Optimization of the Urea Removal in a Wearable Dialysis Device Using Nitrogen-Doped and Phosphorus-Doped Graphene

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ABSTRACT: Dialysis has been recognized as an essential treatment for end-stage renal disease (ESRD). This therapy, however, suffers from several limitations leading to numerous complications in the patients. As dialysis cannot completely substitute healthy kidney functions, the health condition of an ESRD patient is ultimately affected. Wearable artificial kidney (WAK) can resolve the restrictions of blood purification by the dialysis method. However, absorbing large amounts of urea produced in the body is one of the main challenges of these WAK and overcoming this is necessary to improve both functionality and footprint of the device. This study investigates the adsorption capabilities of N- and P-doped graphene nanosorbents for the first time by using molecular dynamic simulation. Urea removal on carbon nanosheets was simulated with different percentages of phosphorus and nitrogen dopants along with the pristine graphene. Specifically, the effects of interaction energy, adsorption percentage, gyration radius, hydrogen bonding, and other molecular dynamic analyses on urea removal were also investigated. The results from this study match well with the existing research, demonstrating the accuracy of the model. The results further suggest that graphene nanosheets doped by 10% nitrogen are likely the most effective in removing urea given that it is associated with the maximum radial distribution function (RDF), the maximum reduction in gyration radius, a high number of hydrogen bonds, and the most negative adsorption energy. This molecular study offers attractive suggestions for the novel adsorbents of artificial kidney devices and paves the way for the development of novel and enhanced urea adsorbents.

1. INTRODUCTION

The kidneys are responsible for balancing the minerals, organic substances, and electrolytes within the blood as well as removing wastes. Kidney-related diseases are prevalent and as much as 10% of the world’s population suffers from renal disorders.1 The end-stage renal disease (ESRD) for example is a common kidney disorder that is affecting more than 3 million people. The ESRD is the final stage of chronic kidney failure (CKD) where more than 90% of the renal function is lost.2–6

Urea is one of the organic substances produced in the body during the oxidation of amino acids. Urea is a common source of nitrogen and the purification of the blood nitrogen is one of the main functions of the kidneys. The concentration of urea increases when the kidney stops functioning and excessive urea disrupts homeostasis, which can be life-threatening.7 In CKD patients who are suffering from ESRD, reduction in renal function predisposes these patients for kidney transplantation or hemodialysis. Hemodialysis is costly and is aggravated by the need to undertake this treatment regularly given that a single treatment is only equivalent to 9–12 h of kidney function.8–11 Therefore, wearable hemodialysis devices are extremely appealing for ESRD patients (Figure 1) as they not only enable dialysis to be performed more conveniently but also the fact that patients can undertake treatment regularly, which means that it will potentially reduce the health service burden of dialysis centers and hospitals.12–16

Urea hydrolysis is distinguished by two key stages. In the first stage, urea is converted to ammonia and carbamate and in the second stage, carbamate is decomposed into ammonia and carbon dioxide in an aqueous environment. Existing dialysis machines use large quantities of enzymes to break down the urea molecule, which is unfeasible for WAK. The use of nanostructures to adsorb blood urea is an attractive alternative to remove urea, which will also help in reducing the weight and volume of WAK machines.12–16 Urea adsorption by mesoporous silica (MS) and activated carbon fiber (ACF)
The aim of the present study is to investigate urea adsorption on single-layer graphene particles in the presence of various amounts of N and P dopants using molecular dynamics simulation for the first time with the goal of providing insight into the experimental configuration needed to optimize the adsorption capabilities of graphene. To do this, urea and adsorbent molecules were placed in a 6 nm cubic box that was filled with water molecules. Then, the simulation was conducted on the interaction between urea and the adsorbent. Urea adsorption was investigated through radial distribution function (RDF), number of hydrogen bond (H-bond), root-mean-square deviation (RMSD), energy analysis and the gyration radius analysis.

2. RESULTS AND DISCUSSION

The aim of the simulation was to investigate the effects of nitrogen and phosphorus dopants in graphene design configurations on urea adsorption. To investigate the effect of nitrogen content, different amounts of carbon atoms were randomly replaced by nitrogen as shown in Figure 2. The design configurations are as follows: N2 (2% of carbon atoms were replaced by nitrogen atoms), N5 (nitrogen atom replaced 5% of carbon atoms), N8 (nitrogen atom replaced 8% of carbon atoms), N10 (nitrogen atoms replaced 10% of carbon atoms), N15 (nitrogen atoms replaced 15% of carbon atoms), PC (50% of the carbons have been replaced by phosphorus atoms) and pristine graphene.

2.1. Validation. In order to validate the simulations, a similar valid article was regarded as the reference work. To this end, the work by Zhang et al.38 was considered in which the phenol and water solutions were studied in the presence of oxidized nanotubes by performing a MD simulation that is in line with our present study with respect to molecular structures, force fields and the details of the simulation systems (in spite of the differences in concept and application). So, the reported method was repeated to check the validity of our systems, where the similar results between our work and the reference can verify the validity of our systems and it can generalize our simulation method. In the reference work, the simulation was carried out on 5424 water molecules along with the 70 urea molecules and adsorbent, in which the OPLSAA force field was adopted in Gromacs software and the RDF analysis was reported. Here, the BCN tube and GO structure were resimulated in accordance with details of the reference work including the dimensions of the box, the simulation time, and the molecular structures. For this purpose, a system
containing 70 phenol molecules and 5500 water molecules and two adsorbents in a $6 \times 6 \times 5 \text{ nm}^3$ box was again modeled and simulated. The comparison between the results acquired from both works as presented in Figure 3 indicates that our results are in good agreement with those reported by Zhang et al.\footnote{Zhang et al.} From these points, it is inferred that the system proposed in the current work is valid so that the other methods employed here are generally verified.

Urea adsorption was analyzed by comparing the initial and final simulation images by image processing software\footnote{VMD software; COUNTRY}. The accumulation of urea molecules around the adsorbent indicates the absorption of urea molecules. For confirmation of the urea adsorption by these adsorbents, the coordinates of molecules are shown at the beginning and end of the simulation. The initial and final images of the N2 simulation are depicted in Figure 4a. Urea molecules concentrated around the N2 adsorbent after 10 ns indicate the successful urea adsorption and the fact that an appropriate interaction energy occurs between urea and N-doped graphene nanosheets. The initial and final images of the N5 simulation are shown in Figure 4b. It is observed that the urea molecules concentrated around the N5 adsorbent after 10 ns, which again verifies the successful adsorption of urea molecules. The similar images for other adsorbents are given in Figure 4c–g, from which it is seen that all considered adsorbents were relatively effective in urea adsorption. The high-quality figures of urea adsorption at the end of simulation are shown in Figure 5. However, the detailed energy analysis will determine the most active sorbent.

The images alone are not sufficient indicators of the urea adsorption. Other analyses, such as RDF, gyration radius, and energy analysis should also be used to assess the intensity of urea adsorption. Before investigating the intensity of urea adsorption, the stability of simulated systems was compared using RSMD analysis.

### 2.2. RMSD Analysis

RMSD is used to determine the particle deviation to ascertain the stability of the simulation where instability is indicated by the number of peak occurrences in the RMSD diagrams. RMSD is defined by the following equation:

$$\text{RMSD} = \sqrt{\frac{1}{M} \sum_{i=1}^{M} (p_i(t) - p_r(t))^2}$$

where $M$ is the number of atoms, $p_i(t)$ is the position of an atom $i$ at time $t$, and $p_r(t)$ is the position of reference atom at time $t$. In a stable simulation, the small changes can be seen in the RMSD diagram.\footnote{The RMSD diagrams for the adsorbent nanosheets performed in this study are shown in Figure 6a–c. The results showed that the absorbent N2 had more fluctuations compared to N15 and N10 (Figure 6d,e). The absorbent N10 demonstrated seemingly less RMSD fluctuations and the range of RMSD fluctuations exhibited by this absorbent is also less compared to N15, which suggested that N10 is more stable than N15 based on the simulation. Figure 6f and g show the RMSD diagrams of PC and graphene simulations. There were more fluctuations in RMSD for the graphene simulation than the PC simulation. Figure 6e, b, and f show the RMSD diagrams of N10, N5, and PC, respectively. The RMSD chart for N10 has less fluctuations than the simulations of N5 and PC, and this suggests that the urea adsorption by N10 was more stable than the other two simulations.}

### 2.3. Hydrogen Bond Analysis

Hydrogen bonds can be formed between hydrogen atoms and highly electronegative atoms (such as oxygen, nitrogen, or fluorine) and also between different molecules. The hydrogen bond is weaker than the covalent and ionic bonds; however, it is stronger than the van der Waals force. The hydrogen bond can be analyzed using the Hydrogen Bond Network in VMD software. The Hydrogen Bond Network analysis was performed to determine the number and strength of hydrogen bonds formed during the simulation. The analysis showed that the number of hydrogen bonds was highest for N10, followed by N5 and N2. The hydrogen bond density also showed that N10 had the highest density, followed by N5 and N2. The hydrogen bond analysis was performed using the following steps:

1. Load the trajectory file into VMD software.
2. Analyze the trajectory file using the Hydrogen Bond Network tool.
3. The hydrogen bond network analysis was performed for all considered adsorbents, as shown in Figure 6a–c. The results showed that the absorbent N2 had more hydrogen bonds compared to N15 and N10 (Figure 6d,e). The absorbent N10 demonstrated seemingly less hydrogen bond fluctuations and the range of hydrogen bond fluctuations exhibited by this absorbent is also less compared to N15, which suggested that N10 is more stable than N15 based on the simulation. Figure 6f and g show the Hydrogen Bond Network diagrams of PC and graphene simulations. There were more fluctuations in Hydrogen Bond Network for the graphene simulation than the PC simulation. Figure 6e, b, and f show the Hydrogen Bond Network diagrams of N10, N5, and PC, respectively. The Hydrogen Bond Network chart for N10 has less fluctuations than the simulations of N5 and PC, and this suggests that the urea adsorption by N10 was more stable than the other two simulations.
The number of hydrogen bonds in simulation suggests that there were more interactions between molecules as well as the higher tendency to attract between the substances. Thus, the number of hydrogen bonds created between the urea and the adsorbent is an indicator of the urea adsorption efficiency. Under proper conditions, the amine functional group can form hydrogen bonds via the hydrogen attached to the amine group. The N-doped adsorbents possessed N atoms which can form hydrogen bonds. Due to the presence of an amine group in the urea molecular structure, hydrogen bonding is hence possible between the amine group and the adsorbent. The numbers of hydrogen bonds created during the simulation for N8, N5, and N2 adsorbents were 0.572427572, 0.417582418, and 0.054945055, respectively (Table 1). The number of hydrogen bonds in PC and graphene adsorption simulations were 0 and 0, respectively (Table 1). Fluorine, oxygen and nitrogen atoms were not present in the molecular structure of the PC adsorbent.

The results of energy analysis for multiple component environments are shown in Figure 7. This figure illustrates the average hydrogen bonds between urea and different two-dimensional nanosheets (2D), urea/water and also water/nanosheets. As shown, in all percentages of N dopants, the hydrogen bonds between water and urea and also water and nanosheets are lower than the hydrogen bonds between urea and nanosheets. This means that the interaction between urea and nanosheets are stronger than interactions between urea and water and as a result, urea tends to be adsorbed on the nanosheet. The number of hydrogen bonds in N15 simulation was greater than in other systems, and also the hydrogen bonds between urea and water is lower than between urea and N15, implying stronger hydrogen interactions between N15 molecules and the urea molecules. Hydrogen bonds are not the only intermolecular bonds. The combination of van der Waals and electrostatic bonds may compensate for the lack of hydrogen bonding.

2.4. Analysis of the Gyration Radius. The gyration radius is one of the measures for studying the adsorption of different materials. It indicates the particle density around its center of gravity. The radius of gyration is defined as eq 2:

\[ R_g = \sqrt{\frac{\sum_{i=1}^{N} r_i^2 m_i}{\sum_{i=1}^{N} m_i}} \]  

where \( N \) is the number of particles, \( r_i \) is the distance of particle \( i \) from the center of gravity, and \( m_i \) is the mass of particle \( i \). Therefore, a final gyration radius that is less than the initial gyration radius suggest that the simulated material would have been compacted during the process. Figure 8 shows reduction in gyration radius, which may represent a urea condensation reaction. During the adsorption process, the density of the adsorbed material around the center of gravity is higher. Hence, a smaller final gyration radius of the urea when compared to the initial gyration radius could suggest that more urea would be absorbed.

The difference between the initial and final gyration radius of urea for the N2, N5, and N8 simulations is shown in Table 2. The gyration radius in the model with N2 simulation is larger than its initial gyration radius. Assuming that the distribution of urea molecules is homogeneous, the difference between the initial and final gyration radius of simulations could be used to infer the density change of urea molecules. While the urea density decreased in N2 simulation, it was increased in both N5 and N8 simulations. The increase in urea density has been greater in the N8 simulation. Analysis of the gyration radius indicated a better urea adsorption by N8 than the samples possessing lower amount of N. The final gyration radius in both simulations was reduced compared to their initial gyration radius. In both simulations of N10 and N15, the...
urea density showed an increment. The difference between the initial and final gyration radius in the N10 simulation was greater, implying that the urea adsorption was more common in N10 simulation. The difference between the initial and final gyration radius of the graphene and PC in Table 2 clariﬁes that the final gyration radius in both simulations was increased compared to their initial gyration radius. The increased rate of the final gyration radius in the PC simulation was lower. The urea adsorption condition was much better in PC simulation than in the pristine graphene. Figure 9 demonstrates the difference between the initial and final gyration radius in all simulations. The N-doped graphene provided better conditions for urea adsorption than the pristine graphene. The greater difference between the initial and final gyration radius in the N10 simulation implies a higher urea density and, accordingly, more urea adsorption by N10.

2.5. Energy Analysis. Energy in molecular dynamics simulations may help in investigating and analyzing the van der Waals and electrostatic bonds. The greater (i.e., more negative) the absolute energy of the van der Waals and the electrostatic bonds, the stronger the interactions in a given reaction simulation. The total energy of the van der Waals and electrostatic bonding is also an indicator of the urea adsorption intensity. Strong interactions between the adsorbent and urea may hence be associated with higher capabilities in urea adsorption. Here, the energy analysis was carried out by the mmpbsa software. The van der Waals and electrostatic energies were calculated for N2, N5, N8, N15, N10, PC, and pristine graphene. The sum of the energies was also averaged.

Table 1. Number of Hydrogen Bonds Formed between Different Adsorbents and Urea Molecules

| adsorbent | N2     | N5     | N8     | N10    | N15    | PC     | graphene |
|-----------|--------|--------|--------|--------|--------|--------|----------|
| average of hydrogen bond values | 0.054945055 | 0.41758242 | 0.572427572 | 0.597472527 | 0.789210789 | 0 | 0 |
during the simulation period. The average energies for the N2, N5, and N8 simulations are $-591.272015$, $-606.1158571$ and $-641.3748651$ kJ/mol (Table 3), respectively. The absolute value of the vdW energy of the N8 simulation was greater, indicating the stronger vdW interactions between urea and the N8 adsorbent than the nanosheets containing lower amounts of nitrogen. The electrostatic energy values between urea and N2, N5, and N8 adsorbents were $-3.823256743$, $-8.121240759$, $-19.66176124$ kJ/mol (Table 3), respectively. The combination of electrostatic and vdW energies is the best indicator of the adsorption intensity. These parameters were $-595.0952717$, $-614.2370979$, and $-661.0366264$ kJ/mol (Table 3) for N2, N5, and N8 samples, respectively. The absolute energy of N8 simulation was more favorable, suggesting the positive effect of increasing the dopant concentration. The further increase in the N dopant contents brought about the van der Waals energy values of $-682.2845325$ and $-545.5910649$ kJ/mol for N10 and N15, respectively (Table 3). Thus, the optimum amount was obtained for the N dopant amount in N10 and the further increase resulted in deterioration of the vdW energy. The energy magnitude of the electrostatic interactions between urea and N10 and N15 adsorbents were $-36.49498801$ and $-93.95795704$ kJ/mol, respectively (Table 3). The total energies for N10 and N15 were $-718.7795205$ and $-639.549022$ kJ/mol, respectively (Table 3). Thus, N10 exhibited a higher absolute energy, implying its stronger interactions with urea and hence more urea adsorption through vdW and electrostatic interactions.

The vdW energy values of PC and graphene were $-545.6664076$ and $-555.6746294$ kJ/mol, respectively (Table 3). In addition, the energy magnitude of the electrostatic interactions between urea and PC or graphene adsorbents were $-22.969921$ and 0 kJ/mol, respectively. Also, the total energies for PC and graphene were $-568.6363287$ and $-555.6746294$ kJ/mol, respectively. The PC exhibited a more negative absolute energy compared to the pristine graphene, implying the impact of the P dopant on improving the interaction energy compared to the pristine graphene. However, the N-doped nanosheets outperformed the P-doped samples and could have an outstanding influence on the interaction energy of the graphene, ameliorating the urea adsorption.

Also, Figure 10a shows the total interaction energy between urea and nanosheets, urea/water and also water/nanosheets. As shown, the total energy analysis revealed that the total energy between urea and nanosheets is stronger than van der Waals and electrostatic energy between urea and water and also water/nanosheets. So, it can be concluded that in competition between nanosheets and water molecules, the urea molecule is adsorbed on the nanosheet surface.

The average energy from the VDW and electrostatic bonds and the total simulation energy of urea adsorption by different nanoparticles are represented in Figure 10b. The N10 simulation exhibited a higher absolute VDW toward urea, suggesting its strongest interactions with urea and thus more urea adsorption through VDW bonds. The VDW bonds are not the only intermolecular bond, and the electrostatic bonds should be also considered in the determination of the most effective adsorbent. The absolute value of the electrostatic energy in N15 was higher than the other adsorbents, indicating its greater electrostatic interactions. The energy from VDW bonds predominated in all simulations. Most urea and nanoparticle bonds were of the VDW type. The mean value of the total VDW and electrostatic energies were considered as the basis for determining the best adsorbent. N10 showed a higher absolute energy toward urea, reflecting its strongest interaction with urea. On further interactions, the N10 simulation also caused more urea adsorption, so it is concluded that the N10 provided the best adsorption ability toward urea in terms of energy analysis. Interestingly, the total energy is not

![Figure 7. Average hydrogen bonds generated during simulation of different nanoparticles.](https://doi.org/10.1021/acsomega.1c05495)

![Figure 8. Densification of urea molecules by reducing the final radius of gyration.](https://pubs.acs.org/journal/acsodf)

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correlated with the amount of nitrogen dopants, for which there is an optimum value to maximize the urea adsorption. It was found that the further increase in N content worsens the VDW bonds and accordingly decreases the total energy.

2.6. RDF Analysis. The radial distribution function (RDF) analysis is the most important method to evaluate the intensity of an adsorption process. The RDF was investigated in systems comprising urea and N2, N5, N8, N10, N15, PC, and graphene adsorbents. This parameter shows the density of urea molecules around the adsorbent. The RDF diagrams are composed of two important parts. The first part includes a maximum intensity of urea molecule adsorption, while the second part indicates the particle density at greater distances from the adsorbent. In the second part, the RDF diagram reaches equilibrium. Upon the adsorption of urea by the adsorbents, urea molecules will condensate around doped graphene nanosheets. The radius at which the maximum RDF occurs is indicative of the distance of the adsorbed urea from the adsorbent. To investigate the intensity of urea adsorption, RDF diagrams of the adsorbents were evaluated. The RDF diagrams of N2, N5, and N8 are presented in Figure 11. The maximum RDF of N8 simulation was 13.445, while the maximum RDF values of N2 and N5 were determined as 12.53 and 12.872, respectively. The greater the maximum RDF of the N8 simulation indicates its higher urea adsorption within a radius of 0.5 nm reflecting more urea adsorption by this adsorbent compared to the N2 and N5.

The maximum RDF values of N10 and N15 adsorbents were 14.543 and 13.213, respectively. Figure 12 depicts the maximum RDF of N10 and N15 simulations in a radius of 0.5 nm. This diagram shows the urea accumulation at a distance of 0.5 nm from the adsorbent. The maximum RDF of N10 was greater than that of N15, indicating its higher urea adsorption.

The maximum RDF values of PC and graphene adsorbents were 11.943 and 11.5, respectively. Figure 13 depicts the maximum RDF of PC and graphene simulations in a radius of 0.5 nm. This diagram shows the urea accumulation at a distance of 0.5 nm from the adsorbent. The maximum RDF of PC was greater than that of the pristine graphene, indicating its higher urea adsorption.

Figure 14 presents the maximum RDF of N2, N5, N8, N10, N15, PC, and the pristine graphene obtained from the simulations within the radius 0.5 nm. Replacing carbon atoms with phosphorus and nitrogen atoms could amend the urea adsorption. N10 exhibited a higher RDF value and hence a stronger urea adsorption. The RDF analyses, gyration radius, and energy analyses were used to compare the adsorption capability of the proposed graphene-based nanoadsorbents. The results obtained from the RDF analysis were in line with the findings of the gyration radius and energy analyses. Overall, it is established that tuning the chemical nature of the graphene nanosorbents through doping can enhance the urea adsorption affinity significantly. This is strong evidence on the viability of incorporating dopants to develop novel urea adsorbents. In further works, the results presented here will be employed to synthesize efficient N-doped graphene-based nanosorbents for urea removal in accordance with guidelines of combinatorial materials science.

2.7. Gibbs Free Energy. Gibbs free energy is a thermodynamic quantity, which indicates the spontaneity degree of a reaction. The Gibbs free energy of the structures calculated by the umbrella simulation was also compared to accurately assess the stability and compare the urea adsorption affinity of the proposed engineered adsorbents. The lower Gibbs free energy indicates higher urea adsorption by the nanoparticles and reveals that the simulated particles would be in a more stable state. Table 4 shows the Gibbs free energy of the simulated systems. The Gibbs free energy of urea adsorption simulation in the presence of N8 was lower than that of the N2 and N5 adsorbents. Urea adsorption simulation in the presence of N8 provided a more stable condition. In addition, N8 could absorb more urea than N2 and N5 nanosheets. The Gibbs free energy of urea absorption simulation in the presence of N10 was less than that in N15 particles. The urea adsorption simulation in the presence of N10 reached more stable conditions than other adsorbents. The Gibbs free energy of urea absorption simulation in the presence of PC was also less than that of graphene but still much more than the N-doped nanosheets.

Table 3. Values of van der Waals, Electrostatic, and Total Energy of the Simulated Systems

| adsorbent | N2       | N5       | N8       | N10      | N15      | PC       | graphene |
|-----------|----------|----------|----------|----------|----------|----------|----------|
| total energy (kJ/mol) | -595.0952717 | -614.237098 | -661.036626 | -718.77952 | -639.549022 | -658.636329 | -555.67463 |
| van der Waals energy (kJ/mol) | -591.272015 | -606.115857 | -641.374865 | -682.284532 | -545.591065 | -545.666408 | -555.67463 |
| electrostatic energy (kJ/mol) | -3.823256743 | -8.12124076 | 19.6617612 | -36.494988 | -93.957957 | -22.969921 | 0 |

Figure 9. Difference between the initial and final gyration radius of the systems.
The Gibbs free energy analysis in presence of various modeled nanosheets is shown in Figure 15. The negative value
Table 4. Gibbs Energy Values for Simulations of Urea Adsorption in the Presence of Nanoparticles

| adsorbent | N2 | N5 | N8 | N10 | N15 | PC | graphene |
|-----------|----|----|----|-----|-----|----|-----------|
| ΔG (kJ/mol) | -6.3 | -7.2 | -8.5 | -11.5 | -8.1 | -6.7 | -5.6 |

Figure 15. Gibbs free energy diagram of simulations of urea in the presence of nanoparticles.

of Gibbs free energy in all simulations indicates the good affinity for urea adsorption by all nanoparticles. Urea particles were stable at the end of the simulation. Moreover, incorporating the N or P dopants into the graphene sheets reduced the Gibbs free energy. Urea adsorption simulation in the presence of N10 had the lowest Gibbs free energy, which is proposed as the best sorbent to absorb urea.

3. CONCLUSIONS

This paper evaluated the urea adsorption by seven different adsorbents which were modeled to optimize the graphene doping for urea adsorption. It was found that the N-doped nanosheets could form hydrogen bonds to amend the urea adsorption, which were lacking in P-doped and pristine graphene. The number of hydrogen bonds formed between N-doped nanosheets and urea was a function of N content. However, further analyses revealed that there is an optimum N dopant content to optimize the urea adsorption. The results clarified that the graphene nanosheets possessing 10% nitrogen could achieve the best performance in terms of total energy and adsorption energy. In addition, the RDF and RMSD analysis indicated that the N-doped nanosheet containing the optimum amount of nitrogen had a much better performance in urea adsorption. Overall, it was established that P and N doping of graphene nanosheets is an effective approach to tune and optimize the graphene-based nanosorbents to achieve the best performance in urea removal and accordingly enable enhanced dialysis, where the nitrogen dopants could bring about an extraordinary performance.

4. MATERIALS AND METHODS

4.1. Simulation Method. The graphene nanosheet structures were made by Nanotube_Modeler_1.7.9 software. In order to investigate the effect of dopants on adsorption characteristics, some carbon atoms were replaced by nitrogen and phosphorous atoms. The obtained structures were optimized based on the density functional theory method (B3LYP function and 6-31+g* basis set) using Gaussian 0975,76 software. The charge was also calculated based on esp charges population, which was then included in the topology file. The OPLSSA force field75,76 topologies of all materials were made by the x2top command and the calculated esp charges were placed in the topology. A 6 nm cube was designed as a simulation box that was filled with 80 urea and 6500 SPC/E water molecules and a modeled graphene-based nanosorbent.

The simulations were performed in four steps:

1) The simulation boxes were optimized to a minimum force of 100 kJ/mol within 50,000 steps, where the time steps were set to 1 fs.

2) The simulation box must then be thermally equilibrated. For this purpose, balancing the temperature (NVT) was performed using the V-rescale algorithm for a duration and temperature of 100 ps and 300 K, respectively.77–79

3) The pressure of the box was then balanced by NPT simulation using the parrinello-rahman algorithm at a duration and pressure of 100 ps and 1 bar, respectively.80–82

4) The final simulation was performed by the LINCS algorithm considering a H-bond limit. The cutoff radius was also set to 1.4 nm. The simulation was then run for 10 ns.

Furthermore, by using the Umbrella simulation, the Gibbs free energy changes were calculated. After completing the EM and NPT steps, the system was ready to simulate the Umbrella. A 5 × 5 × 20 nm simulation box was considered for performing the umbrella simulation. First, position restraining was carried out for nanoparticles. To conduct the Pull code step, an adsorbed urea molecule was pulled 10 nm in the Z direction. Then, 1000 configurations with a constant distance of 0.01 nm were extracted. Other simulations were performed on all extracted configurations for 5 ns. Next, the Gibbs free energy changes were obtained by performing the Weighted Histogram Analysis Method (WHAM) on all configurations.83

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