}) is calculated by the equation of $E_{ad} = E_{APAP + electrode} - E_{electrode} -$

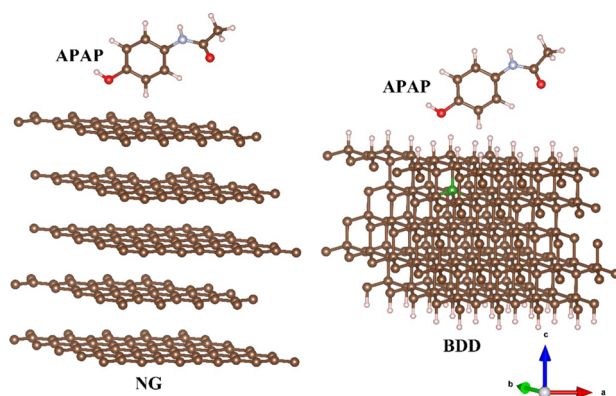


Figure 8. Crystal structure of APAP with NG and APAP with BDD. Brown, pink, red, gray, and green balls represent C, H, O, N, and B, respectively.

E_{APAP} , where $E_{\text{APAP} + \text{electrode}}$ is the total energy of the combined APAP and electrodes of H-NG-BDD (or BDD), and $E_{\text{electrode}}$ and E_{APAP} are the energy of the electrode and a single APAP molecule, respectively. The calculated E_{ad} values of APAP molecules on H-NG-BDD and BDD in Table 3 are -0.220 and

Table 3. Calculated E_{ad} of APAP Molecules on NG and BDD

samples	$E_{\text{APAP} + \text{electrode}}$ (eV)	$E_{\text{electrode}}$ (eV)	E_{APAP} (eV)	E_{ad} (eV)
NG	−1609.97	−1482.27	−127.47	−0.22
BDD	−1712.49	−1584.91	−127.47	−0.12

-0.115 eV, respectively. It means that the surface of the H-NG-BDD electrode has a stronger adsorption capacity for APAP because of the lower E_{ad} . NG is grown on BDD directly, thus the binding force between NG and BDD is firm. NG has a stronger adsorption to APAP, and the background current of BDD is low. The better performance of the H-NG-BDD electrode could be attributed to the synergistic effect of BDD and NG as follows: the BDD substrate exhibits low background signals; the strong interfacial force between NG and BDD substrate offers a stable electrode; NG has stronger adsorption to APAP; and the defective sheets of NG provides active sites for electrocatalytic APAP.

2.6. Interference Analysis. Dopamine, uric acid, ascorbic acid, and tryptophan could exist with APAP in biological samples, and thus interferes with the analysis of detecting APAP important in practical electrochemical APAP sensors. A total of 10-fold concentration ($85 \mu\text{M}$) of dopamine, uric acid, and tryptophan is added in 0.1 M of PBS ($\text{pH} = 7.4$) mixed to APAP with a concentration of $8.5 \mu\text{M}$. It is clear that the H-NG-BDD electrode could distinguish the oxidation peaks of each interference well (black line in Figure 9). The uric acid peak is submerged and cannot be identified when the concentration of APAP reaches $50 \mu\text{M}$ (red line in Figure 9). The results prove that the detection of APAP is evidently distinguished from the mixtures and without sensitivity to ascorbic acid. From the DNPV curves, the oxidation peaks of interference with great separation imply the excellent selectivity of H-NG-BDD and possibility of developing a sensor with various sensing platforms.

2.7. Reproducibility and Stability of the Sensor. The reproducibility of H-NG-BDD is investigated by CV for 10 repetitive measurements of $5 \mu\text{M}$ of APAP. The relative

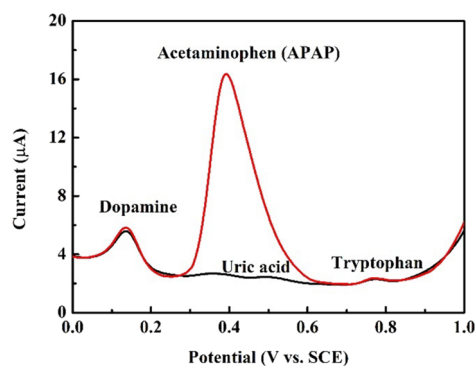


Figure 9. DNPV diagrams of $8.5 \mu\text{M}$ APAP (black line) and $50 \mu\text{M}$ APAP (red line) with the $85 \mu\text{M}$ concentration of dopamine, uric acid, ascorbic acid, and tryptophan on the H-NG-BDD electrode.

standard deviation less than 2.3% reveals the excellent reproducibility at the H-NG-BDD electrode. Furthermore, five H-NG-BDD electrodes prepared under the same condition were applied for detecting $5 \mu\text{M}$ of APAP, and the low relative standard deviation of 3.6% for the current response suggests a good electrode-to-electrode reproducibility. The stability of the H-NG-BDD electrode for testing the APAP solution remained for 10 days. After one experiment, the electrode is cleaned by the repeated cycling of CV and washed by deionized water and then stored in a refrigerator at 4°C . For $5 \mu\text{M}$ APAP, the peak current responses fluctuate in the region of -2.7 to 3.8% compared to the initial peak current (Figure S4), revealing the stability and accuracy of the H-NG-BDD electrode.

2.8. Analysis of Real Samples. The H-NG-BDD electrode was used to evaluate the performance of commercial drug samples containing APAP. Two drug tablets were analyzed to determine the concentration of APAP by DNPV. Tylenol (Johnson Inc., Canada) and Baifuning (Shanghai Squibb Ltd., China) tablets containing 500 mg of APAP were dissolved in PBS ($\text{pH} 7.4$) first, then filtered through a cellulose acetate membrane (pore size $0.45 \mu\text{m}$; US), and finally diluted to an appropriate concentration range for an electrochemical analysis. The measurement results of APAP concentration are shown in Table 4. The results show that the electrode is a promising electrochemical sensor for the accurate detection of APAP.

Table 4. Measurements of APAP in Paracetamol Samples

samples	added (μM)	detected (μM)	recovery (%)	RSD (%)
tablet1	10	9.8	98%	1.2
tablet1	20	19.8	99%	3.1
tablet2	30	30.6	102%	2.2
tablet2	40	41.2	103%	2.4

3. CONCLUSIONS

In the present study, we have developed a highly electroactive H-NG-BDD film by a one-step growing process. The NG grown on the (111) facets of BDD comes from the reconstruction after boron doping at a high temperature. The sensor based on H-NG-BDD exhibits a good linear range from 0.02 to $50 \mu\text{M}$ for detecting APAP and realizes a low detection limit of 5 nM . The redox mechanism of APAP on the H-NG-BDD belongs to a two-electron and two-proton process. Furthermore, the adsorption between APAP and the

H-NG-BDD electrode indicates that the APAP is easier to be detected according to the theoretical calculation. The H-NG-BDD sensor shows high selectivity, reproducibility, and stability for monitoring APAP. The H-NG-BDD electrode would have a very broad application prospect in the electrochemical analysis of other drugs and not only limited to APAP.

4. METHODS

4.1. Materials. APAP (guaranteed reagent) was obtained from Sigma-Aldrich. Dopamine, uric acid, and tryptophan were used of analytical grade from Sigma-Aldrich. NaH_2PO_4 and Na_2HPO_4 (analytical grade) were purchased from Sigma-Aldrich and prepared with water purified by a Barnstead Ultrapure filtration system. PBS was used as a solvent to dilute various detected compounds throughout the experiment.

4.2. Preparation of the NG-BDD Electrode. First, the mirror-polished Si substrate was scratched with nanodiamond powders (10 nm) for 30 min. Second, the substrate was ultrasonicated with nanodiamond powders in an acetone solution for 90 min to increase the nucleation points. At last, the Si substrate was cleaned by ultrasonic treatment with acetone, ethanol, and purified water for 10 min and dried with nitrogen. The NG-BDD films were produced on the treated Si wafers by microwave plasma CVD at 2.45 GHz. CH_4/H_2 flow rates were 2/150 sccm, and the liquid $\text{B}(\text{OCH}_3)_3$ (incorporated boron source) at room temperature was carried by bubbling H_2 gas of which flow rates were 2 sccm. The NG-BDD films were deposited for 6 h with a thickness of 5 μm at a pressure of 8.8 kPa at the temperature between 950 and 1050 $^\circ\text{C}$.

4.3. Characteristic Apparatus. A scanning electron microscope (SEM, JSM-6480LV) was used to characterize the surface morphologies of the NG-BDD films. The analysis of the XPS was performed using a VG ESCALAB MK II with a monochromated Al $K\alpha$ source. The crystal structure of the products was characterized by XRD (Rigaku D/Max-Ra) using Cu $K\alpha$ radiation at a wavelength of 1.5418 Å. The structure of the NG-BDD electrodes was obtained by Raman spectroscopy (Renishaw in Via Raman microscope equipped with 514 nm laser excitation).

4.4. Electrochemical Measurements. In a three-electrode system, platinum wire, saturated calomel electrode, and NG-BDD electrodes were served as the counter, reference, and working electrodes, respectively. The area of the NG-BDD electrode was 0.10 cm^2 . The EIS texts were measured in a solution containing 5 mM $\text{Fe}(\text{CN})_6^{3-/4-}$ and 0.1 M KCl. The electrochemical measurements carried out in a PBS of NG-BDD electrodes were investigated by using CV and DNPV using an electrochemical workstation (CHI 760E) at room temperature.

4.5. Calculation Methods. DFT-based Vienna Ab initio Simulation Package code⁴⁹ was used for investigating the interaction between an APAP molecule and BDD (or NG). The Perdew–Burke–Ernzerhof of generalized gradient approximation⁵⁰ was chosen for the exchange–correlation functional. A kinetic cut-off energy of 400 eV and Monkhorst–Pack k-meshes with a grid spacing of $2\pi \times 0.2 \text{ \AA}^{-1}$ were adopted to ensure the energy convergence. The 4×4 supercells were used.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.0c06141>.

Relationship between an oxidation peak current and scan rate from the CV curves of 10 mM acetaminophen; relationship between an oxidation peak current and the natural logarithm of scan rate from CV curves of 10 mM acetaminophen; relationship between oxidation potential and pH obtained from the DNPV diagrams of 10 mM acetaminophen; and bar graph of the oxidation peak current responses the 1st to 10th day by DNPV (PDF)

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Notes

The authors declare no competing financial interest.

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