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Pressure-Responsive Polymers

Direct Correlation between Local Pressure and Fluorescence Output in Mechanoresponsive Polyelectrolyte Brushes**

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In recent years, there has been huge progress in the development of stimuli-responsive polymeric materials,[1] and especially mechanoresponsive polymers, which convert mechanical stimuli into optical, electrical or chemical signals are a particularly attractive class of materials.[2–5] An ultimate goal of such materials would be to emulate the unique responsiveness of human skin, which can detect gentle touches of around 1 kPa at a spatial resolution of about 40 μm.[6]

Here, we introduce a new concept for optical force mapping based on mechanoresponsive polyelectrolyte brushes, which in addition to their response to force also respond to changes in the chemical environment.[7] Dense, strong polyelectrolyte brushes are hard to compress due to the increase of the osmotic pressure of the counter-ions and the excluded volume interactions between the individual chains.[8,9] Thus, they are not mechanically responsive per se, and to generate an optical signal a "mechanophore"[10] needs to be introduced. Previously, we used a pH-sensitive dye to act as a mechanosensitive building block, where the dissociation constant of the dye was a function of brush compression.[7] However, the dye was only infiltrated into the brush and not a covalent part of it. Furthermore, only qualitative information on the correlation between pressure and optical response was obtained. The key advance in the present work is the quantitative characterization of the mechanoresponsive properties of polyelectrolyte brushes functionalized by covalent attachment of fluorescent dye molecules. We have determined a response function $I(p)$, which correlates local fluorescence intensity (I) to local pressure (p) and we have found an excellent pressure sensitivity in the order of 10 kPa and a lateral resolution better than 1 μm.

Our experimental platform consists of cationic poly[2-(methacryloyloxy)ethyl]trimethyl ammoniumchloride (PMETAC) brushes with a covalently attached fluorescent dye, 5(6)carboxyfluorescein (CF) (Figure 1; see Supporting Information (SI) for details on synthesis). To these brushes a defined force was applied using soft colloidal probe atomic force microscopy (AFM),[11,12] where an elastomeric particle is pressed against the substrate surface of interest with well-defined forces while the contact area between particle and substrate is monitored in situ with confocal laser scanning microscopy (CLSM) (Further information in SI 1).

A standard force experiment on PMETAC copolymer brushes with 10% fluorescently labeled monomers is shown in Figure 2. When approaching the bead to the surface (Figure 2a–c), a dark area was observed where the bead was in contact with the brush. With increasing force, the contact area became larger due to elastic deformation of the polydimethylsiloxane (PDMS) bead. When retracting the bead from the brush (Figure 2d–f), the radius of the dark contact area decreased with a significant hysteresis as a result of adhesion forces acting between the bead and the brush.[13] The most striking feature of the retract cycle was a bright "rim" surrounding the edge of the contact area. Control experiments on neutral brushes showed virtually no changes in fluorescence upon compression (see insets in Figure 2a–f) while cationic brushes with different concentrations of dye showed qualitatively the same response as shown in Figure 2. The rates of compression and release were chosen such that the deformation kinetics of the bead did not interfere with the brush response to changes in pressure, with the fluorescent signal stabilizing well before the acquisition time of 1–2 s. The fluorescence output remained constant for at least several minutes and the response was completely reversible. When the bead was detached from the surface, the initial value of the fluorescence intensity was recovered. As demonstrated in Figure 3, force cycles could be repeated for at least four times without significant changes of the response.

Looking at the molecular nature of the polyelectrolyte brush, the question arises why the fluorescence intensity of the brushes is a function of the applied force. Studies on CF

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Supporting information for this article (full experimental details on polymer brush formation and characterization and determination of fluorescent monomer loading in brushes as well as a detailed description of soft colloidal probe experiments and JKR analysis) is available on the WWW under http://dx.doi.org/10.1002/anie.201102560.

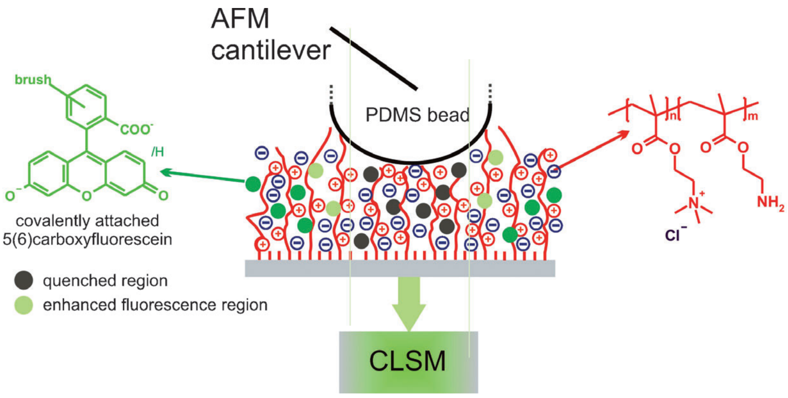

Figure 1. Experimental design to measure the fluorescence-based readout of the effect of mechanical compression of functionalized polyelectrolyte brushes using a soft colloidal probe.

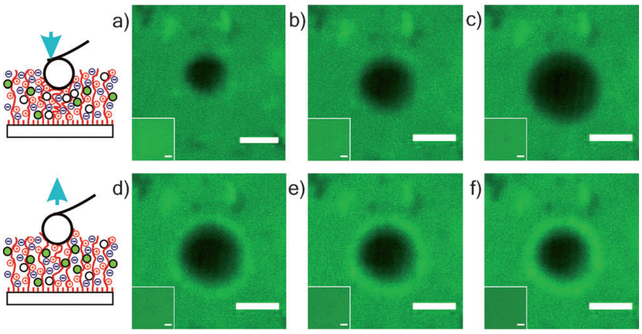

Figure 2. Representative compression experiment on fluorescently labeled PMETAC brushes in water. a–c) Fluorescence images during approach, using loads of 0.7, 2.8, and 5.6 μN. d–f) Fluorescence images during retraction, using loads of 2.8, 0.7, and −1.4 μN. Scale bars represent a length of 5 μm. Insets show absence of any changes in fluorescence intensity during compression experiments on neutral brushes at loads of 0.3 (a), 1.3 (b), and 1.9 μN (c) during the approach and 1.3 (d), 0.8 (e), and −0.5 μN (f) when retracting.

encapsulated in liposomes at 0.2 M showed 97 % fluorescence concentration quenching, with the residual fluorescence arising from dye molecules interacting with lipid.[14] Furthermore, CF forms non-fluorescent complexes with quaternary ammonium group containing polymers,[15] which we also observed when METAC is added to a CF solution (SI 3). Considering the high loading of dye in our brushes (0.1–0.4 M), and the possibility for the dye to complex with the cationic PMETAC brushes, we believe that the variations in fluorescence intensity are caused by reversible association of CF with the polymer brush. Compression leads to a higher local concentration of quaternary ammonium groups and an additional driving force for remaining free dye to form non-fluorescent complexes thereby extinguishing the remaining CF fluorescence. Conversely, the adhesion of the brushes to the beads leads to stretching of the chains and lowering of the local METAC concentration and hence a local higher concentration of dissociated dye molecules and a slightly brighter rim.

This molecular picture of the response of the dye-functionalized brushes to mechanical deformation can be quantified by modeling the contact situation underneath the PDMS bead with the theory developed by Johnson, Kendall and Roberts (JKR theory, see SI 5.1 for a discussion of assumptions).[16,17] In a simplified approach, the PDMS bead is regarded as an elastic bead in contact with the polyelectrolyte brush as a hard adhesive substrate. In such a situation, JKR theory predicts that the pressure distribution underneath the bead is governed by the interplay between compression and adhesion. Analytically, the pressure profile underneath the bead can be described by Equations (1) and (2):

$$p(r) = p_0\left(1-\frac{r^2}{a^2}\right)^{1/2} + p_1\left(1-\frac{r^2}{a^2}\right)^{-1/2} \quad (1)$$

$$p_0 = \frac{3Ka}{2\pi R} \text{ and } p_1 = -\sqrt{\frac{3Kw}{2\pi a}} \quad (2)$$

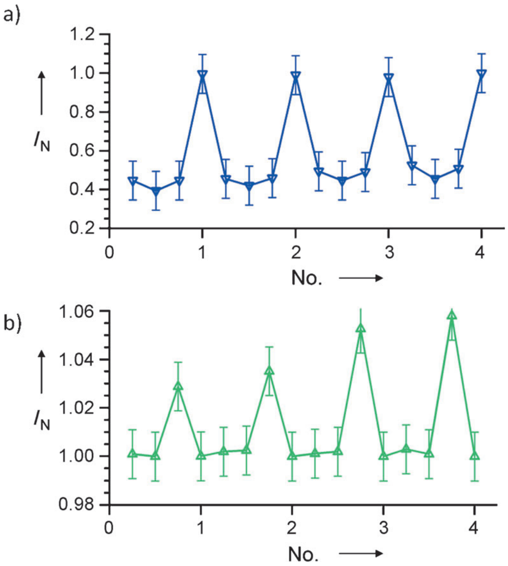

Figure 3. Reversibility of the response to compression and retraction of the bead measured in the a) dark center and b) bright edge, respectively. Values are the average of 3 measurements. One cycle shows the response I_N (normalized by the background intensity) to 0.6 μN and 2.9 μN loads during approach and a 0.6 μN load and completely withdrawn state during retraction.

where R is the effective radius of curvature, K is the effective elastic modulus of the system, w is the thermodynamic work of adhesion per unit area, $a(R,K,w,P)$ is the contact radius, and r is the distance from the axis of cylindrically symmetric systems. Elastic deformation of the bead on the surface leads to a positive contribution to the pressure and a zone of compressive stress underneath the bead [first part in Eq. (1)]. At the edge of the contact area, adhesive contributions dominate, resulting in a region with negative pressure (tension) [second part in Eq. (1)]. This tensile stress is very high at the edges.

We can now correlate the computed pressure profiles with extracted intensity profiles (obtained from data analysis with Image J). Figure 4a shows the calculated pressure profile for an adhesive contact using JKR theory (w, K and P measured by force spectroscopy, a calculated and measured, r measured by CLSM) and the experimentally obtained fluorescence intensity profiles. One finds a decrease in fluorescence intensity (as compared to the background intensity) in areas of compression and a slight increase of fluorescence in areas of tension. These lateral variations of fluorescence intensity can be explained by the variations in local pressure in the contact area, as described by Equation (1): when a load is applied by the bead, the spherical bead shape results in a higher pressure in the center of the contact area, which decreases with increasing distance from the center. In our case additional adhesive interactions are present, leading to a transition to negative stresses at the edge of the contact. When the measured fluorescence intensity is correlated with the calculated lateral pressure variation, we obtain the response function $I(p)$, that is, the dependency of the local fluorescence intensity as a function of local pressure (Figure 4b). Figure 4b shows data for applied loads ranging from 0.9 to 4.5 µN while retracting, and clearly shows that all $I(p)$ data collapse onto one master curve, independent of the applied external load.

Brush compression can also be induced by the addition of salts,[18,19] and Figure 4c shows that the response function drastically alters as the NaCl concentration is increased from 0.1 M to 1 M, with fluorescence intensity dropping strongly at high salt concentrations. Importantly, the dependency of the relative intensity I_N (absolute intensity divided by the background intensity) on p is only weakly changing with salt concentration. Thus normalization provides a means to eliminate the effects of salt concentration on fluorescence over a broad range (zero up to greater than 1 M NaCl). The fluorescence output and responsiveness of the brushes can be switched off by the addition of 0.1 M $NaClO_4$, which leads to hydrophobic collapse and dehydration of the brushes.[20]

In summary, we have demonstrated mechanoresponsive polyelectrolyte brushes which show a strong correlation between local fluorescence intensity and local (calculated) pressures. The response of the surface to mechanical stimuli was completely reversible and provided a sensitivity under 10 kPa. The combination of very high lateral resolution over

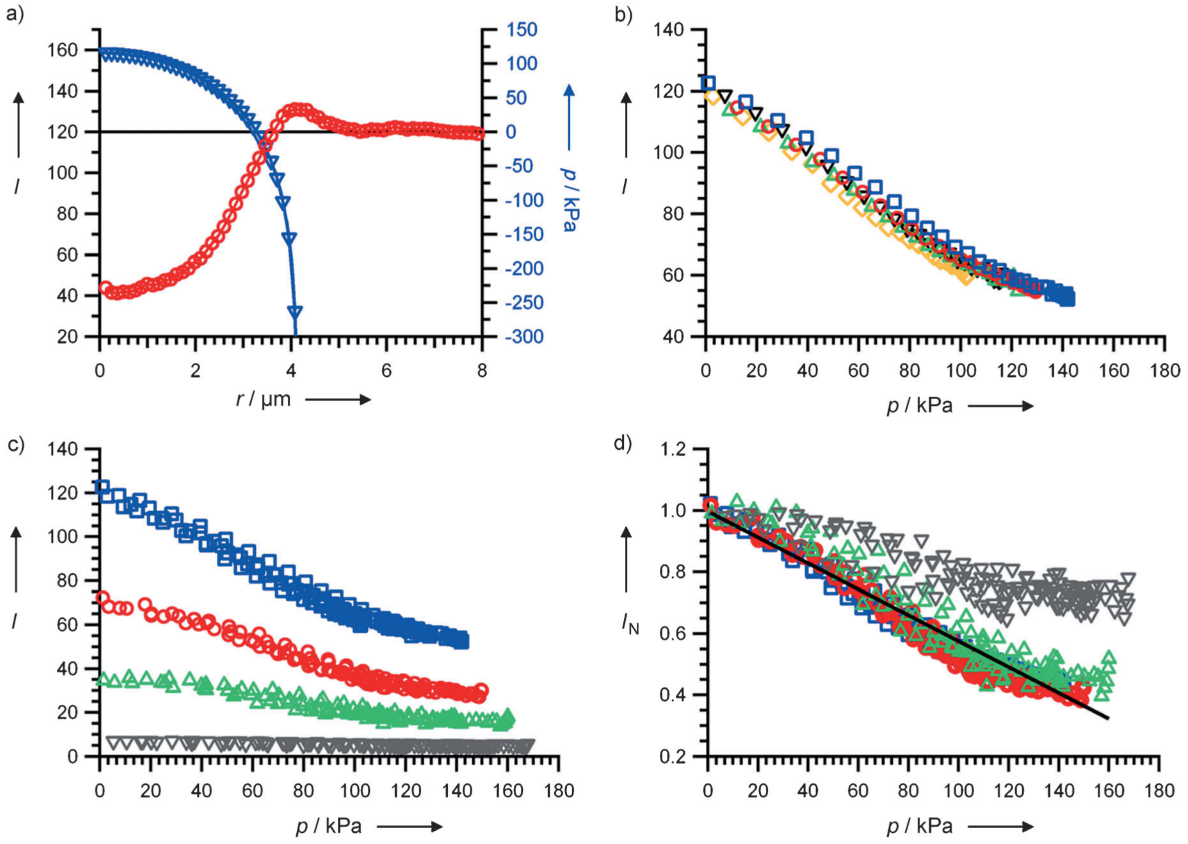

Figure 4. a) Extracted intensity profile and calculated pressure profile on applied load (1780 nN) in water while retracting (Young's modulus $E = 0.8$ MPa, adhesion energy per unit area $w = 19$ mJ m^{-2}): red ○, intensity profile; blue ▽, pressure profile. b) Response functions $I(p)$ correlating fluorescence intensity vs. calculated pressures under spherical bead at five different loads: blue □, 4.5 ± 0.9 µN; red ○, 3.6 ± 0.7 µN; green △, 2.7 ± 0.5 µN; gray ▽, 1.8 ± 0.4 µN, yellow ◇, 0.9 ± 0.2 µN. c) Response functions acquired in Millipore H_2O (blue □), 0.1 M NaCl (red ○), 1.0 M NaCl (green △), 0.1 M $NaClO_4$ (black ▽). Each dataset contains five different forces while retracting. d) Data of (c) normalized by the background intensity. Data for H_2O, 0.1 M NaCl, and 1.0 M NaCl fall on a common mastercurve, shown by the linear fit (black line). (Further details in SI 5.3.)

large areas, good pressure sensitivity, response times in at least the sub-second range and the ability to measure compression and tension simultaneously makes this sensor an outstanding starting point towards mechanoresponsive surfaces with potential applications in for example robotics or fundamental studies on bioadhesion phenomena.

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