Detection of Covid-19 through a Heptanal Biomarker Using Transition Metal Doped Graphene

Anthony Zhu and Xuan Luo*

ABSTRACT: A rapid and noninvasive way to monitor the spread of COVID-19 is the detection of SARS-CoV-2 biomarkers from exhaled breath. Heptanal was identified as a key biomarker which was significantly elevated in the breath of SARS-CoV-2 patients. In this study, the adsorption behaviors of heptanal on pristine and transition metal (Pd, Pt, and Ag) doped graphene were studied based on density functional theory. The results indicated that heptanal was weakly adsorbed on pristine graphene with an adsorption energy of $-0.015 \text{ eV}$ while it was strongly adsorbed on Pd-, Pt-, and Ag-doped graphene with adsorption energies of $-0.404$, $-0.356$, and $-0.755 \text{ eV}$, respectively. Also, the electronic properties of Pd-, Pt-, and Ag-doped graphene changed more dramatically after heptanal adsorption than pristine graphene. The recovery times were estimated to be $6.13 \times 10^{-6}$, $9.57 \times 10^{-7}$, and $4.83 \text{ s}$ for Pd-, Pt-, and Ag-doped graphene, respectively, showing that Pd-, Pt-, and Ag-doped graphene are suitable as reversible sensors. Our results conclude that Pd-, Pt-, and Ag-doped graphene are potential candidates as gas sensors for heptanal detection, and Ag-doped graphene is the most promising one.

1. INTRODUCTION

With the 2020 outbreak of COVID-19 caused by the coronavirus (SARS-CoV-2), many serious threats to global health have been produced. As of November 2021, there have been over 200 million reported cases of COVID-19 with more than 5 million reported deaths worldwide according to the World Health Organization (WHO) Coronavirus (COVID-19) Dashboard. Research institutes and pharmaceutical industries have made extensive efforts to gain knowledge about this new virus including diagnostics and therapeutics, as well as vaccine development. Large scale testing to detect COVID-19 is an essential strategy for the containment of the pandemic, especially in congregate settings such as airports or schools. Currently, COVID-19 is mainly diagnosed through the identification of the viral gene region using polymerase chain reaction (PCR) and the detection of antigens in samples collected from the upper respiratory tract. However, these tests can be uncomfortable, can be expensive, and can require laboratory equipment with trained professionals. Because of these drawbacks, a rapid, noninvasive and cost-effective way to detect COVID-19 would be valuable. Recently, an extremely appealing approach to consistently monitor the spread of COVID-19 through the detection of SARS-CoV-2 biomarkers from exhaled breath was reported.

Breath analysis is a rapid, noninvasive method for disease diagnosis. It has been demonstrated that viruses induce cells to produce metabolites, which lead to volatile organic compounds (VOCs) being exhaled. These VOCs, which act as biomarkers for diseases and disorders, can be the targets of breath diagnostics to assess the health status of patients. More than 870 kinds of VOCs in the human breath have been identified to provide vital information about dysfunctions or metabolic disorders in the human body. For instance, the breath of patients infected with tuberculosis (TB) shows increased levels of several benzene and aldehyde derivatives, and acetone is highly related to diabetes detection. Using VOCs to detect various diseases and metabolic disorders such as cancers, kidney failure, liver disease, and Alzheimer’s disease has been studied in the past, and a similar approach has been recently expanded to include COVID-19 diagnosis. From studies conducted by Berna et al. and Miller et al., heptanal has been identified as one of the key biomarkers which was significantly elevated in the breath of SARS-CoV-2 patients.

There are several major technologies in VOC detection, including gas chromatography–mass spectrometry (GCMS) and chemo-resistive devices, as well as sensor-based diagnosis. Recognized as the gold standard, GC-MS has been widely used in clinical trials in breath VOC detection. However, it is time-consuming and requires bulky, expensive equipment and highly trained professionals. Compared to GC-MS, nanomaterial based gas sensors are one of the most...
preferable sensors due to their simple structure, rapid response, high sensitivity and low cost.³⁰⁻⁵³ Many two-dimensional (2D) materials have been investigated substantially for VOC detection, including graphene, silicene, phosphorene, and TM-doped graphene. However, graphene has unique physical and electrochemical properties including high electrical conductivity and high electrochemically active surface area. In the past year, graphene has also caught tremendous attention from researchers for COVID-19 detection, and several studies have been published. Researchers have explored many approaches to detect COVID-19. However, type 2 diabetes is the most common disease. A graphene-like BC 6N nanosheet was disclosed as a promising candidate for the breath analysis of VOCs. It was also reported that Ag-doped graphene exhibited excellent sensitivity toward NO. Therefore, Pd, Pt, and Ag have been chosen as dopants to improve the sensitivity of graphene toward VOCs.

Graphene is one of the most favored 2D materials in gas sensor applications. It is a single layer, two-dimensional honeycomb lattice network of sp²-hybridized carbon atoms. This unique structure gives graphene superior physical and electrochemical properties including high electrical conductivity and high electrochemically active surface area. In the past year, graphene has also caught tremendous attention from researchers for COVID-19 detection, and several studies have shown promising results for graphene as a biosensor. However, pristine graphene has a zero band gap and is insensitive to gas molecules. Numerous studies have demonstrated that by doping graphene with transition metals (TM), especially palladium, platinum, and silver (Pd, Pt, and Ag), the doped graphene significantly improves the adsorption properties of gas molecules. Ma et al. have found that the sensitivities of graphene toward CO, NH₃, O₂, and NO₂ were dramatically enhanced by Pd doping. Another study showed stronger adsorption of cysteine molecules on Pt-doped graphene, compared to pristine graphene. It was also reported that Ag-doped graphene exhibited excellent sensitivity toward NO. Therefore, Pd, Pt, and Ag have been chosen as dopants to improve the sensitivity of graphene toward heptanal.

In this study, the effectiveness of pristine graphene and transition metal (Pd, Pt, and Ag) doped graphene to detect heptanal, a key biomarker of COVID-19, has been investigated. Using first-principles calculations based on density functional theory (DFT), the atomic structures and electronic structures of pristine and TM-doped graphene were studied. Furthermore, the calculated results of heptanal adsorption on pristine and TM-doped graphene were analyzed and compared to find a suitable sensor for heptanal detection. The magnetic properties of TM-doped graphene were not analyzed in this study.

### 2. METHODS

#### 2.1. Computational Details

All first-principles calculations were carried out based on DFT using the Generalized Gradient Approximation (GGA) with Perdew–Burke–Ernzerhof (PBE) exchange-correlation functional implemented in the ABINIT code. The Projected Augmented Wave (PAW) method was used to generate pseudopotentials using the AtomPAW code.

#### 2.2. Convergence Details

To ensure the accuracy of the calculations, the values for kinetic energy cutoffs, k-point mesh, and vacuum were converged. The convergence total energy tolerance on the self-consistent field (SCF) was set to be when the difference between two consecutive calculations of total energy was less than 1.0 × 10⁻¹⁰ Ha twice. Using the converged value, structural optimization was performed, and the force tolerance on the SCF was set to be 1.0 × 10⁻⁶ Ha/Bohr between consecutive forces twice. The structural optimization was conducted using the Broyden–Fletcher–Goldfarb–Shanno minimization (BFGS) with a maximal force tolerance of 2.0 × 10⁻⁵ Ha/Bohr or 0.01 eV/Å.

#### 2.3. Atomic Structure

A 4 × 4 × 1 supercell of graphene with 32 C atoms was used for the calculations. TM (Pd, Pt, and Ag) doped graphene was constructed by substituting one C atom with a TM atom. The defect formation energy (E_form) of an atom on the graphene sheet is given by

\[ E_{form} = E_{TMG} - E_{PG} + E_{C} - E_{TM} \]  

where E_{TMG}, E_{PG}, E_{C} and E_{TM} are the total energies of the TM-doped graphene sheet, total energy of pristine graphene sheet, and chemical potentials for C and TM atoms, respectively.

#### 2.4. Adsorption Calculations

Heptanal was placed above the graphene sheet in different configurations to analyze its adsorption behavior. Total energies were calculated for the heptanal adsorbed graphene system, pristine or TM-doped graphene sheet, and pure heptanal molecule. The adsorption energy (E_ads) was calculated using

\[ E_{ads} = E_{surr+mol} - E_{surr} - E_{mol} \]  

where E_{surr+mol}, E_{surr}, and E_{mol} represent the total energies of the heptanal-adsorbed graphene system, pristine or TM-doped graphene sheet, and pure heptanal, respectively.

#### 2.5. Electronic Structure

The band structure of the graphene system was calculated before and after the adsorption of heptanal, and it was plotted using high symmetry k-points \( \Gamma (0, 0, 0), K (\frac{\pi}{a}, \frac{\pi}{a}, 0), M (\frac{\pi}{a}, \frac{\pi}{a}, 0), \) and \( \Gamma (0, 0, 0) \).

For the adsorption of heptanal, the projected density of states (PDOS) was plotted using the tetrahedron method for the heptanal adsorbed pristine and TM-doped graphene systems. The atoms chosen for projections were the atoms closest to the site of the heptanal adsorption. Therefore, the PDOS of the 2p orbital of oxygen in heptanal and the 2p orbital of carbon in graphene or the d orbital of the TM dopants were plotted for heptanal adsorbed pristine or TM-doped graphene systems.

The interaction of graphene and heptanal was further confirmed by the charge transfer between them. The charge transfer \( \Delta \rho \) was calculated by

\[ \Delta \rho = \rho_{surr+mol} - \rho_{surr} - \rho_{mol} \]  

where \( \rho_{surr+mol}, \rho_{surr}, \) and \( \rho_{mol} \) represent the charge of heptanal-adsorbed graphene system, pristine or TM-doped graphene sheet, and pure heptanal, respectively.

#### Table 1. Electron Configurations and Radius Cutoffs for Generating PAW Pseudopotentials of Each Element Used in This Study

| element       | electron configuration | radius cutoffs (Bohr) |
|---------------|------------------------|-----------------------|
| hydrogen (H)  | 1s¹                    | 0.99                  |
| carbon (C)    | [He]2s²2p²             | 1.51                  |
| oxygen (O)    | [He]2s²2p⁴            | 1.41                  |
| palladium (Pd)| [Ar 3d⁸4s²]5s¹4d⁶     | 2.51                  |
| platinum (Pt) | [Xe 4f¹⁰]6s¹5d⁹       | 2.50                  |
| silver (Ag)   | [Kr]5s¹4d¹⁰           | 2.50                  |
2.6. Recovery Time, Conductivity, and Sensitivity.

The recovery time of the pristine and TM-doped graphene systems after heptanal adsorption was estimated. Based on the conventional transition state theory, \( \nu \), the recovery time \( (\tau) \) of graphene system after heptanal adsorption can be estimated using

\[
\tau = \nu^{-1} e^{-\frac{E_{ad}}{k_B T}}
\]

where \( \nu \) represents the attempt frequency \( (\nu = 10^{13} \text{s}^{-1} \text{for visible light}) \), \( E_{ad} \) represents the adsorption energy, \( T \) represents the thermodynamic temperature \( (T = 300 \text{K for room temperature}) \), and \( k_B \) represents the Boltzmann constant \( (k_B = 8.617 \times 10^{-5} \text{eV K}^{-1}) \).

The electrical conductivity \( \sigma \) of graphene system can be determined by

\[
\sigma \propto \exp\left(-\frac{E_g}{2k_B T}\right)
\]

where \( E_g \), \( k_B \), and \( T \) represent the band gap of the graphene system, the Boltzmann constant, and the thermodynamic temperature, respectively.

The sensitivity \( (S) \) of the graphene sheet, another important factor for heptanal sensing, was also evaluated. The sensitivity was defined as the variation of the electrical conductivity \( (\sigma) \) of the graphene sheet before and after heptanal adsorption as follows:

\[
S = \frac{\sigma_{surf} - \sigma_{surf+mol}}{\sigma_{surf}} \times 100
\]

Here, \( \sigma_{surf} \) and \( \sigma_{surf+mol} \) represent the conductivity of the pristine or TM-doped graphene sheet, and the conductivity of heptanal adsorbed graphene system, respectively.

3. RESULTS AND DISCUSSION

In this section, the adsorption characteristics of heptanal on pristine graphene (PG) were studied first. In order to improve the sensitivity of graphene toward heptanal, TM (Pd, Pt, and Ag) atoms were substitutionally doped into the graphene sheet. Then, the TM-doped graphene systems (PdG, PtG, and AgG) were analyzed upon heptanal adsorption. Adsorption energy, charge transfer, recovery time, band structure, PDOS, and sensitivity were evaluated and compared for all heptanal-adsorbed graphene systems, in order to find the most effective sensor for heptanal.

3.1. Heptanal Adsorption on Pristine Graphene. The optimized structures of pure heptanal (C\(_7\)H\(_{14}\)O) molecule and a 4 × 4 supercell of pristine graphene are illustrated in Figure 1. The calculated C–O bond length of heptanal molecule was 1.22 Å, and the bond angles of O–C–C and O–C–H were measured to be 125.6\(^\circ\) and 120.2\(^\circ\), respectively. For pristine graphene, the C–C bond length, C–C–C bond angle, and lattice constant were calculated to be 1.42 Å, 120\(^\circ\), and 2.47 Å, respectively. The band structure of pristine graphene is illustrated in Figure 7a, and it was observed that the dirac point is located at symmetry point \( K \) which shows a zero direct band gap. The calculated results of pristine graphene are in accordance with recent theoretical studies and also are in good agreement with a previous experimental study which shows the results of 1.42 Å for the C–C bond, 2.46 Å for the lattice constant, and zero band gap for pristine graphene. The calculated bond length, bond angle and lattice constant (9.86 Å) for 4 × 4 supercell of pristine graphene were listed in Table 2.

### Table 2. Optimized Structural Parameters of 4 × 4 Graphene Sheet: Lattice Constant \( (a) \), Bond Length \( (d) \) of C–C in Pristine or C-TM in TM-Doped Graphene, Bond Angle \( (\theta) \) of C–C–C in Pristine or C–TM–C in TM-Doped Graphene, Defect Formation Energy \( (E_{form}) \), and Bandgap \( (E_g) \)

| configuration      | \( a \) (Å) | \( d \) (Å) | \( \theta \) (deg) | \( E_{form} \) (eV) | \( E_g \) (eV) |
|--------------------|-------------|-------------|-------------------|--------------------|--------------|
| pristine graphene  | 9.86        | 1.42        | 120.0             | –                  | –            |
| Pd-doped graphene  | 10.06       | 1.94        | 88.9              | 6.291              | 0.293        |
| Pt-doped graphene  | 9.92        | 1.94        | 90.3              | 6.277              | 0.221        |
| Ag-doped graphene  | 9.90        | 2.14        | 77.4              | 8.965              | metallic     |

In order to find the most favorable adsorption configuration and study the interactions between heptanal and pristine graphene, different sizes of graphene supercells and different orientations were investigated, including aligning heptanal perpendicular or parallel to the graphene sheet. First heptanal was aligned perpendicularly with the O atom above the center of a carbon hexagon of pristine graphene using 2 × 2, 3 × 3, and 4 × 4 supercells. The configurations of heptanal on pristine graphene before and after the relaxation are illustrated in Figure 2. As shown in Figure 2a, heptanal stays perpendicular above the graphene sheet in the 2 × 2 supercell. This is likely due to the interactions between the periodic images of heptanal. When a 3 × 3 or 4 × 4 supercells of graphene is used, heptanal tends to adopt a parallel orientation after relaxation, as illustrated in Figures 2b and c. Based on the analysis on heptanal adsorption orientations and the size of the graphene sheet, a parallel

![Figure 1](https://example.com/figure1.png)
orientation of heptanal and a 4 × 4 supercell of graphene to minimize the interactions between periodic images of heptanal were used throughout the rest of this study.

There were three different adsorption sites considered for heptanal with the O atom above the hollow site (H represents the center of a carbon hexagon), the bridge site (B represents the center of a C−C bond), and the top site (T represents a carbon atom) of pristine graphene, as illustrated in Figure 1b. To find the most stable adsorption site, these structures were fully optimized and presented in Figure 3. The final adsorption distances between the O atom of heptanal and the nearest C atom of pristine graphene were measured to be 3.756, 3.346, and 3.459 Å for H, T, and B sites, respectively, as listed in Table 3. The large adsorption distances indicate weak interactions between heptanal and pristine graphene. Using eq 2, the adsorption energies of heptanal on pristine graphene were calculated, as shown in Table 3. The calculated adsorption energies were −0.015, −0.009, and 0.004 eV for H, B, and T sites, respectively, $E_{ad}(H) < E_{ad}(B) < E_{ad}(T)$. A positive adsorption energy indicates an endothermic reaction with a nonspontaneous adsorption while a negative adsorption energy indicates an exothermic reaction with a spontaneous adsorption. The more negative the adsorption energy is, the stronger the interaction between heptanal and graphene would be. These obtained values for all three sites suggest weak interactions between the heptanal molecule and pristine graphene. The most stable adsorption site with the most negative adsorption energy was chosen for further evaluation in this study. Among those three adsorption sites, the most stable adsorption site was determined to be the hollow site.

To work as an effective sensor, the interactions between the gas molecule and the substrate should be strong enough to retain the molecule on the substrate. However, the interactions should not be too strong so the desorption of the molecule from the substrate can take place in a very short period of time and the substrate can recover to its previous state. From eq 4, it is expected that a smaller adsorption energy will result in a very short recovery time, which means a faster desorption process of molecule. But the recovery time of nanosecond or less would be too short for a gas detection in a real environment because the sensor cannot hold the gas molecule.58 On the other hand, increasing the adsorption energy will elongate the recovery time dramatically in an exponential manner at a fixed temperature. In visible light and at room temperature, the recovery time for the desorption of heptanal from pristine graphene was estimated to be $1.79 \times 10^{-12}$ s, as listed in Table 4. This obtained short recovery time is due to the small adsorption energy and indicates that pristine graphene is not suitable for the detection of heptanal.

This weak interaction between heptanal and pristine graphene was further confirmed by the charge transfer of the heptanal adsorbed pristine graphene system. The charge transfer isosurface was plotted, as shown in Figure 6. The yellow region represents electron acceptors, and the blue region represents electron donors. The larger the charge transfer is, the more suitable the system is for heptanal adsorption. When a chemical bond is formed between the molecule and the

Figure 2. Configurations of heptanal on (a) 2 × 2 supercell, (b) 3 × 3 supercell, and (c) 4 × 4 supercell of pristine graphene. Top and bottom rows illustrate the configurations before and after the optimization, respectively. C, H, and O atoms are represented by gray, white, and red, respectively.

Figure 3. Top and side views of the optimized configurations of heptanal adsorption on pristine graphene for (a) hollow site, (b) top site, and (c) bridge site. C, H, and O atoms are represented by gray, white, and red, respectively.

Table 3. Adsorption Energy ($E_{ad}$) and the Final Adsorption Distance ($h$) between the O Atom of Heptanal and the Nearest C Atom of Pristine Graphene after Heptanal Adsorption for H, T, and B Adsorption Sites

| adsorption site | $E_{ad}$ (eV) | $h$ (Å) |
|-----------------|---------------|---------|
| hollow (H)      | −0.015        | 3.756   |
| top (T)         | 0.004         | 3.346   |
| bridge (B)      | −0.009        | 3.459   |
and protruded out of the graphene sheet, as shown in Figure 4. The TM atoms’ protrusion out of the graphene structure and elongation of the TM-C bond length are due to the larger atomic radii of the TM atoms than carbon atoms. The bond lengths of the TM atoms and nearest neighboring C atoms in PdG, PtG, and AgG, and their corresponding bond angles were presented in Table 2. The measured TM–C bond lengths were 1.94, 1.94, and 2.14 Å for PdG, PtG, and AgG, respectively and these results are in good agreement with previous studies.45,48,49 Compared to Pd and Pt atoms, Ag–C shows the biggest bond elongation. The bond angles of the C–Pd–C, C–Pt–C, and C–Ag–C were found to be 88.9°, 90.3°, and 77.4° respectively. The lattice constants for PdG, PtG, and AgG were measured to be 10.06, 9.92, and 9.90 Å, respectively, increased from pristine graphene’s lattice constant of 9.86 Å, and PdG shows the largest increase.

The structural stability of the TM-doped graphene sheets was studied regarding the defect formation energy using eq 1. The defect formation energies were calculated to be 6.29, 6.28, and 8.96 eV for PdG, PtG, and AgG, respectively. While PdG and PtG resulted in similar defect formation energies, AgG produced the largest among them. Compared to the formation energy of a single C vacancy in the graphene sheet (7.5 eV),46 it is observed that the formation energies of the Pd, Pt in the graphene sheet are smaller, indicating that PdG and PtG can be easily formed.

To investigate the effects of the TM dopants on the electronic properties of pristine graphene, the band structures were calculated for PdG, PtG, and AgG, as plotted in Figure 7. It was observed that the band structures near the Fermi level of graphene change significantly after TM doping. The band gap of graphene was opened when doped with Pd or Pt, and the band gaps of PdG and PtG were found to be 0.293 and 0.221 eV, respectively, whereas AgG behaved as a metal with the valence band maximum (VBM) located near Γ point, and conduction band minimum (CBM) located at K point.

In order to study the heptanal adsorption behavior on TM-doped graphene sheet, heptanal was placed with the O atom above the TM dopants of graphene sheet. All structures were fully relaxed and the optimized configurations of the heptanal adsorbed TM-doped graphene systems were depicted in Figure 5. It was discovered that upon exposure to the TM-doped graphene, heptanal makes a bond through the O atom with TM dopants. Compared to heptanal adsorbed pristine graphene system which mostly retains its planarity, the adsorption of heptanal induces significant pulling and buckling in the TM-doped graphene sheet around the dopant sites, due to the interactions between heptanal and TM dopants. This was confirmed by measuring the changes of bond length of C–O in heptanal and TM-C in TM-doped graphene after

Table 4. Adsorption Energy ($E_{ad}$), the Adsorption Distance ($h$) between the O Atom of Heptanal and the Closest C or TM Atom of Graphene, Band Gap ($E_g$), and Recovery Time ($\tau$) for Heptanal-Adsorbed Pristine or TM-Doped Graphene Systems

| System          | $E_{ad}$ (eV) | $h$ (Å) | $E_g$ (eV) | $\tau$ (s) |
|-----------------|---------------|---------|------------|------------|
| pristine graphene | -0.015        | 3.756   | 0.010      | 1.79 × 10^{-12} |
| Pd-doped graphene  | -0.404        | 2.206   | 0.265      | 6.13 × 10^{-6}  |
| Pt-doped graphene  | -0.356        | 2.149   | 0.199      | 9.57 × 10^{-7}  |
| Ag-doped graphene  | -0.755        | 2.189   | 0.309      | 4.83 |

To be a reliable sensor, the electrical properties of the sensor need to be altered upon the exposure of gas molecules, in addition to having an acceptable adsorption energy. Electronic band structures of pristine graphene before and after heptanal adsorption were presented in Figures 7, parts a and b. It can be seen that, upon heptanal adsorption, the electronic band structure of pristine graphene remained almost unchanged near the Fermi level and the band gap was slightly increased from 0 to 0.010 eV. Based on eqs 5 and 6, it is concluded that pristine graphene has a low sensitivity toward heptanal due to the minor change in band gap.

The PDOS was also calculated after heptanal adsorption on pristine graphene. Figure 8a shows the PDOS plot of the O atom of heptanal with a neighboring C atom of pristine graphene. It can be seen that the hybridization of the O 2p orbital of heptanal and the C 2p orbital in pristine graphene is not obvious, indicating a weak interaction between heptanal and pristine graphene. The calculated results of band structure and PDOS are in good agreement with the obtained small value of adsorption energy for heptanal-adsorbed pristine graphene system.

### 3.2. Heptanal Adsorption on TM-Doped Graphene

In order to improve the sensing properties of pristine graphene, substitutional doping using TM atoms (Pd, Pt, and Ag) was adopted to modify the graphene sheet, as previous studies have demonstrated that substitutional doping to graphene sheet improved the adsorption of molecules.45,46,48,57 After one carbon atom in graphene was substituted by a transition metal atom, it was observed that optimized PdG, PtG, and AgG produced differences in their atomic structures, compared to the flat structure of pristine graphene. Pd, Pt and Ag atoms deformed the six-membered ring (6MR) near the doping site

**Figure 4.** Top and side views of optimized atomic structures of (a) Pd-doped graphene, (b) Pt-doped graphene, (c) Ag-doped graphene. C, Pd, Pt, and Ag atoms are represented by gray, blue, yellow, and green, respectively.
heptanal adsorption. The average bond lengths of Pd–C, Pt–C, and Ag–C were elongated after heptanal adsorption and were measured to be 1.96, 1.97, and 2.29 Å, respectively. The bond length of Ag–C showed the largest increase of 7%. This implies that there is attraction between TM atoms of graphene and O atom of heptanal. The adsorption distance between TM atoms and O atom in heptanal were measured and presented in Table 4. In PdG and PtG, heptanal remained on top of the TM atoms of graphene sheet, with the adsorption distances of 2.206 and 2.149 Å, respectively. While in AgG, heptanal adopted a tilted orientation and moved away from the Ag atom of the graphene sheet with an adsorption distance of 2.189 Å. The adsorption distances of heptanal on all TM-doped graphene sheets were dramatically decreased from pristine graphene (3.576 Å).

It was observed that TM-doped graphene systems significantly increased the adsorption energies of heptanal compared to pristine graphene. The adsorption energies of heptanal were calculated to be $-0.404$, $-0.356$, and $-0.755$ eV respectively, for PdG, PtG, and AgG, as illustrated in Table 4. Among the three TM-doped graphene systems, AgG shows the most negative adsorption energy, indicating the best adsorption system for heptanal. Bigger adsorption energies and significantly reduced adsorption distances indicate much stronger adsorption of heptanal on PdG, PtG, and AgG, compared to PG. Using the eq 4, in visible light and at room temperature, the recovery times of heptanal-adsorbed PdG, PtG, and AgG systems were estimated to be $6.13 \times 10^{-6}$, $9.57 \times 10^{-7}$, and $4.83$ s, respectively, as illustrated in Table 4. These short recovery times indicate that all TM-doped graphene are suitable for the reversible detection of heptanal.

The charge transfer of heptanal adsorbed TM-doped graphene sheets were calculated in order to further study the adsorption properties of heptanal. As shown in parts b–d of Figure 6, the yellow and blue regions overlap significantly, indicating the exchange of electrons between heptanal and TM-doped graphene sheet, and strong chemisorptions are observed. It can be seen that the electron accumulations are mainly between the O atom of heptanal and the TM dopants, indicating covalent characteristics for the interactions between heptanal and TM-doped graphene.

To investigate the effects of heptanal adsorption on the electronic properties of TM-doped graphene, the electronic band structures and PDOS of PdG, PtG, and AgG after heptanal adsorption were calculated and analyzed. Parts d, f, and h of Figure 7 showed the band structures of PdG, PtG, and AgG after heptanal adsorption. It was noted that both of the band gaps of PdG and PtG were slightly decreased from 0.293 to 0.265 eV for PdG, and from 0.221 to 0.199 eV for PtG, after heptanal adsorption. From Figure 7, it can be seen that the effect of heptanal adsorption has little impact on the band structure of PdG and PtG. In the case of heptanal adsorption on AgG, the band structure was changed significantly from the metallic nature before heptanal adsorption to a band gap of 0.309 eV. From the eq 5, it is concluded that the band gap ($E_g$) is a key factor determining the electrical conductivity of a substrate, and the conductivity is correlated with the negative value of $E_g$ exponentially. So, with a fixed temperature, even a small change in band gap causes considerable change in electrical conductivity. Based on this, the PdG and PtG systems are expected to be more conductive after heptanal adsorption due to the decrease in their band gaps. Based on the eq 6, it is obvious that the sensitivity would increase from PG due to the changes in conductivity. Hence, the sensitivities of PdG, PtG, and AgG are significantly increased from PG, and AgG shows the highest sensitivity toward heptanal.

The PDOS after heptanal adsorption on TM-doped graphene were analyzed in order to investigate the interactions between heptanal and TM-doped graphene. Figures 8b, c, and d showed the PDOS plots of the interacting oxygen atom of heptanal with the TM atoms of the TM-doped graphene sheets. Compared to PG, the PDOS of TM-doped graphene...
systems show more peaks. In PdG, it is observed that there are overlapping peaks around $-3.2$, $0.5$, and $2.0$ eV between O 2p and Pd 4d orbitals, showing strong hybridization. Similarly, the overlapping peaks around $-3.2$ and $1.0$ eV between O 2p and Pt 5d orbitals in PtG, and the overlapping peaks located around $-3.5$, $-0.2$, and $2.0$ eV between O 2p and Ag 4d orbitals in AgG were noticed. These indicate there are interactions between heptanal and TM-doped graphene sheets.

Figure 7. Band structures before and after heptanal adsorption on (a and b) pristine graphene, (c and d) Pd-doped graphene, (e and f) Pt-doped graphene, and (g and h) Ag-doped graphene, with the Fermi level set at zero.
during the adsorption process, which might be due to the formation of a bond between the TM atom in graphene and O atom in heptanal.

The obtained results of adsorption energies, recovery time, charge transfer, band structures and PDOS suggest that the TM-doped graphene has the potential to be an effective sensor to detect heptanal reversibly. Among all TM-doped graphene, Ag-doped graphene could be the most promising candidate to be a highly sensitive gas sensor for heptanal detection.

4. CONCLUSION

In summary, by using first-principles calculations based on density functional theory, the adsorption behavior of heptanal on pristine and TM- (Pd-, Pt-, and Ag-) doped graphene were investigated. The electronic properties of TM-doped graphene presented dramatic changes after heptanal adsorption, compared to pristine graphene. The obtained results of the adsorption distance, adsorption energy, and charge transfer indicated that heptanal was weakly adsorbed on pristine graphene while strongly adsorbed on TM-doped graphene. Because of the moderate adsorption energies, the calculated recovery times for TM-doped graphene were very short which implied that they are suitable to be used as reversible sensors. Considering the calculated results for electronic properties, recovery time, and sensitivities, it can be concluded that Pd-, Pt-, and Ag-doped graphene are potential candidates as gas sensors for heptanal detection, and Ag-doped graphene is the most promising one.

Figure 8. Projected density of states after heptanal adsorption on (a) pristine graphene, (b) Pd-doped graphene, (c) Pt-doped graphene, and (d) Ag-doped graphene, with the Fermi level set to 0 and indicated by the green dashed lines. The red, violet, blue, cyan, and turquoise lines represent the O-2p orbital, C-2p orbital, Pd-4d orbital, Pt-5d orbital, and Ag-4d orbital, respectively.

AUTHOR INFORMATION

Corresponding Author
Xuan Luo — National Graphene Research and Development Center, Springfield, Virginia 22151, United States; Phone: +001 (202)384-5595; Email: xluo@ngrd.org

Author
Anthony Zhu — National Graphene Research and Development Center, Springfield, Virginia 22151, United States; orcid.org/0000-0003-2816-865X

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.jpckb.1c09580

Notes
The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We would like to thank Dr. Geifei Qian for providing the technical assistance for this study. There was no financial support received for this study.

REFERENCES

(1) Hu, B.; Guo, H.; Zhou, P.; Shi, Z.-L. Characteristics of SARS-CoV-2 and COVID-19. Nat. Rev. Microbiol. 2021, 19, 141–154.
(2) El Zowalaty, M. E.; Järhult, J. D. From SARS to COVID-19: A Previously Unknown SARS - related Coronavirus (SARS-CoV-2) of Pandemic Potential Infecting Humans-Call for a One Health Approach. One Health 2020, 9, 100124.
(3) Lai, C.-C.; Shih, T.-P.; Ko, W.-C.; Tang, H.-J.; Hsueh, P.-R. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
and Coronavirus Disease-2019 (COVID-19): The Epidemic and the Challenges. Int. J. Antimicrob. Agents 2020, 55, 105924.

(4) Giovannini, G.; Haick, H.; Garoli, D. Detecting COVID-19 from Breath: A Game Changer for a Big Challenge. ACS Sens 2021, 6, 1408–1417.

(5) Berna, A. Z.; Akaho, E. H.; Harris, R. M.; Congdon, M.; Korn, E.; Neher, S.; M’Farrej, M.; Burns, J.; Odom John, A. R. Reproducible Breath Metabolite Changes in Children with SARS-CoV-2 Infection. ACS Infect. Dis 2021, 7, 2596–2603.

(6) Li, X.; Li, J.; Ge, Q.; Du, Y.; Li, G.; Li, W.; Zhang, T.; Tan, L.; Zhang, R.; Yuan, X.; et al. Detecting SARS-CoV-2 in the Breath of COVID-19 Patients. Front. Med. 2021, 8, 210.

(7) Davis, C. E.; Schivo, M.; Kenyon, N. J. A Breath of Fresh Air - the Potential for COVID-19 Breath Diagnostics. EBioMedicine 2021, 63, 103183.

(8) Aghaei, S.; Aasi, A.; Farhangdoust, S.; Panchapakesan, B. Graphene-like BC6N nanosheets are Potential Candidates for Detection of Volatile Organic Compounds (VOCs) in Human Breath: A DFT Study. Appl. Surf. Sci. 2021, 536, 147756.

(9) Das, S.; Pal, M. Review—Non-Invasive Monitoring of Human Health by Exhaled Breath Analysis: A Comprehensive Review. J. Electrochem. Soc. 2020, 167, 037562.

(10) Park, C. H.; Schroeder, V.; Kim, B. J.; Swager, T. M. Ionic Liquid-Carbon Nanotube Sensor Arrays for Human Breath Related Volatile Organic Compounds. ACS Sens 2018, 3, 2423–2437.

(11) Lukman Hekiem, N. L.; Md Raili, A. B.; Mat Hattar, M. A.; Ahmad, F. B.; Nordin, A. N.; Rahim, R. A.; Za’bah, N. F. Advanced Vapour Sensing Materials: Existing and Latent to Acoustic Wave Sensors for VOCs Detection as the Potential Exhaled Breath Biomarkers for Lung Cancer. Sens. Actuators, B 2021, 329, 112792.

(12) Srushy, P.; Nagarajan, V.; Chandiramouli, R. Interaction Studies of Kidney Biomarker Volatiles on Black Phosphorene Nanoring: A First-principles Investigation. J. Mol. Graphics Modell. 2020, 97, 107566.

(13) Srimathi, U.; Nagarajan, V.; Chandiramouli, R. Germanane Nanosheet as a Novel Biosensor for Liver Cirrhosis Based on Adsorption of Biomarker Volatiles - A DFT Study. Appl. Surf. Sci. 2019, 475, 990–998.

(14) Majidi, R.; Nada'fan, M. Application of Nitrogenated Holey Graphene for Detection of Volatile Organic Biomarkers in Exhaled Breath of Humans with Chronic Kidney Disease: A Density Functional Theory Study. J. Comput. Electron. 2021, 20, 1930–1937.

(15) Ruskiewicz, D. M.; Sanders, D.; O’Brien, R.; Hempel, F.; Reed, M. J.; Riepe, A. C.; Bailie, K.; Brodrick, E.; Darnley, K.; Ellerkem, R.; et al. Diagnosis of COVID-19 by Analysis of Breath with Gas Chromatography-ion Mobility Spectrometry - A Feasibility Study. EClinicalMedicine 2020, 29–30, 100609.

(16) Miller, T. C.; Morgera, S. D.; Saddow, S. E.; Takshi, A.; Mularkey, M.; Palm, M. Neural Connections and Endogenous Biochemistry - Potentially Useful in Electronic-nose Diagnostics for Coronavirus Diseases. Neuroinmunol. Neuroinflammation 2021, 8, 284–296.

(17) Dewulf, J.; Van Langenhove, H.; Wittmann, G. Analysis of Volatile Organic Compounds Using Gas Chromatograph. TrAC Trends Anal. Chem. 2002, 21, 637–646.

(18) Galstyan, V.; D’Arco, A.; Di Fabrizio, M.; Poli, N.; Lupi, S.; Comini, E. Detection of Volatile Organic Compounds: From Chemical Gas Sensors to Terahertz Spectroscopy. Rev. Anal. Chem. 2021, 40, 33–57.

(19) Konvalina, G.; Haick, H. Sensors for Breath Testing: From Nanomaterials to Comprehensive Disease Detection. Acc. Chem. Res. 2014, 47, 66–76.

(20) Wilson, A. D. Noninvasive Early Disease Diagnosis by Electronic-Nose and Related VOC-Detection Devices. Biosens 2020, 10, 73.

(21) Zhang, L.; Khan, K.; Zou, J.; Zhang, H.; Li, Y. Recent Advances in Emerging 2D Material-Based Gas Sensors: Potential in Disease Diagnosis. Adv. Mater. Interfaces 2019, 6, 1901329.
Viruses: A Perspective in View of COVID-19. Carbon Trends 2021, 2, 100011.

(41) Torrente-Rodríguez, R.; Lukas, H.; Tu, J.; Min, J.; Yang, Y.; Xu, C.; Rossiter, H.; Gao, W. SARS-CoV-2 RapidPlex: A Graphene-based Multiplexed Telemedicine Platform for Rapid and Low-Cost COVID-19 Diagnosis and Monitoring. Matter 2020, 3, 1981–1998.

(42) Mallakpour, S.; Azadi, E.; Hussain, C. M. Fight Against COVID-19 Pandemic with the Help of Carbon-based Nanomaterials. New J. Chem. 2021, 45, 8832–8846.

(43) Wang, W.; Zhao, X.; Ren, J. Electronic Structure and Optical Properties of B- or N-doped Graphene Adsorbed Methanol Molecule: First-principles Calculations. J. Optoelectron. Adv. Mater. 2021, 23, 72–78.

(44) Zhou, X.; Zhao, C.; Wu, G.; Chen, J.; Li, Y. DFT Study on the Electronic Structure and Optical Properties of N, Al, and N-Al Doped Graphene. Appl. Surf. Sci. 2018, 459, 354–362.

(45) Li, Y.; Sun, X.; Zhou, L.; Ning, P.; Tang, L. Density Functional Theory Analysis of Selective Adsorption of AsH3 on Transition Metal-doped Graphene. J. Mol. Model. 2019, 25, 145.

(46) Shukri, M.; Saimin, M.; Yaakob, M.; Yahya, M.; Taib, M. Structural and Electronic Properties of CO and NO Gas Molecules on Pd-doped Vacancy Graphene: A First Principles Study. Appl. Surf. Sci. 2019, 494, 817–828.

(47) Ma, F.; Zhang, Z.; Jia, H.; Liu, X.; Hao, Y.; Xu, B. Adsorption of Cysteine Molecule on Intrinsic and Pt-doped Graphene: A First-principle Study. J. Mol. Struct.: THEOCHEM 2010, 955, 134–139.

(48) Lee, Y.; Lee, S.; Hwang, Y.; Chung, Y.-C. Modulating Magnetic Characteristics of Pt Embedded Graphene by Gas Adsorption (N2, O2, NO2, SO2). Appl. Surf. Sci. 2014, 289, 445–449.

(49) Ma, L.; Zhang, J.-M.; Xu, K.-W.; Ji, V. A First-principles Study on Gas Sensing Properties of Graphene and Pd-doped Graphene. Appl. Surf. Sci. 2015, 343, 121–127.

(50) Nesbet, R. K. Reference-State Density Functional Theory. J. Phys. Chem. 1996, 100, 6104–6106.

(51) Perdew, J. P.; Burke, K.; Emnerzhof, M. Generalized Gradient Approximation Made Simple. Phys. Rev. Lett. 1996, 77, 3865–3868.

(52) Gonze, X.; Amadon, B.; Anglade, P.-M.; Beuken, J.-M.; Bottin, F.; Boulanger, P.; Bruneval, F.; Caliste, D.; Caracas, R.; Cote, M.; et al. ABINIT: First-principles Approach of Materials and Nano-system Properties. Comput. Phys. Commun. 2009, 180, 2582–2615.

(53) Blochl, P. Projector Augmented-wave Method. Phys. Rev. B 1994, 50, 17953–17979.

(54) Holzwarth, N. A. W.; Tackett, A. R.; Matthews, G. E. A Projector Augmented Wave (PAW) Code for Electronic Structure Calculations, Part I: atompaw for Generating Atom-centered Functions. Comput. Phys. Commun. 2001, 135, 329–347.

(55) Head, J. D.; Zerner, M. C. A Broyden–Fletcher–Goldfarb–Shanno Optimization Procedure for Molecular Geometries. Chem. Phys. Lett. 1985, 122, 264–270.

(56) Pitt, I. G.; Gilbert, R. G.; Ryan, K. R. Application of Transition-State Theory to Gas-Surface Reactions: Barrierless Adsorption on Clean Surfaces. J. Phys. Chem. 1994, 98, 13001–13010.

(57) Zhang, J.-N.; Ma, L.; Zhang, M.; Zhang, J.-M. Effects of Gas Adsorption on Electronic and Optical Properties of Palladium-doped Graphene: First-principles Study. Physica E Low Dimens. Syst. Nanostruct. 2020, 118, 113879.

(58) Aasi, A.; Mehdi Aghaei, S.; Panchapakesan, B. Outstanding Performance of Transition-Metal-Decorated Single-Layer Graphene-like BC3N Nanosheets for Disease Biomarker Detection in Human Breath. ACS Omega 2021, 6, 4696–4707.

(59) Schwierz, F. Graphene Transistors. Nat. Nanotechnol. 2010, 5, 487–496.

(60) Banhart, F.; Kotakoski, J.; Krasheninnikov, A. V. Structural Defects in Graphene. ACS Nano 2011, 5, 26–41.