Rupture Mechanism of Aromatic Systems from Graphite Probed with Molecular Dynamics Simulations

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Intermolecular interactions involving aromatic rings are of pivotal importance in many areas of chemistry, biology, and materials science. Mimicking recent atomic force microscopy (AFM) experiments that measured the adhesion forces of single π–π complexes, here interactions between pyrene/coronene and graphite have been probed by force-probe molecular dynamics (FPMD) simulations. The pyrene or coronene molecule was connected to a virtual spring through a flexible poly(ethylene glycol) (PEG) linker and was pulled away from graphite in water under constant velocity. Pyrene and coronene showed similar unbinding pathways featuring four states, with a transition and an intermediate state connecting the bound and unbound states in terms of distance and interplanar angles. Transient conformations with tilted orientations (~40°) and with one side of the aromatic structure still in contact with the graphite surface (~70°) were identified as the transition and intermediate states, respectively, similar to previously observed perpendicularly stacked benzene dimers. The distance to transition state xₚ was determined to be 0.23 ± 0.03 nm both for pyrene/graphite and coronene/graphite. The complexes share similar unbinding pathways, but coronene binds to graphite more strongly than to pyrene.

Introduction

π–π interactions between aromatic systems are ubiquitous in molecular structures and important in diverse phenomena, including biological recognition and supramolecular self-assembly.1–9 Pyrene and coronene molecules with conjugated extended π-electron systems have been demonstrated to have a very high affinity for graphite surfaces.9,10 The high stability of the π–π interactions formed between these aromatic systems and the graphitic surface of carbon nanotubes has attracted growing interest from experimentalists. Electrochemical, photophysical, and fluorescence techniques have been employed to study the π–π interactions between pyrene and nanotubes. Recently, the adhesion force between pyrene and graphite in an aqueous solution was probed using single-molecule force spectroscopy and was reported to be ~0.5 pN in equilibrium.11 In this experiment, a single pyrene molecule was attached to the tip of a force microscope via a flexible PEG linker. Detachment of the pyrene molecule from graphite and the involved forces were monitored while moving the tip away from the surface. The molecular basis of the adhesion strength of aromatic systems on graphite and the dissociation mechanism, however, remains largely unknown.

Here, we use force-probe molecular dynamics (FPMD) simulations to study the molecular pathway of the unbinding of pyrene and coronene from graphite. FPMD has proven to be a powerful tool for investigating the mechanisms of single molecules.12–14 In particular, FPMD simulations have been used to explore the unbinding pathway of a pair of interacting molecules, where the applied force lowers the activation-energy barriers along the unbinding pathways leading to dissociation. Here, the dissociation pathways of pyrene and coronene from graphite were characterized by studying the unbinding mechanism and required rupture forces for different loading rates.

A classical molecular mechanics description as used in the FPMD simulations can implicitly account only for π–π interactions. However, it enables us to explicitly include the stochastic nature of unbinding under force, including solvent interactions and entropic effects, both of which are known to be crucial in hydrophobic interactions as considered here.15 In fact, the adhesion strength of benzene dimers decreases by a factor of 2 when going from vacuum to water.16–19 Even though the classical treatment does not directly consider quantum effects, it is able

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to capture the interaction strength and geometries of aromatic molecules quantitatively.\textsuperscript{17,20} The alternative, high-level ab initio calculations with the correct treatment of stacking interactions\textsuperscript{21} is computationally prohibitive when aiming at a dynamic picture of the force-induced unbinding mechanism. We find coronene to dissociate from graphite at higher forces than pyrene, as expected. However, the two molecules share a very similar unbinding pathway involving an intermediate state in which the aromatic system is tilted relative to the graphitic surface by 50–85\textdegree/C\textsuperscript{176} for pyrene and by 65–85\textdegree/C\textsuperscript{176} for coronene.

Methods

Modeling and Equilibration. Simulations were carried out with the Gromacs 3.3.1 software package.\textsuperscript{22} The model setup for modeling the \(\pi-\pi\) interactions between pyrene/coronene and graphite in an aqueous medium is shown in Figure 1. Complexes between a single layer of graphite that is \(\sim\)5.0 nm in diameter and a single molecule of pyrene or coronene were modeled, respectively. To eliminate boundary artifacts, dangling bonds were terminated with hydrogen atoms. A flexible poly(ethylene glycol) (PEG) linker consisting of CH\textsubscript{2} CH\textsubscript{2} O monomers was connected to pyrene and coronene. The OPLS-AA (optimized potentials for liquid simulations-all atoms) force field\textsuperscript{23} was applied to graphite and the pyrene/coronene-PEG complex. All of the molecules were solvated in a triclinic box with TIP4P water molecules,\textsuperscript{24} resulting in a system size of \(\sim\)38 000/58 000 atoms for the complexes of pyrene–graphite/coronene–graphite, respectively. Simulations were carried out with periodic boundary conditions to remove artificial boundary effects. Lennard-Jones interactions were calculated with a cutoff of 1.0 nm. At a distance of less than 1.0 nm, electrostatic interactions were calculated explicitly, whereas long-range electrostatic interactions were calculated using the particle-mesh Ewald method.\textsuperscript{25} All bonds were constrained using the LINCS (linear constraint solver) algorithm.\textsuperscript{26} The integration time step was 2 fs in all molecular dynamics (MD) simulations. An energy minimization, using the steepest descent method, was followed by an MD simulation with position restraints on the solute atoms. The simulation system was then equilibrated for 1 ns. The interplanar spacing, 0.45 nm, was close to that of a coronene dimer (0.43 nm) calculated using the density functional theory (DFT) method.\textsuperscript{27} The C–C bond length was about 0.14 nm, and the C–H distance was about 0.109 nm, which are in good agreement with those in refs 27–29, the resulting trajectory from which starting points were used for the FPMD simulations. (See below.)

Force-Probe Molecular Dynamics Simulations. We performed force-probe molecular dynamics (FPMD) simulations to assess the unbinding pathways of pyrene and coronene from...
graphite. Several equilibrated structures obtained from the free MD simulations were exposed to an external stress applied to the PEG chain to monitor the rupture. The pull vector is along the x axis, and the pulling velocity varied from 0.01 to 15 m/s at room temperature (27 °C) with a spring constant of 0.25 N/m. The terminal carbon atom of the PEG linker was subjected to a pulling force by moving the virtual springs with the respective constant velocity away from the substrate graphite, of which the center of mass was fixed to prevent it from translating and rotating. To investigate how the spring stiffness and temperature will influence the unbinding force, FPMD simulations to monitor the unbinding of the coronene–graphite complex were performed. The pulling velocities and temperatures were varied from 0.01 to 15 m/s and from 11 to 43 °C respectively, and two spring constants, 0.25 and 0.83 N/m, at 27 °C were compared. All FPMD simulations used the same simulation parameters as the equilibrium simulations. (See above.) The applied pulling velocities and time per simulation are listed in the Supporting Information (Table 1). Simulation times varied from 0.2 ns (fast pulling) to ∼200 ns (slow pulling). The simulations with high velocities (beyond 0.1 m/s) showed a large scattering in the rupture force and therefore were repeated several times. We obtained the rupture force \( f_r \) from

\[
\Delta f = k \Delta x
\]  

where \( k \) is the spring constant and \( \Delta x \) is the change in the spring position. We smoothed the unbinding force profiles by Gaussian filtering to filter out high-frequency components arising from random thermal motion and obtained the maximum forces of unbinding. In the FPMD simulations, the stiffness of the pulling spring is comparable to that of the PEG linker (\( \sim 0.64 \) N/m), which should not be neglected in estimating the effective loading rate. According to the definition of the loading rate, the loading rate \( \dot{r} \) was determined directly from the increase in force \( (f) \) with time \( (\dot{f}) \) \( (\dot{r} = \frac{df}{dt}) \). Analogous to the experiment, \(^{11}\) the loading rate \( \dot{r} \) was derived from the slope of the force–time curve.

Results and Discussion

**Unbinding Pathways of Pyrene and Coronene from Graphite.** In these simulations, the applied pulling velocities are from 0.01 to 15 m/s, and the applied spring constant and the simulation temperature were set to be 0.25 N/m and 27 °C, respectively. Representative unbinding force and distance profiles of the coronene–graphite system are shown in Figure 1a,b. By monitoring molecular distances and interplanar angles, we identified a transition (tr) and an intermediate state (im) between the bound (b) and unbound (ub) states. The bound state is marked as b, where the distance between the center of mass of pyrene/coronene and graphite is minimal, and the small aromatic molecule is oriented parallel to graphite to form an optimal stacking interactions (Figure 1).

We identified the transition-state region (marked tr) of the dissociation process of pyrene/coronene from graphite in water from the sudden decrease in force and the paucity of states. In this transient orientation, one side of the aromatic structure is still in contact with the graphite surface, with the plane of the aromatic ring tilted relative to the graphitic plane. As shown in the Supporting Information (Figure S1), for a few representative FPMD simulations independent rupture events have very similar transition regions in common, independent of the pulling force (as well as independent of the aromatic moiety, i.e. coronene/pyrene, data not shown).

To assess the distance between the transition state and the bound state quantitatively, we measured rupture forces, averaged over several trajectories at different loading rates. Figure 2 shows the rupture forces observed for the unbinding of pyrene (triangles and solid line) and coronene (circles and dashed line) from graphite against the logarithm of the loading rate. The coronene–graphite complex is, as expected, overall more stable. We use a revised Bell formula\(^{30}\)

\[
f^* = f - \frac{1}{2}k_B T \ln \frac{r_f x_{tr}}{k_B T}
\]  

where \( f^* \) being the direct observed rupture force, \( k_B \) being the Boltzmann constant, \( T \) being the absolute temperature, \( x_{tr} \) being the distance from the free-energy minimum to the mechanically probed transition state, \( r_f \) being the loading rate, and \( k_B T \) being the equilibrium unbinding rate. We validated this formula by performing simulations of the unbinding of coronene from graphite with two different spring constants of 0.25 and 0.83 N/m (Supporting Information Figure S2). Whereas the rupture forces obtained with the different spring stiffness differ for the same loading rate when using the original Bell formula, \(^{31-33}\) the data collapses onto a linear curve when using eq 2. Also, within the range of loading rates covered by the FPMD simulations, we find a linear increase in force with the logarithm of the loading rate. Fitting the revised Bell formula to the simulated data in Figure 2 yields a distance from the bound state to the transition state \( (x_{tr}) \) of 0.23 ± 0.03 nm for both pyrene and coronene. Thus, apparently the two molecules share a similar transition-state structure, resulting in a similar force dependence of the adhesion lifetime. As suggested by the force spectroscopy experiments, a crossover into a regime without a dependence of rupture forces on loading rates exists for pyrene at slow loading. We estimate a lifetime of binding of 0.3 ms for the pyrene–graphite complex, assuming the interaction to be at equilibrium on longer timescales. However, a change in slope near the crossover is likely,\(^{34}\) so the estimation of a millisecond timescale represents a lower limit for the adhesion lifetime.

We next identified the tilt angle between the aromatic interaction partners. Figure 3 shows the interplanar angles as a function of the logarithm of the loading rate.

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**Figure 2.** Rupture forces observed for the unbinding of pyrene (−•−) and coronene (−○−) from graphite as a function of the logarithm of the loading rate.

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\(^{33}\) Bell, G. I. Science 1978, 200, 618.

of the minimum distance \(d_{\text{min}}\) between pyrene/coronene and graphite. The transition states are identified from the paucity of states scattered in the range of 15–50°/C for pyrene and 22–65°/C for coronene.

Before the final dissociation of pyrene/coronene from graphite, we find the small molecule to dwell in an orientation nearly perpendicular to the graphite, marked (im) in Figure 1. As shown in Figure 3, the interplanar angles \(\alpha_{\text{im}}\) in the intermediate state are centered in the range of 50–85°/C for pyrene and 65–85°/C for coronene. The distances from the bound to the intermediate states \(x_{\text{im}}\) are in the range of 0.26–0.36 nm for pyrene and 0.35–0.41 nm for coronene (Figure 4). In this nearly perpendicular orientation, the molecules remain in contact with graphite and the larger \(x_{\text{im}}\) of coronene simply stems from its larger molecular size.

We note that most of the individual rupture trajectories for both pyrene and coronene feature an intermediate state as described above, as visible from the overlay of all rupture events in Figures 3 and 4 and from Supporting Information Figure S1.

Finally, the force drops quickly to zero and the distance increases steeply, marked ub in Figure 1. The unbound state is reached when the remaining direct interaction between the CH groups of the aromatic pyrene/coronene system and graphite as found in the intermediate state is finally ruptured. As a rough estimation of the distance between bound and unbound states along the reaction coordinate (the pulling direction), we calculated the potential energy along this coordinate (Supporting Information Figure S3). We defined the unbound state to be reached when the potential energy drops to zero and obtained distances from the bound to the unbound state \(x_{\text{ub}}\) to be around 0.8 and 0.9 nm for pyrene and coronene, respectively.

Temperature Dependence of the Unbinding of the Coronene–Graphite Complex. The temperature dependence of unbinding forces of noncovalent bonds has been investigated using atomic force microscopy (AFM) measurements.\(^3(5,36)\) Here, the temperature dependence of the \(\pi-\pi\) noncovalent interactions between coronene and graphite was determined by FPMD simulations at 11, 27, and 43 °C. The pulling velocity ranged from 0.015 to 15 m/s, and the spring constant was maintained at 0.25 N/m. The resulting rupture forces versus the logarithmic loading rate \(\ln(r_f)\) are shown in Supporting Information Figure S4. We fitted the obtained rupture forces versus \(\ln(r_f)\) to the revised Bell formula (eq 2).\(^3(0)\) The distances to the transition state \(x_{\text{tr}}\) were measured to be 0.25, 0.24, and 0.23 nm for 11, 27, and 43 °C, respectively, thus slightly decreasing with increasing temperature. Also, an increased temperature causes a slight decrease in the rupture force at any loading rate. This suggests that the stability of the coronene and graphite complex depends on temperature, with stronger stacking interactions at lower temperature. In our model, the direct interaction energy of the aromatic molecules is independent of the temperature. Therefore, the observed increase in stability and the stiffening of the adhesion potential (as indicated by the decrease in \(x_{\text{tr}}\)) are likely to be due to a strengthening of the hydrophobic effect at elevated temperature.

**Conclusions**

Taking these results together, we sketched a schematic 3D energy landscape to describing the unbinding of the pyrene–graphite and coronene–graphite complexes (Table 1 and Figure 5). From the dissociation dynamics of the aromatic stacking complexes under force, we identified the transition (tr)


Table 1. Data Obtained from the Unbinding of Pyrene and Coronene from Graphite

<table>
<thead>
<tr>
<th></th>
<th>pyrene and graphite</th>
<th>coronene and graphite</th>
</tr>
</thead>
<tbody>
<tr>
<td>$x_{tr}$</td>
<td>$0.23 \pm 0.03$ nm</td>
<td>$0.23 \pm 0.03$ nm</td>
</tr>
<tr>
<td>$x_{im}$</td>
<td>$0.26-0.36$ nm</td>
<td>$0.35-0.41$ nm</td>
</tr>
<tr>
<td>$x_{ub}$</td>
<td>$0.8$ nm</td>
<td>$0.9$ nm</td>
</tr>
<tr>
<td>$\alpha_{tr}$</td>
<td>$15-50^\circ$</td>
<td>$22-65^\circ$</td>
</tr>
<tr>
<td>$\alpha_{im}$</td>
<td>$50-85^\circ$</td>
<td>$65-85^\circ$</td>
</tr>
<tr>
<td>$\Delta E$</td>
<td>$6.2$ kcal/mol</td>
<td></td>
</tr>
</tbody>
</table>

Figure 5. Three-dimensional energy landscape of the energetics of unbinding for pyrene/coronene from graphite.

and intermediate (im) states connecting the bound (b) and unbound (ub) structures in terms of distances and interplanar angles. Both the pyrene–graphite and coronene–graphite system shared similar unbound pathways. The small aromatic molecules, pyrene and coronene, are oriented parallel to graphite to form an optimal stacking interactions in the bound states (b). Transient conformations with tilted orientations and one side of the aromatic structure still in contact with the graphite surface were identified as the transition ($\alpha_{tr} = 15-50^\circ$ for pyrene and $22-65^\circ$ for coronene, respectively) and intermediate ($\alpha_{im} = 50-85^\circ$ for pyrene and $65-85^\circ$ for coronene, respectively) states. The distances to the transition states $x_{tr}$ were both determined to be $0.23 \pm 0.03$ nm. Pyrene–graphite and coronene–graphite thus share a similar transition state, resulting in a similar force dependency of the adhesion lifetime. Interestingly, a stable benzene dimer has been found with a perpendicular orientation similar to that of our intermediate states, giving us confidence in our classical mechanical description of the aromatic π-system stacking interaction investigated here. The unbound state (ub) is reached when the remaining contact in this perpendicular orientation is lost. The unbinding distances from the bound states to the unbound states $x_{ub}$ are roughly measured to be $0.8$ nm for pyrene and $0.9$ nm for coronene. From $x_{ub}$ given the experimentally determined equilibrium force of $\sim 55$ pN, we calculate a pyrene–graphite interaction free energy of $6.2$ kcal/mol. The value is roughly 4 times higher than that of a benzene dimer, which is measured to be $1-1.5$ kcal/mol in solution. We thus predict the binding affinity to scale approximately with the size of the aromatic system. Coronene, as the larger aromatic system, shows larger rupture forces. The binding energy can thus be expected to be significantly larger than $6.2$ kcal/mol, namely in the range of $10$ kcal/mol.

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Supporting Information Available: Simulation details, effects of the spring constant and temperature, and histograms of the unbinding distance. This material is available free of charge via the Internet at http://pubs.acs.org.