Title

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Abstract

1 Introduction

First synthesized in 2004 [14], graphene has since experienced an explosive growth in interest [17]. For pristine graphene, it's interactions with other particles are mainly due to Van der Waals forces and $\pi - \pi$ stacking. [26] As pristine graphene is chemically inert [6] a classical description of it is expected to suffice in simulations. Multiple molecular dynamics studies on the interactions between proteins and carbon based nanoparticles (CBNs) –such as graphene– have been published [1,4,5,7,8,13,16,22,25,26]

2 Methods

2.1 Free Energy Methods

The Helmholtz free energy of adsorption of an amino acid onto a graphene layer (ΔA_{ads}) can be obtained from the difference in free energy of the Adsorbed and Free states:

$$\Delta A^{ads} = A^{near} - A^{free} \tag{1}$$

Where the near and free states are defined based on the reaction coordinate $\xi(\mathbf{r})$. $\xi(\mathbf{r})$ depends on the coordinates of the system ($\mathbf{r}$) and is equal to the distance between the graphene layer and the $\alpha-$carbon of the amino acid projected onto a vector normal to the graphene layer. For a graphene layer prepared along the XY plane, this is equivalent to the distance along the Z–axis. The cut-off ranges for the near and far states will be defined based on the PMFs (potentials of mean force) along $\xi(\mathbf{r})$ of the amino acids, which can be found in the supplementary materials TODO.

The free energy of a state is related to the probability of the state via:

$$A^i = -k_B T \ln(p_i) \tag{2}$$

Where k_B is Boltzmann's constant and T is the temperature. Replacing Eq. (2) in Eq. (1) we get an expression to calculate the free energy of adsorption from the probabilities of the near and free states:

$$\Delta A^{ads} = -k_B T \ln(\frac{p_{near}}{p_{free}}) \tag{3}$$

If the PMF along ξ has been estimated for the discrete states $\{\xi_1, \xi_2, ..., \xi_N\}$, the probability of a state ξ_j can be estimated with:

$$p_{\xi_j} = \frac{e^{-\beta \text{ PMF}(\xi_j)}}{\sum_{i=1}^{N} e^{-\beta \text{ PMF}(\xi_i)}} \tag{4}$$

where β is the thermodynamic beta ($\frac{1}{k_B T}$). To estimate the probability of a state with multiple possible ξ values, the numerator is replaced with a sum over the individual values of ξ. In this way, the probabilities of the adsorbed and free states can be estimated with:

$$p_{near} = \frac{\sum_{j \in near} e^{-\beta \text{ PMF}(\xi_j)}}{\sum_{i=1}^{N} e^{-\beta \text{ PMF}(\xi_i)}} \tag{5}$$

$$p_{free} = \frac{\sum_{j \in free} e^{-\beta \text{ PMF}(\xi_j)}}{\sum_{i=1}^{N} e^{-\beta \text{ PMF}(\xi_i)}} \tag{6}$$

Replacing Eqs. (5) and (6) in Eq. (3) we have an expression to calculate the free energy of adsorption from a PMF of ξ, regardless of how the PMF was obtained:

$$\Delta A^{ads} = -k_B T \ln\left(\frac{\sum_{j \in near} e^{-\beta \text{ PMF}(\xi_j)}}{\sum_{k \in free} e^{-\beta \text{ PMF}(\xi_k)}}\right) \tag{7}$$

or, equivalently:

$$\Delta A^{ads} = -k_B T \ln\left(\frac{\sum_{j \in near} p_{\xi_j}}{\sum_{k \in free} p_{\xi_k}}\right) \tag{8}$$

On the following sections, two different methods used to obtain a PMF along ξ will be described.

2.1.1 Umbrella Sampling

Umbrella sampling [24] was used to obtain the PMF along reaction coordinate by sampling multiple windows of ξ. Each sample was obtained from a simulation where the Hamiltonian included the following potential:

$$\mathcal{V}^{US}(\mathbf{r}, k^{US}, \xi^0) = \frac{1}{2} k^{US} [\xi^0 - \xi(\mathbf{r})]^2 \tag{9}$$

where ξ^0 is the center of the sampling window and k^{US} is an harmonic constant. For simulations of amino acids over pristine graphene ξ^0 took values from 0.3 to 1.5 nm in 0.05 nm steps, while k^{US} took values from 1000 to 12000 $[kJ \cdot mol \cdot nm^2]$ adjusted to ensure a good overlap in the sampling of different windows while retaining a high sampling of the window's center.

The biased samples of ξ obtained from these windows were used to obtain the unbiased PMF using an implementation of the Weighted Histogram Analysis Method (WHAM) [11,12]

developed by Grossfield [9]. This implementation of WHAM outputs –in addition to the free energy/probability along ξ– the (dimensionless) free energy of each window, F_i. Knowing the F_i of every we can unbias our samples of any property T, to get an average for the window:

$$\langle T(\xi')\rangle = \frac{\sum_i^S \sum_j^{N_i} T_{i,j} e^{-\beta[F_i - \mathcal{V}^{US}(\mathbf{r_j})]} \delta\xi_{i,j}}{\sum_i^S \sum_j^{N_i} e^{-\beta[F_i - \mathcal{V}^{US}(\mathbf{r_j})]} \delta\xi_{i,j}} \qquad (10)$$

where

2.1.2 Well-Tempered Multiple Walker Metadynamics

2.2 Molecular Dynamics Simulation

MD simulations were performed using the GROMOS11 [19,21] and the NAMD 2.14 simulation packages [15]. Details of the simulations will be presented separately for each program.

2.2.1 GROMOS

The SHAKE algorithm [20] was employed to constrain all bonds to their reference values with a relative tolerance of 10^{-4}, allowing for a time-step of 2 fs using the leapfrog algorithm [10]. For water, the SPC model was used [2]. Non-bonded interactions were computed using a triple range cut-off. Interactions within the short-range cut-off of 0.8 nm were computed every time-step, from a pair-list that was generated every 5 steps. At these time points, interactions between 0.8 and 1.4 nm were also computed which were kept constant between these updates. A reaction-field contribution was added to electrostatic interactions approximating for a homogeneous medium outside the 1.4 nm long-range cut-off, employing the relative permittivity of SPC water (61) [23]. All interactions were calculated using the GROMOS 54a8 potential energy function, with all graphene atoms modeled as neutral sp^2 carbons [18]. After a steepest-descent minimization to remove bad contacts, all velocities were randomly assigned from a Maxwell-Boltzmann distribution at 298 K. All simulations were run coupled to thermostats using the weak-coupling algorithm [3]. The solute, graphene and solvent atoms were independently coupled to different heat baths. Additionally, the graphene layer was coupled to separate baths for regulation of its center of mass motion and its rotational and internal degrees of freedom. This totaled 4 heat baths.

2.2.2 NAMD

3 Results

3.1 Adsorption Free Energy

3.2 Adsorption Entropy

3.3 Adsorption Energy

3.4 Diffusion

4 Conclusions

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