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RESEARCH ARTICLE

Cooperativity of Catechols and Amines in High Performance Dry/Wet Adhesives

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Abstract: The outstanding adhesive performance of mussel byssal threads has been a beacon of inspiration for materials scientists over the past few decades. Historically, presence of a significant amount of the unique catecholic amino acid dihydroxyphenylalanine (Dopa) has been considered to play a key role in strong dry and wet adhesive properties of the byssal interfacial proteins. In recent years, molecular and microscopic level studies using short peptides or small molecule analogs have investigated the roles of other amino acids in mussel adhesion. In particular, these studies have highlighted the cohesive role of cation-π interactions as well as the adhesive synergy between Dopa and flanking lysine residues. Inspired to design advanced synthetic adhesives that exploit amino-catechol synergy, we synthesized polymeric pressure sensitive adhesives (PSAs) by copolymerizing traditional PSA monomers, butyl acrylate and acrylic acid, with mussel-inspired lysine- and aromatic-rich monomers. Of particular interest was to compare the consequences of decoupling amino and catechol moieties from each other (i.e. incorporated as separate monomers) versus a monomer architecture in which the catechol and amine were coupled together in a fixed orientation in the monomer side chain. Comprehensive multi-scale adhesion assays were used to probe performance at the molecular, microscopic and macroscopic levels through a combination of AFM-assisted force spectroscopy, peel and static shear adhesion. We showed that coupling of catechols and amines together within the same monomer side chain produced optimal cooperative effects in improving macroscopic adhesion performance. The findings in this study improve our understanding of underlying principles of mussel adhesion and provide a solid framework for rational design of high-performance bioinspired adhesives.

The remarkable wet adhesion of marine mussel byssus has been a major source of bioinspiration for materials scientists during the recent decades.[1] These sessile organisms are able to tenaciously attach to various surfaces in turbulent, wet, and saline habitats using their byssal threads.[1a, 2] Since many man-made adhesives fail in the presence of moisture, surface contaminants or salts, incorporation of concepts from mussel adhesives into synthetic materials has been a long-standing pursuit for researchers.[3] To achieve this goal, many fundamental studies have been conducted in order to understand the underlying principles of mussel adhesion. Early investigations attributed the unique adhesive properties of mussel plaques to the presence of unusually high contents (20-30 mol%) of the post-transitionally modified 3,4-dihydroxyphenylalanine (Dopa) residues in the mussel foot proteins (Mfps-3,5) at the protein-substrate interface.[1a, 4] Fundamental studies later confirmed the critical role of catechol moiety in adhesive and cohesive properties of these interfacial proteins using surface forces apparatus (SFA) and single molecule force spectroscopy (SMFS).[5] These initial observations sparked an era of substantial scientific interest in designing catechol-containing synthetic peptides and polymers to mimic the mussel plaque adhesion.[6] Although incorporating catechols alone shows great promise in improving adhesive performance,[6c, 7] such simplified approaches are unable to capture the complex interplay between different amino acids in Mfps.

Recently, a few seminal studies have suggested the critical role of other amino acids besides Dopa on the strong adhesion of Mfps. For instance, a possible synergy between Dopa and positively charged amino acids such as lysine (Lys) and arginine (Arg) has been proposed.[8] These amino acids are frequently positioned adjacent to Dopa residues in Mfps.[1a] Although still a subject of active investigation, presence of these cationic residues and their close proximity to Dopa are thought to improve the interfacial adhesion by providing additional surface binding opportunities as well as repelling the hydration layer and thus preparing a pristine surface for effective catechol interaction.[8-9] In addition to acting as surface primer, amine groups are also believed to amplify the cation-π interactions and enhance cohesive properties.[10] Cation-π interactions are among the most important non-covalent interactions employed in nature to stabilize and tune the structure and function of many biological molecules.[11] In particular, interactions between hydrophobic aromatic amino acids such as phenylalanine and tyrosine with cationic residues has been shown to play an essential role in self-assembly, molecular cohesion and adhesion, as well as formation of secondary structures in proteins and peptides.[12] Interestingly, a few recent

investigations have suggested that the aromatic-rich nature of Mfps provide a clue as to the important function of cation-π interactions in tuning the underwater adhesion of mussel plaques.[10a, 12b, 12c, 13]

Although these recent findings have improved our understanding of the underlying mechanisms for the remarkable adhesion of Mfps, many important questions still remain unanswered. For instance, it is not clear whether the synergistic effects between catechols and amines are limited to only enhancing the interfacial adhesion or if cohesive properties are also affected. More importantly, a controversy still exists on whether the adjacency of the catecholic and cationic moieties is crucial in establishing the cooperative effects. In addition, it remains unclear whether catechol groups are inherently essential to observe strong synergy with amines or if similar properties can be achieved by employing phenyl instead of catechol in the bioinspired molecular designs. Finally, most of the previous investigations have focused on studying the adhesion of nanometer thin films of small molecules or short peptides using SFA measurements. Although these experiments provide invaluable molecular mechanistic insights, validity of translating these results across many length scales to design polymer adhesives for practical applications remains an open question.

Here, we examined the cooperative effects of amine and aromatic groups incorporated into a common pressure sensitive adhesive (PSA) polymer based on acrylic acid (AA) and butyl acrylate (BA). The polymers were subjected to a variety of multi-scale adhesion measurements including AFM-based force spectroscopy at molecular and microscopic levels as well as macroscopic peel and static shear adhesion, providing fundamental insights into the mechanism and strength of the interfacial interactions between the polymers and the surface. The rational approach to polymer design combined with comprehensive multi-scale adhesion characterizations allowed us to decouple the interfacial adhesive and intermolecular cohesive contributions of each functional motif on the overall performance and provided new insights into mussel adhesion principles.

Results and Discussion

PSAs have become an integral component in many consumer products with widespread applications including adhesive tapes, labels, protective coatings, and medical bandages.[14] Among different classes of PSAs, linear or slightly cross-linked acrylic based polymers with a high content of BA or other monomers with low glass transition temperature (T_g) are extensively used in these contexts.[14c, 15] Although the conventional PSA formulations show satisfactory performance for non-demanding applications there are a few challenges associated these compositions.[14b, 14d] For instance, the adhesive properties of PSAs in wet conditions are generally significantly inferior to their performance in ambient.[14d] In a previous effort to improve their wet adhesion, we applied the mussel inspiration principles to the base PSA polymers and showed that catechol PSAs outperformed conventional benchmarks in different industry standard tests even at a low ~3mol% catechol content.[6b] In addition to the inferior under water performance, another major shortcoming of conventional PSAs is their poor cohesive strength and low toughness. PSAs commonly take the form of viscoelastic polymers with a sufficiently low modulus to allow for good contact with the substrate upon application of light pressure.[15-16] However, the low modulus can lead to poor cohesive strength which can substantially limit the use of PSAs to low stress applications.[14c, 16] Although a few strategies have been previously proposed to improve the cohesive strength of PSAs, optimizing the adhesive and cohesive properties of PSAs has proven to be a challenging task, as improving one property often comes at the expense of another.[6b, 14d, 16]

The promising results of our earlier study motivated us to take a step further and apply the recently highlighted mussel adhesion propositions to our PSA design in order to tackle the above challenges. To examine the synergy between catechols and cationic amine groups in PSAs, we designed and synthesized several mussel-inspired Lys- and aromatic-rich monomers (**Figure 1**). The monomer designs were inspired by the high Dopa and Lys content and common appearance of adjacent Lys-Dopa pairs in Mfps, as well as recent findings regarding the potential of cation-π interactions between cationic and aromatic residues in tuning the adhesive performance.[8a, 8c, 10a] Acrylic-based PSAs can be considered an ideal platform for studying the effects of mussel-inspired monomers in improving the adhesive performance owing to their widespread practical use and their synthetic modularity in monomer composition. Thus, we proceeded to polymerize our mussel-inspired monomers with AA and BA co-monomers using conventional free-radical polymerization to yield high molecular weight PSAs (**Figure 1**). Full synthetic schemes and experimental details for monomer and polymer preparation are provided in the supporting information (**Schemes S1-S6**). The chemical structure and successful synthesis of each compound was confirmed by ^{1}H NMR, ^{13}C NMR, and ESI-MS measurements (**Figures S2-S39**). The library of synthesized polymers along with the selective deprotection of the amine and catechol moieties (**Schemes S6-S7**) allowed us to effectively decouple the adhesive and cohesive contributions of each functional group on the overall adhesive performance and investigate possible cooperative effects.

In order to isolate the effect of composition on adhesion, we chose to keep the functional monomer feed ratio fixed at 2.85 mol% (**Table 1**), as this concentration of catechol was demonstrated to be sufficient for boosting the adhesive performance of acrylic PSAs.[6b] Calculations based on the integration of area under the peaks from functional groups in the NMR spectra showed that the compositional drifts from the intended feed ratio in the polymerization were not significant (**Table S2** and **Figures S29-S34**). Molecular weight and T_g values of polymers were measured using gel permeation chromatography (GPC) and differential scanning calorimetry (DSC) and are listed in **Table 1** (also **Table S1**, **Figures S40-S41**). Compared to the control PSA polymer ($BA_{91.4\%}$:$AA_{8.6\%}$), the functional polymers had higher M_w which can be attributed to the enhanced non-covalent and covalent interactions between the polymer chains owing to the presence of catechol groups, as described previously in more detail.[6b] The small variations observed between the molecular weight and T_g of the functional polymers can further underline that physical properties of PSAs are not expected to be a major contributor to the differences noticed in their adhesive performance.[17]

After a thorough physical and chemical characterization of PSAs, we proceeded to evaluate their interfacial adhesion using an Atomic Force Microscope (AFM). Owing to its high force resolution and displacement sensitivity, AFM-assisted force spectroscopy has been recognized as a versatile technique in studying physical behavior and mechanical properties of polymeric films.[18] Depending on the cantilever probe used in the measurements, a range of molecular or micro-scale interfacial phenomena can be investigated using this technique. For example, colloidal probe spectroscopy (CPS) is a widely employed method to measure adhesive forces acting between

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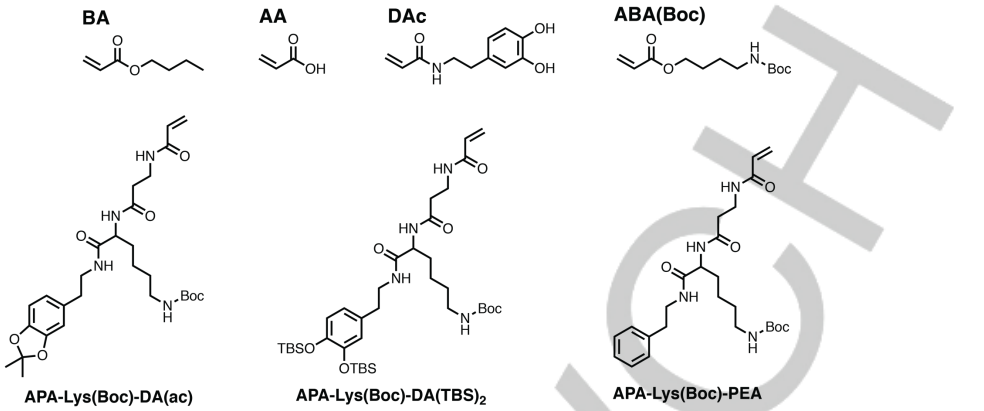
Monomers



Polymers

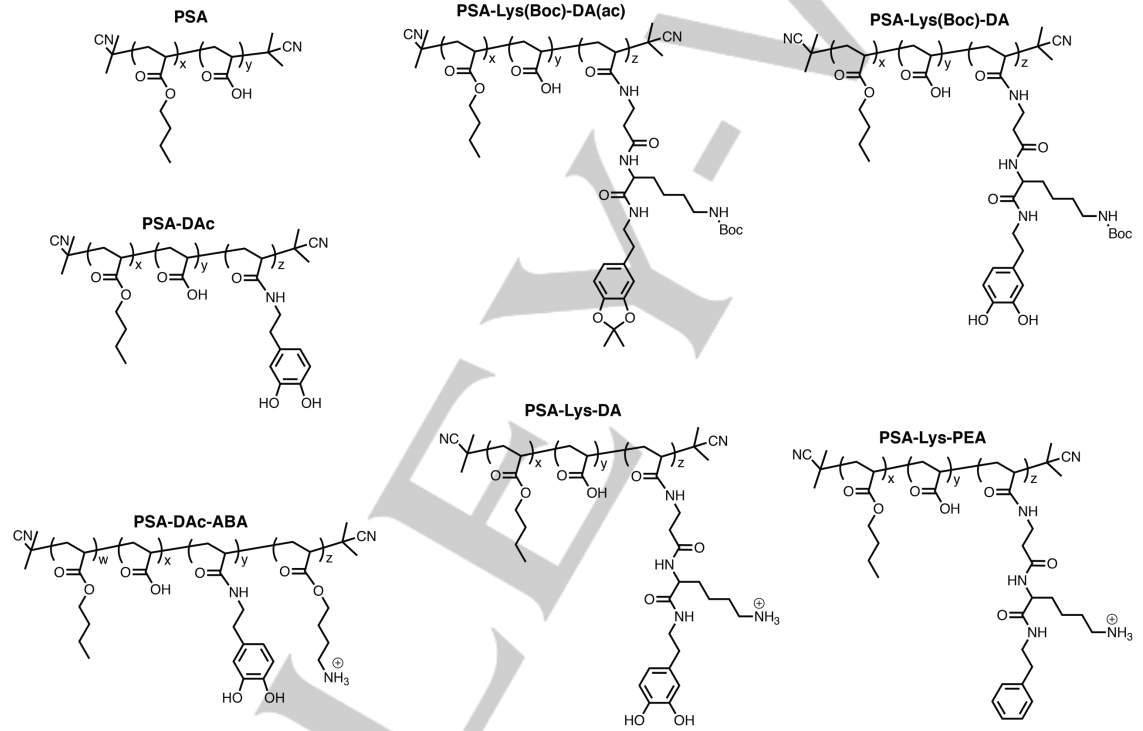


Figure 1. Structure of conventional and various mussel-inspired monomers used to synthesize a library of PSAs via free-radical polymerization.

Table 1. Monomer feed composition (mol%), molecular weight values, polydispersity index, and T_g of synthesized PSAs.

Polymer	Feed Composition (mol%)					M_n (kDa)	M_w (kDa)	Đ	T_g (˚C)
	BA	AA	Dipeptide Monomer	DAc	ABA				
PSA	91.4%	8.6%	-	-	-	116	346	3.0	-41
PSA-DAc	88.4%	8.74%	-	2.85%	-	280	599	2.14	-32
PSA-Lys(Boc)-DA(ac)	88.4%	8.74%	2.85%	-	-	157	377	2.40	-30
PSA-Lys(Boc)-DA	88.4%	8.74%	2.85%	-	-	204	413	2.03	-32
PSA-Lys-DA	88.4%	8.74%	2.85%	-	-	233	827	3.54	-28
PSA-Lys-PEA	88.4%	8.74%	2.85%	-	-	153	352	2.30	-30
PSA-DAc-ABA	85.6%	8.74%	-	2.85%	2.85%	193	544	2.82	-23

a colloidal particle (i.e., micrometer-sized spherical particle) attached to a cantilever beam and a planar substrate.[19] Single molecule force spectroscopy (SMFS) is another powerful AFM-based characterization method which is well suited to investigate and quantitively measure the strength of chemical bonds as well as adhesive interactions acting between molecules and surfaces.[20] This technique has been widely used in the past for studying the adhesion of mussel-inspired peptides and polymers and advances have been summarized in a recent review by Li et al.[5a] SMFS measurements are complementary to the CPS experiments and when combined together can provide a more comprehensive picture of the molecular basis underlying adhesive and cohesive properties of materials. In the present work, we utilized both SMFS and CPS techniques to study adhesive performance of PSA polymers in order to decouple cohesive contributions from interfacial adhesive interactions acting between polymer chains and the surface.

SMFS experiments were performed initially to gain a fundamental insight into the molecular phenomena underlying the interfacial adhesive properties of PSAs. In our experiments a sharp AFM cantilever (tip radius ~10-20 nm) was brought into contact with PSA films on mica substrate and retracted at a specified speed while the force of interaction between the probe and the polymer film was measured. A schematic of the experimental setup as well as a representative F-D curve for PSA-Lys-DA is shown in **Figure 2a**. The sequential rupture of polymer-surface interactions during retraction of the cantilever lead to the appearance of sawtooth-like peaks in the F-D curves, reminiscent of what is observed during unfolding of globular polyproteins during stretching.[18d, 21] These rupture events can then be fitted using polymer elasticity models to confirm single molecule behavior and extract the strength of polymer-surface interactions (**Figure S43**). Histograms and median values of rupture force for PSAs are presented in **Figure 2** and **Table 2**, respectively (also **Table S3** and **Figure S45**). We first tested the control PSA polymer where a median rupture force of 118 pN was measured (**Figure 2b**). This value is in the range of weak non-covalent interactions such as hydrogen bonding and charge-charge interactions and can be attributed to the presence of AA in the polymer which can accommodate these interactions with the substrate.[22] Results of measurements on PSA-DAc indicated that incorporation of catechol groups into the polymer can lead to a notable increase in the median rupture force to ~236 pN, possibly owing to the myriad of interfacial interactions that catechol can form with the mica surface including strong hydrogen bonding and bidentate complexation.

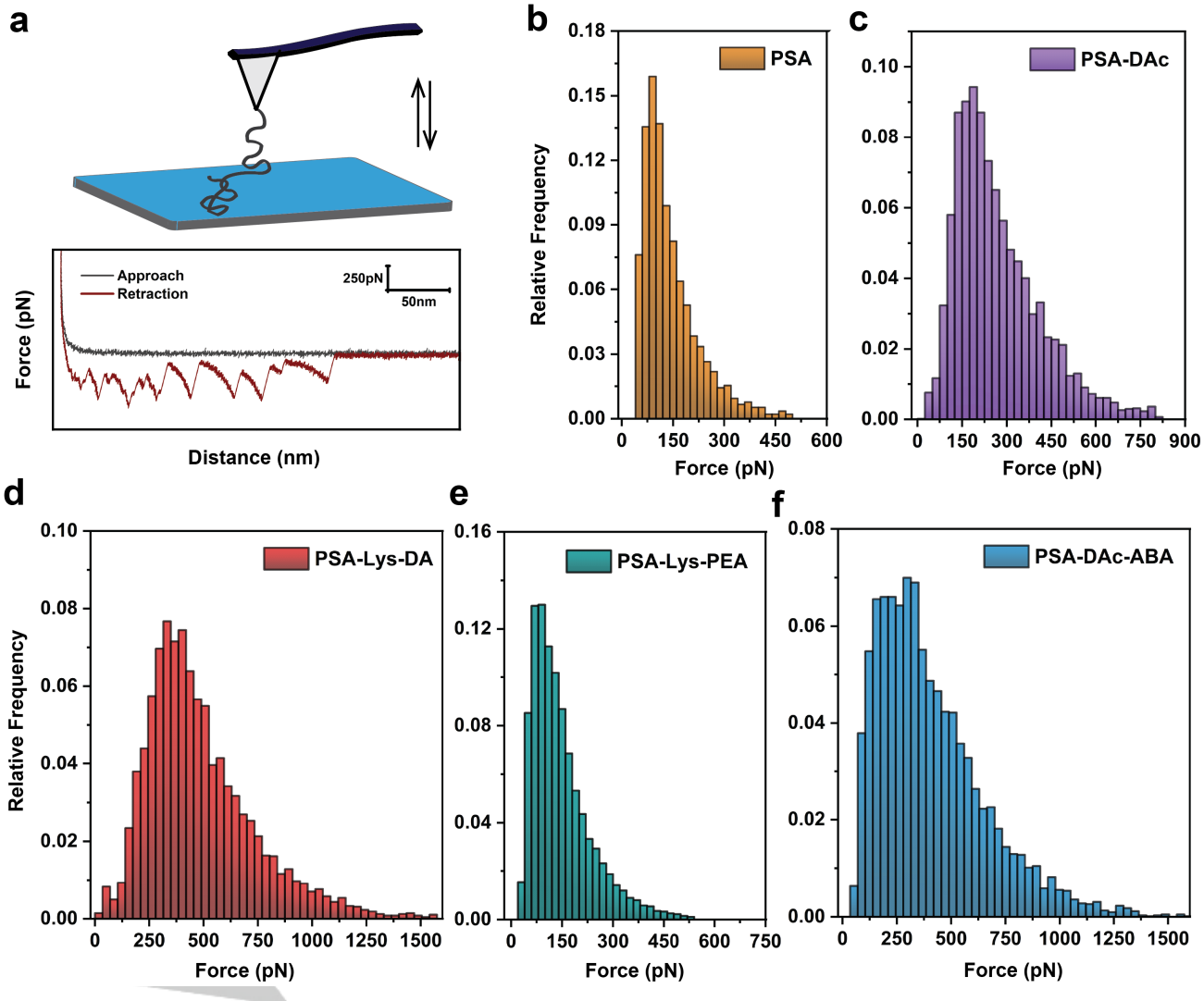


Figure 2. SMFS characterization of PSA polymers. (a) experimental schematic and a representative F-D curve for PSA-Lys-DA are shown. Histograms of the rupture forces are shown in **(b)** PSA, **(c)** PSA-DAc, **(d)** PSA-Lys-DA, **(e)** PSA-Lys-PEA, **(f)** PSA-DAc-ABA.

We observed a stark increase in the rupture forces for PSA-Lys-DA compared to PSA and PSA-DAc polymers, confirming the cooperative effects between catechols and positively charged amines at the single molecule level. The elevated rupture forces for PSA-Lys-DA can be attributed to the potential role of positive charges of Lys in removal of solvation layer from the surface for a more effective catechol interaction as well as possible cooperative surface binding leading to an increased interaction strength and lifetime as suggested previously by Cao and colleagues.[8] Next, we proceeded to study the interfacial adhesion of PSA-Lys-PEA to evaluate the effects of cation-π interactions in improving the polymer-surface interactions. Interestingly, we observed a median rupture force of ~125 pN for PSA-Lys-PEA. The sharp contrast in the rupture forces detected for PSA-Lys-DA and PSA-Lys-PEA clearly highlights the advantages of catechols over unsubstituted phenyl rings for improving interfacial interactions with substrates.

After observing the performance of PSA-Lys-DA we were intrigued to study the effects of the molecular architecture and adjacency of amine and catechol groups on the interfacial adhesion. Since Lys and Dopa residues are most commonly positioned adjacent to each other along the backbone in Mfp-3 and 5, it was initially hypothesized that the close proximity of the cationic Lys residues and catecholic motifs are necessary to establish the synergistic effects.[8a, 8c] However, recently it has been suggested that the adjacency of the two functional motifs might not be required for the synergistic effects and only co-presence of cationic and catecholic groups might lead to major improvements in adhesive performance.[9a] To further test this notion we studied interfacial adhesion of PSA-DAc-ABA. The median rupture force for PSA-DAc-ABA was ~351 pN, much higher than that of the of amine-free PSA-DAc and only modestly less than the values observed for PSA-Lys-DA. Compared to PSA-Lys-DA, catechol- and amine-containing monomers are located randomly along the backbone in PSA-DAc-ABA, resulting in a stochastic distribution of spacing between DAc and ABA groups in the polymer chains. The SMFS results indicate that even when randomly distributed, the amine groups can possibly be partially effective in desolvating the surface and facilitating the interaction of catechols with the substrate. More importantly, in SMFS measurements the polymer chains can be picked up at any random point along their contour length. Owing to this random attachment to the probe as well as flexibility of the backbone and the presence of a large number of amine and catechol groups in polymer molecules, the synergistic effect due to the simultaneous rupture of catechol- and amine-surface interactions might still be observed, leading to elevated rupture forces as compared to PSA-DAc.

Next, we proceeded to perform CPS experiments on PSAs in order to complement the SMFS studies and to gain a microscopic view of adhesion performance.[19c, 19d] In our measurements an AFM cantilever with a colloidal probe of silica (SiO_2, diameter = 3.5 μm) was used and brought into contact with a PSA film adsorbed on mica substrate. Schematic of the experimental setup as well as a representative F-D curve for PSA-Lys-DA are shown in **Figure 3a**. A characteristic feature in most of the collected F-D curves was the appearance of multiple spikes in the retraction trace. The presence of these spikes can be attributed to detachment of multiple polymer chains from either the colloidal probe or the substrate upon retraction of the AFM cantilever, or alternatively to rupture of specific polymer-surface adhesive interactions between individual chains and the surface. As a result, extracting only the maximum detachment force from the F-D curves is not a proper measure of the overall adhesive interactions. More importantly, owing to the viscoelastic nature of the polymer as well as roughness and asperities on the colloidal particle, accurate determination of the contact geometry and radius can be challenging.[19a-c, 23] Hence, the adhesion energy values calculated based on the contact mechanics models can be subject to large errors introduced from the estimated contact radius. An alternative approach to estimate the magnitude of the overall adhesive strength between the polymer film and the substrate in the contact area is to integrate the area under the retraction trace in the F-D curves.[24] The calculated quantity has the units of energy and will be referred to as separation work (W) here.[6b, 25] The separation work calculated here is related to the energy that is required to detach the probe from the substrate.[19b]

Histograms and median values of W for the PSA polymers are presented in **Figure 3** and **Table 2**, respectively (also **Table S4** and **Figure S46**). CPS results show that incorporating catechol as DAc into the polymer backbone can lead to a 20-fold increase in the separation work. A similar trend was observed in our earlier study where incorporating 5 wt% dopamine methacrylamide into PSAs resulted in a significant increase in the separation work for SiO_2 probes.[6b] The large increase in adhesion to silica upon incorporation of DAc may be attributed to strong binding mechanisms such as hydrogen bonding and bidentate complexation as described in detail previously.[1c, 5b, 6b] As expected, incorporating a protected form of the bifunctional monomer Lys-DA into the polymer backbone did not result in major changes in adhesion compared to the control PSA polymer (**Figure S44**). However, upon removal of the protecting groups the resulting PSA-Lys-DA outperformed all other polymers by showing a remarkable ~36-fold increase in the separation work compared to the control PSA. This striking increase further highlights that co-presence of amine and catechol groups can lead to significant improvements in adhesive performance of PSA polymers. The cooperative effects between amines and catechols can be attributed to the role of positive charges of amines in removing solvation layer and providing an immaculate surface for catechol interaction or resulted from a better load distribution through synergistic surface binding of the two groups as suggested in previous molecular studies.[8-9]

To determine if similar adhesive performance can be achieved by substituting phenyl for catechol groups in the monomer design, we tested the adhesion of PSA-Lys-Phe. Although the results showed a notable ~10x improvement in the separation work compared to the control PSA, PSA-Lys-Phe underperformed both PSA-Lys-DA and PSA-DAc. Considering the results obtained in CPS and SMFS experiments together, the findings indicate the potential benefits of cation-π interactions in improving the cohesive interactions between the macromolecules leading to an enhanced adhesion as measured here in the CPS experiments as well as in previous SFA studies.[10a, 12b, 12c] Nevertheless, the SMFS results imply that Lys-PEA pairs have minimal effects in strengthening the interfacial adhesive interactions with surfaces. In other words, due to the nature of the CPS and SFA experiments where detachment of an ensemble of molecules is studied, cohesive interactions between the molecules can affect the measured values for separation work or work of adhesion. Thus, possible contributions of intermolecular cohesive and interfacial adhesive interactions on the improved performance cannot be equivocally deconvoluted solely based on the results these measurements.

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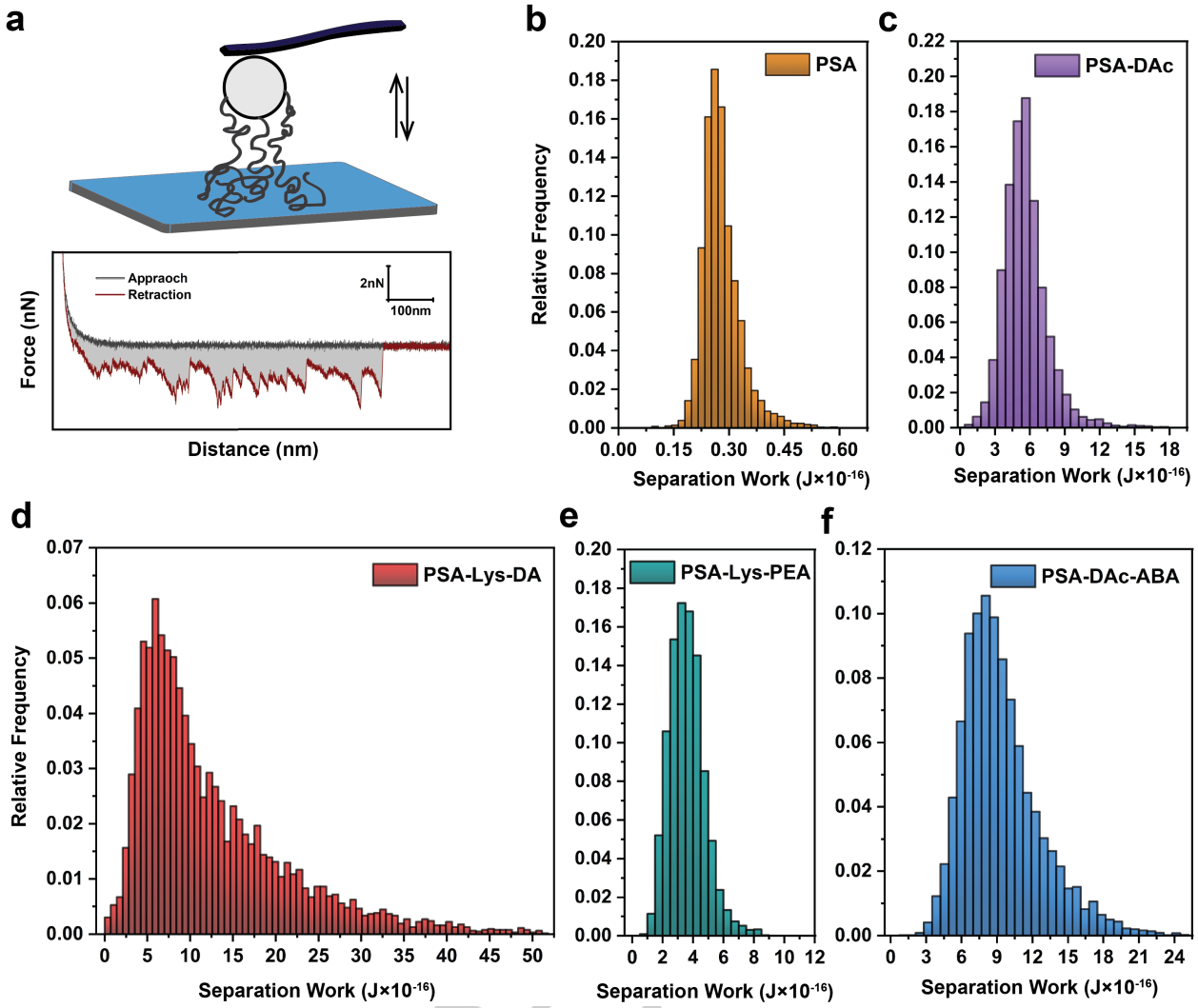

Figure 3. CPS characterization of PSA polymers. (a) experimental schematic and a representative F-D curve for PSA-Lys-DA are shown. Histograms of the separation work are shown in **(b)** PSA, **(c)** PSA-DAc, **(d)** PSA-Lys-DA, **(e)** PSA-Lys-PEA, **(f)** PSA-DAc-ABA.

To gauge the possible role of molecular architecture and proximity of catechol and amine groups on the adhesive performance of PSAs, we performed CPS experiments on PSA-DAc-ABA. Interestingly, the polymer displayed a median separation work close to that of PSA-Lys-DA polymer. The trend observed in CPS measurements is similar to what was noted earlier in SMFS experiments and can indicate that architecture of the polymer and the adjacency of catechol- and amine-containing groups might not be necessary in establishing the cooperative effects to improve the adhesion, at least when measured at the microscopic or molecular levels. Similar observations have been made recently by Degen et al.,[9a] where results of SFA measurements implied that incorporating glycine residues as spacer between the cationic and catecholic groups did not lead to significant changes in the force required to separate peptide-coated mica surfaces.

Despite the wealth of mechanistic information that interfacial adhesion measurements on thin-films can provide, the bulk behavior still cannot be unambiguously predicted from CPS and SMFS experiments that probe the microscopic and molecular levels, respectively. Thus, we proceeded to perform static shear and 180° peel measurements as industry-standard macroscale adhesion tests. Combined with the results obtained in the interfacial adhesion measurements, this holistic multi-scale approach could allow us to decouple the adhesive and cohesive contributions as well as effects of polymer composition and architecture on the PSA performance.

For the macroscopic adhesion measurements, the PET films were coated with PSAs, dried and then cut into 1 inch-wide strips to prepare test samples (**Figure S1**). The shear holding power of the adhesives was evaluated in both dry and wet conditions by adhering the PSA tapes onto a stainless steel test plate and measuring the time to rupture under the influence of a constant shear force (**Figure S47**). This test simulates a constant load creep condition and can be used for determining the shear failure time, a measure of the cohesive strength or shear holding power of the adhesive. Similar to the results obtained in our previous study, incorporation of catechol groups into the polymer backbone led to a substantial increase in the failure time for PSA-DAc as compared to the control PSA, from 14 and 8 to 123 and 77 minutes under dry and wet conditions, respectively (**Figure 4a**). While the improved shear holding power of the PSA-DAc can be mostly attributed to the enhanced cohesive and intermolecular interactions due to the presence of catechol groups, we should note that in addition to the chemical composition, the shear failure times are also dependent on additional factors including M_w and T_g.

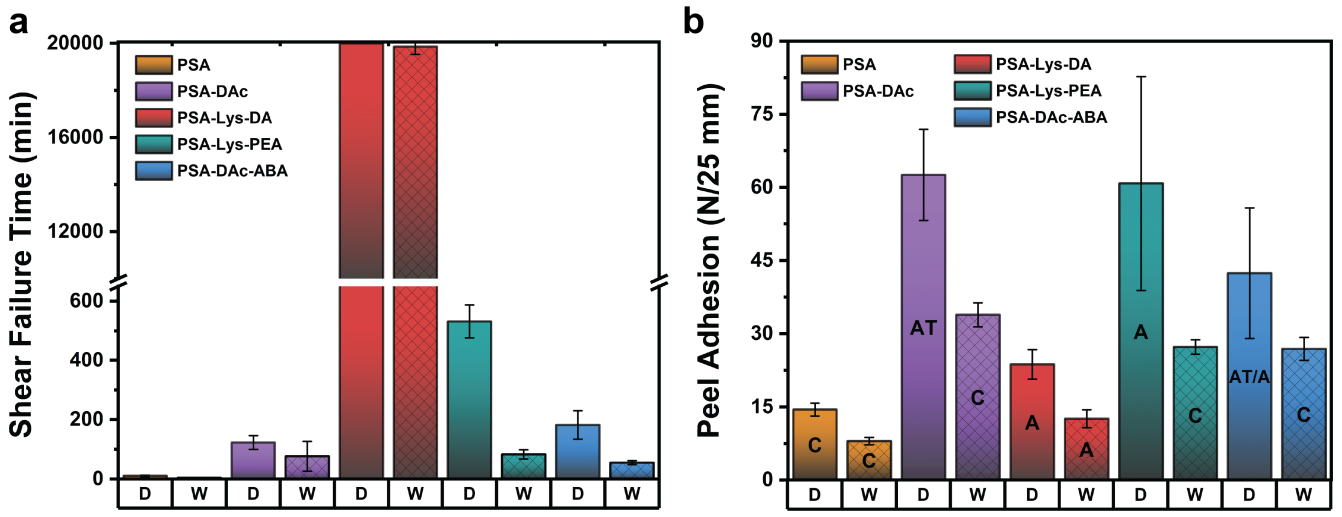

Figure 4. Macroscopic characterization of PSA tapes. **(a)** Shear failure time after 10 min conditioning in ambient (D) and wet (W) conditions. **(b)** 180° peel adhesion after 24 h conditioning in ambient (D) and wet (W) conditions. The failure modes are denoted as: C=cohesive, A=adhesive, and AT=adhesive transfer.

The most interesting finding was the remarkably large failure times observed for PSA-Lys-DA, which was on the order of 20,000 minutes or more compared to <600 minutes for all other samples. This outstanding performance can indicate the significant enhancements in the intermolecular interactions in PSA-Lys-DA, possibly owing to the augmented covalent and non-covalent interactions such as additional hydrogen bonding due to the presence of amine groups as well as strong cation-π interactions between the charged amine and catechol motifs, in a similar manner to their recently highlighted role in improving cohesive strength of Mfps.[10a, 26]

To understand the effects of the aromatic molecular structure on the strength of the cohesive cation-π interactions, we tested the shear holding power of PSA-Lys-PEA. Interestingly, the failure time in wet condition was not statistically different from that shown by PSA-DAc, although PSA-Lys-PEA outperformed other polymers except for PSA-Lys-DA when considering dry shear holding power. The results underline the key role of cation-π interactions in boosting the cohesive strength of the adhesive films. However, when compared against PSA-Lys-DA, the catechol-containing polymer displayed significantly larger failure times, both in ambient and wet conditions. Such a notable difference between failure times of PSA-Lys-DA and PSA-Lys-PEA polymers can possibly be attributed to the role of hydroxyl groups of the catechol in providing additional opportunities for intermolecular hydrogen bonding as well as acting as an anionic site for auxiliary charge interactions with cationic Lys groups.

To evaluate the possible impact of molecular design on cation-π interactions and cohesive strength of catechol-amine containing polymers, we studied shear holding power of PSA-DAc-ABA. Surprisingly, we did not observe a substantial increase in the dry and wet failure times as compared to PSA-DAc. Unlike the behavior noted at the molecular level in this study and recent SFA measurements by others,[9a] the static shear test results indicate that close proximity of cation-aromatic binding pairs can significantly affect the macroscopic cohesive strength. The results might also explain why marine mussels have evolved to secrete adhesive proteins with Dopa and Lys pairs located mostly adjacent to each other rather than separated by spacer amino acids such as glycine. The findings here also motivates further studies to investigate the effects of proximity of catechol and cationic amine moieties in mussel inspired adhesives across many length scales.

In addition to shear, conventional 180˚ peel adhesion tests were performed both in dry conditions and after immersion in water for 24 hours prior to the measurement (**Figure S48**). The results of the peel adhesion for PSA-DAc show that both dry and wet adhesion increase ~4-fold compared to the control PSA polymer (**Figure 4b** and **Table 2**). More importantly, the failure mode also changes from cohesive to adhesive transfer in ambient condition. This behavior can be attributed to the strong interactions of catechol with the metal substrate as compared to the PET backing material which leads to detachment of the polymer from the backing layer. In the case of PSA-Lys-DA polymer, although both dry and wet performance was improved compared to the control PSA, the increase in peel adhesion was not as significant as that observed for PSA-DAc. However, the most interesting observation was the change in the failure mode from cohesive to adhesive for both dry and wet measurements. This behavior can be ascribed to the magnified intermolecular and cohesive forces between the polymer chains in PSA-Lys-DA owing to the presence of cation-π interactions. The adhesive and cohesive performance of PSA-Lys-DA, in terms of both force values and failure mode, may be attractive for many practical applications of PSAs.

Peel adhesion results of PSA-Lys-PEA showed significant improvements in comparison to the control PSA which can partly be attributed to the increase in the T_g and consequently changes in the mechanical properties at room temperature. In dry condition, adhesive failure was observed, which can further underline enhancements in the intermolecular interactions resulting from cation-aromatic pairs in the polymer backbone. The PSA-DAc-ABA polymer showed average peel adhesion values between those measured for PSA-DAc and PSA-Lys-DA. However, since T_g of this polymer is somewhat different from those of the other two polymers, interpretation and direct comparison between the peel adhesion values should be done with caution.

Overall, the results of the static shear and peel adhesion measurements highlight the importance of balancing adhesive and cohesive properties to achieve optimal performance of mussel-inspired PSAs. In this sense, the performance shown by PSA-Lys-DA clearly stands out compared to all other polymers for its remarkable

shear strength conferred by strong cohesive interactions between catechol and amine functional groups. In addition, PSA-Lys-DA also showed improvements in both dry and wet peel adhesion compared to the control PSA, and more importantly we observed a change in the failure mode from cohesive to adhesive which is preferred for many practical applications.

Table 2. Summary of the adhesion characterization results of PSAs measured using SMFS, CPS, static shear test, and 180˚ peel adhesion experiments. The values in parenthesis for SMFS and CPS results correspond to the total number of events used to calculate the averages.

	Single Molecule Force Spectroscopy (SMFS)	Colloidal Probe Spectroscopy (CPS)	Shear Failure Time (min)		Peel Adhesion (N/25mm)	
Polymer	**Median Rupture Force (pN)**	**Median Separation Work ($J\times10^{-16}$)**	**Dry**	**Wet**	**Dry**	**Wet**
PSA	118 (2862)	0.27 (10996)	10.5 ± 3.3	3.9 ± 1.3	14.5 ± 1.3	8 ± 0.7
PSA-DAc	235.8 (6088)	5.41 (8061)	122.9 ± 23.5	76.7 ± 50	62.5 ± 9.3	33.9 ± 2.4
PSA-Lys-DA	430 (4822)	9.72 (6292)	>20000	19858.6 ± 327.4	23.7 ± 3	12.6 ± 1.8
PSA-Lys-PEA	125 (29728)	3.51 (8850)	531.6 ± 55.6	82.9 ± 15.4	60.8 ± 22	27.3 ± 1.5
PSA-DAc-ABA	350.7 (7568)	8.76 (8020)	182.1 ± 47.8	55.2 ± 7	42.4 ± 13.4	26.9 ± 2.3

Conclusion

Altogether, in this work we applied the recently highlighted compositional and structural aspects of Mfps into our modular PSA designs and investigated the effects of molecular architecture and aromatic structure on the cooperative adhesive effects of catechols and amines. An important finding of this work is that comprehensive adhesion measurements across different length scales are crucial in decoupling contributions from interfacial adhesive and intermolecular cohesive interactions on overall PSA performance, highlighting the benefits of a multi-scale approach.

Our results from AFM-based molecular and microscopic force spectroscopy experiments showed significant improvements in interfacial adhesion of catechol-amine PSAs compared to the amine-free polymers, possibly owing to the synergistic effects between catechols and amines. Macroscopic adhesion results further indicated that coexistence of catechol and amine moieties in a hybrid monomer architecture can lead to optimization of overall performance of the catechol-amine adhesives and developing PSAs with remarkable resistance to flow under shear. Moreover, by substituting phenyl for catechol in the hybrid monomer structure we showed that incorporating phenyl-amine pairs into polymer backbone cannot provide a clear benefit in improving interfacial adhesion with surfaces. However, PSA with phenyl and amine groups coupled together demonstrated a satisfactory performance in macroscopic shear and peel adhesion tests, underlining the key role of cation-aromatic pairs as compelling molecular modules in enabling robust cohesion of mussel-inspired adhesives and hydrogels. Finally, since the precise positioning of catechol and amine motifs adjacent to each other in a fixed architecture is synthetically demanding, the intriguing possibility of achieving similar synergistic effects through a random distribution of these groups motivated us to study adhesive performance of PSA polymer with catechol and amine moieties incorporated as separate monomers. Interestingly, both SMFS and CPS results indicated that molecular architecture and adjacency of these groups is not necessary for establishing the synergistic effects. However, the cooperative effects between catechols and amines were not observed at macroscopic level in static shear or peel adhesion tests when amine and catechol groups were decoupled from each other in monomer architecture.

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Keywords: Mussels • Catechol-amine Synergy • Bioinspired • Adhesives • AFM Force Spectroscopy

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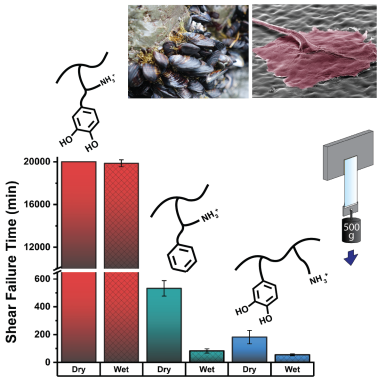

We report design and synthesis of a new generation of amino-catechol adhesives by copolymerization of traditional monomers with novel mussel-inspired monomers. Our multi-scale adhesion characterization results indicated that coexistence of catechol and amine moieties in a hybrid monomer architecture can lead to optimization of overall performance of the catechol-amine adhesives and developing PSAs with remarkable resistance to flow under shear.