Elastic Contact Induced Self-Organized Patterning of Hydrogel Films

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ABSTRACT: When a flat rigid stamp contacts the surface of a soft hydrogel film, a competition between the adhesive and elastic forces engenders an isotropic, labyrinth pattern on the length scale of ∼3*H*, where *H* is the film thickness, We present here a very simple, self-organized technique for aligning and modulating these patterns by using a patterned stamp and by changing the film thickness and the stamp−film intersurface distance. Many complex structures such as an array of femtoliter beakers and doubly periodic channels are generated from a simple stamp. The elastic nature of the patterns allows in-situ tuning, manipulation, and reconfiguration of structures. The patterns can also be made permanent by drying of the hydrogel.

Introduction

Hydrogels are an important class of material in a wide range of chemical and biological applications because of their biocompatibility and response to a host of stimuli like pH, ionic strength,[1] temperature,[2] electric field,[3] light,[4] presence of chemical species,[5] etc. Hydrogel films thus find important applications in substrata for cell cultures and cell immobilization, tissue engineering,[8] biological and chemical sensors, electrophoretic separation and chromatography, drug delivery,[9] flow actuators in microfluidics,[10] and many other applications. Micropatterned hydrogels are also useful in enhancing the effectiveness of sensors, preparation of arrays of tiny beakers for confined chemistry and DNA chip applications, probing of cell behavior on patterned surfaces, microfluidics, and lab-on-a-chip applications.[6−8,10−17] Previously, patterning of hydrogels has been primarily performed by photopolymerization of liquid monomers/precursors, by micromolding in capillaries,[10−19] or by transfer of pattern from a photoresist coating on the gel patterned by conventional optical lithographic techniques[20−22] followed by etching. Finally, room temperature imprint lithographies require application of very high, uniform pressures and specialized equipment.[23]

We propose here a very simple and rapid technique for self-organized mesopatterning of thin hydrogel films, which is based on the surface instability and isotropic deformations of a thin soft elastic film when it is brought in adhesive proximity to another flat rigid surface or stamp.[24−29] Previous experiments on the elastic contact instability are limited to cross-linked PDMS elastomers using a flat stamp[24] or a macroscopically curved glass coverslip.[25,27] The former produces an isotropic labyrinth structure,[24] and the latter results in a line of fingers[24,27] near the contact zone. We show for the first time that the isotropic elastic patterns seen previously in PDMS elastomers can also be engendered in hydrogels with a flat stamp. More importantly, these isotropic patterns can be aligned, ordered, and modulated by using a patterned stamp and by changing the film thickness and the stamp−film intersurface distance. The elastic contact instability can generate a variety of complex ordered structures from the *same* stamp, thus pointing a way toward an in-situ control, manipulation, and reconfiguration of “structures on demand”. The patterning occurs spontaneously at room temperature in the solid phase directly in a single step without the application of outside pressure as in the imprint lithographies,[23] and the technique is not limited to photopolymerized gels. The gentle nature of the elastic deformations in this technique also ensures minimal chemical and plastic deformation induced mechanical alterations and damage to the gel.

The proposed technique is based on the self-organization in thin soft films when they are confined by the adhesive forces such as the van der Waals and electrostatic. Such highly confined films are inherently metastable or unstable and thus readily self-organize their shapes to reduce the total energy. In particular, it is known that thin flat PDMS elastomeric films deform spontaneously when brought in contact with another rigid flat surface, and the resulting isotropic labyrinth like structures exhibit a characteristic wavelength.[24−29] The wavelength shows a short length scale (of the order of the film thickness), which depends linearly on film thickness. Interestingly, the lateral length scale of the instability patterns is independent of the mechanical properties of the film and also independent of the nature and strength of the adhesive interaction between the film and the stamp surface.[24−29] On the basis of the in-situ optical microscopy observations in relatively thick (tens to hundreds of microns) PDMS elastic films, it is known that the length scale of the structures is about 3*H* to 4*H*, where *H* is the film thickness. The origin and characteristics of this contact instability at soft interfaces are also theoretically understood[25,26,28,29] by considering the competition between the attractive adhesive interactions which are destabilizing and the elastic restoring force which tends to stabilize the surface. The surface instability is initiated at small critical intersurface separation distances (∼10 nm) when the adhesive attractive interaction energy overcomes the elastic deformation energy penalty.[24−28] However, after the initiation of the instability, the patterns formed by the adhesion of the film surface to the stamp do not completely disappear when the stamp is withdrawn away from the film. Complete detachment of the stamp or debonding occurs at intersurface distances far exceeding the distance at which the instability is first initiated on approach of the stamp. This “bonding−debonding” hysteresis has been theoretically shown to be caused by the pinning of the patterns in locally metastable states during the stamp pull-off.[28] These theoretical ideas point to the possibility of controlling the length scale and morphology of the instability patterns by the modulation of the

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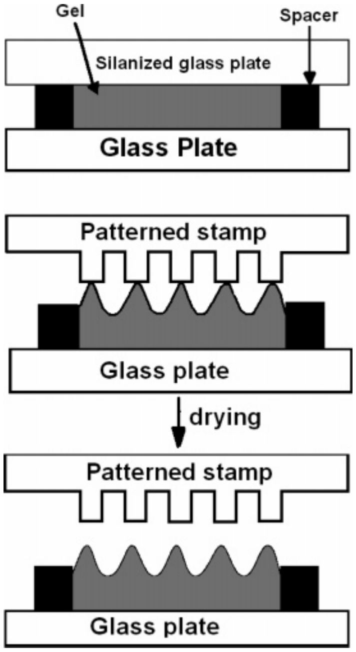

Figure 1. Schematic of a thin hydrogel film casting and patterning by elastic contact lithography.

film thickness, by the use of prepatterned stamps,[30] and by changing the stamp−film intersurface distance (vertical amplitude of the patterns).

In what follows, we demonstrate the elastic contact instability and its modulation and control in hydrogel films. The technique also has the potential to develop into a new soft lithography which may be referred to as "elastic contact lithography (ECL)". In view of its theoretical underpinnings, the technique is also applicable for a simple, direct patterning of a variety of soft solids other than hydrogels, including radiation-insensitive materials. The technique appears to be especially suitable for the laboratory scale, bulk-meso applications probing the cellular responses, confined chemistry, optical properties, etc., where fidelity requirements are not as stringent as in device manufacturing. In some tissue culture and artificial organ applications,[8] hydrogels to be patterned have embedded cells necessitating patterning by gentle methods without excessive pressures, temperatures, radiation exposure, and etching.

Materials and Methods

The polyacrylamide hydrogels were prepared by the polymerization of acrylamide and *N*,*N*-methylenebis(acrylamide) (MBAA, cross-linking agent) in aqueous phase. A solution of acrylamide (10% w/v) and MBAA (4% w/v) in water was prepared, to which *N*,*N*,*N*,*N*-tetramethylethylenediamine (TEMED) (1.25% w/v) was added as catalyst, and the free radical polymerization reaction was initiated by the addition of ammonium persulfate (0.5% w/v). The reaction was allowed to proceed at room temperature, and the gelation time was about 5 min.

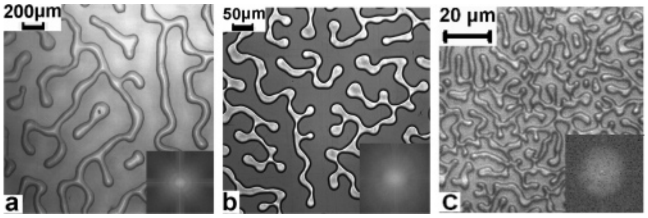

Figure 2. Optical micrographs of elastic instability patterns in hydrogel films when a flat stamp is first brought in adhesive contact with the film. The film thickness and the wavelengths of the isotropic labyrinths correspond to (a) $H = 60$ μm, $\lambda = 196.8 \pm 14.65$ μm, (b) $H = 20$ μm, $\lambda = 56.69 \pm 7.28$ μm, and (c) $H = 2$ μm, $\lambda = 5.89 \pm 0.615$ μm.

The reaction mixture was cast between two cleaned glass plates; one of the plates was silanized with *n*-octadecyltricholorosilane (OTS) for easy release of gel from the glass plate, and photoresist spacers were formed on the other plate to control the thickness of the hydrogel thin films cast. The height of the spacers varied between 1 and 60 μm. Glass plates were silanized by immersion in the silanizing solution consisting of 0.3 mM OTS in a 7:3 mixture of hexadecane and chloroform. The schematic of the process of producing thin hydrogel films is shown in Figure 1. The polymerization reaction results in the formation of the gel in about 5 min at room temperature of about 25 °C. The glass plates were separated, leaving the thin film of gel on the nonsilanized glass plate. The gel layer was dried for 10−60 s before bringing it in contact with a stamp. The soft gels that could be patterned had more than 70% w/w water content at the time of casting. Patterns were generated by bringing a stamp (prepatterned or flat) into close adhesive proximity to the film. The patterns were made permanent by a complete drying of the film, which preserved the pattern. Silanized silicon wafer stamps (flat and patterned) were used for easy release from the patterned film. The patterns could be observed in situ under an optical microscope (Leica DMLM) before removal of the stamp, and the dried patterned gels were investigated by intermittent contact mode atomic force microscopy (Molecular Imaging) after removal of the stamp. The intersurface distance was measured by the height of the structures.

Results and Discussion

Figure 1 represents schematically the process of casting a thin hydrogel film and the key steps in the elastic contact lithography to pattern the film. The hydrogel film deforms spontaneously to form an isotropic labyrinth structures when it comes in contact with a flat rigid stamp, as shown in the optical micrographs of Figure 2. The dominant wavelengths of the patterns as determined from the FFTs of the images are shown in the insets. The pattern wavelength varies with the film thickness: 196.8 ± 14.65 μm for a 60 μm thick film (Figure 2a), 56.69 ± 7.28 μm for a 20 μm film (Figure 2b), and 5.89 ± 0.615 μm for a 2 μm film. The pattern length scales are thus in line with the expectations of the theory for elastic contact instability, which predicts $\lambda \sim 3H$.[25,26,28,29] The structures thus formed relax to the original flat film morphology when the stamp was completely withdrawn. However they could be preserved by drying prior to the removal of the contactor. The lateral length scales of the structures did not change systematically upon variation of the water content of the film (70−85% w/w), whenever the film was soft enough to form the patterns. Films below 70% water content were found to be too stiff for the initiation of the elastic contact instability. The independence of the length scale on the elastic modulus is also known in experiments with PDMS elastomeric films[25,27] and theoretically anticipated[24−28] as discussed below.

The linear dependence of the length scale on the film thickness can be understood by the following simplified scaling analysis. The elastic strain energy (per unit area) of the film surface deformation is given by[25,26,28] $U \sim \mu H(\partial v/\partial x + \partial u/\partial z)^2$, where μ is the elastic modulus, H is mean film thickness, x and z are the lateral and the normal directions, and u and v are the components of the displacement field in the x and z directions, respectively. The displacement continuity equation, $(\partial u/\partial x + \partial v/\partial z) = 0$, together with the characteristic length scales, $x \sim \lambda$, $z \sim H$, and $v \sim \delta$ (vertical amplitude of the pattern), finally give a simple scaling for the elastic stored energy due to the shear and normal deformations of the film:

$$U \sim \mu H\delta^2(\lambda^{-1} + \lambda H^{-2})^2$$

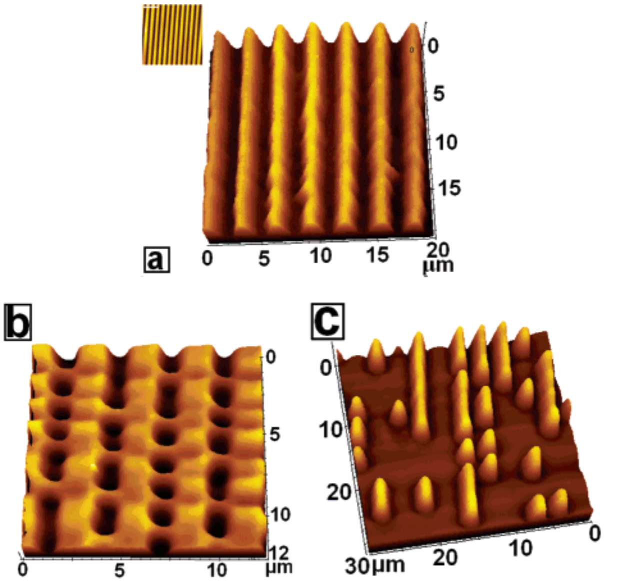

Figure 3. AFM images of the patterns formed in a hydrogel film of thickness 1.14 μm by elastic contact lithography using a stamp shown in the inset of (a). (a) Positive replica of the stamp formed in the film; pattern height = 143.53 ± 11.64 nm. (b) Array of femtoliter beakers formed by a closer proximity of the stamp; pattern height = 104.67 ± 9.66 nm. (c) Ridges of (a) fragment into columns at increased separation; pattern height = 205.54 ± 7.15 nm.

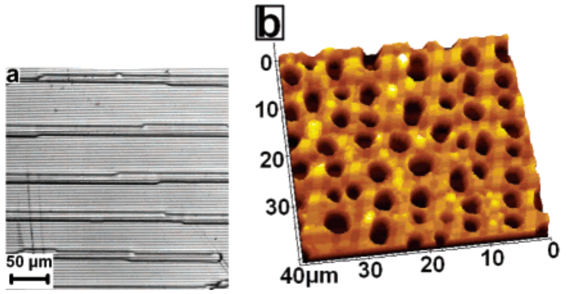

Figure 4. Patterns formed in hydrogel films when the stamp pitch (~3 μm) is smaller than the instability wavelength, $\lambda \sim 3H$. (a) Regions of complete contact (ridges) are separated by the elastic instability length scale in a 20 μm thick film. (b) Incompletely aligned beakers form when the film thickness is about 2 μm.

Basically, the energy penalty for deformations increases both for very short ($\lambda \ll H$) and for very long ($\lambda \gg H$) waves, and thus the minimum elastic energy pattern (for which $\partial U/\partial\lambda = 0$) has a length scale of the order of the film thickness, $\lambda \sim H$. A detailed linear stability analysis of the governing equations provides the numerical prefactor, $\lambda \approx 3H$.[25,26] Interestingly, the analysis shows that the lateral length scale at the onset of instability is independent of the elastic modulus of the film. A nonlinear analysis[28] further shows that the length scale in fact also remains rather robust regardless of the stamp−film separation because of the pinning of the structures in a local metastable state. However, the 2-D nonlinear analysis[28] does not address the issue of the precise 3D morphology of the structures that are experimentally explored here.

The isotropic structures of Figure 2 can be aligned to yield regular patterns by the use of a prepatterned contactor. The patterned silicon contactor used was an array of protruding stripes of height, width, and periodicity of 200 nm, 1.5 μm, and 3 μm, respectively, as shown in the inset of Figure 3a. On bringing the patterned contactor in close proximity to the film, the regions of the film below the protrusions of the stamp experience greater adhesive interactions and thus deform to produce a *positive* replica of the ridges of the stamp, as shown in Figure 3a. The height of the features determined by AFM scans is 143.53 ± 11.64 nm. The pattern could be modulated by a simple displacement of the stamp in the normal direction with respect to the film. Interestingly, on a closer approach of the patterned stamp, the ridges are compressed and a secondary structure evolves to join the parallel ridges, periodically leading to an array of femtoliter beakers shown in Figure 3b. The center to center distance or the periodicity of the beakers corresponds to 2.88 ± 0.18 μm, which is again close to the elastic instability wavelength of $3H$. The height of the ridges in this configuration is 104.67 ± 9.66 nm. Thus, the self-organization by a mere vertical displacement of the stamp engenders a transition to 2-D instability and pattern even though the stamp features are strictly 1-D parallel channels in this case. On the other hand, increasing the stamp separation distance compared to that in Figure 3a results in the fragmentation of 1-D ridges into pillars that are oriented along the protrusions of the stamp and are of height 205.54 ± 7.15 nm (Figure 3c).

Another example below shows that the self-organized patterns follow the length scale of the elastic contact instability rather than the periodicity of the stamp. When the wavelength (~$3H$) of the contact instability becomes much larger than the stamp pitch, for example, when the film thickness is increased, the patterns in the film are still oriented along the features on the stamp, but the spacing between the ridges formed remains close to ~$3H$. For example, Figure 4a is the optical micrograph of the patterns formed by bringing in contact a stamp of 3 μm periodicity with a 20 μm thick film. The parallel ridges in contact with the protrusions of the stamp are now separated by a distance of 54.36 ± 5.94 μm, which again nearly corresponds to the elastic instability scaling of $3H$. Thus, ridges do not form under every protrusion of the stamp, and also, a single ridge spans across many protrusions. The ridges show some localized lateral bulging, but these could not be coaxed into the beaker-like 2-D structure of Figure 3b because of large interridge separation distance in this case. However, when the mismatch between the elastic instability length scale and the stamp periodicity is less, isolated depressions such as shown in Figure 4b could still form. In this case ($H = 2$ μm, $\lambda \sim 6$ μm, stamp pitch ~ 3 μm), a secondary beaker-like pattern is indeed observed, but its 1-D alignment along the stamp protrusions is less strict.

The above examples show that the pattern morphology and length scale can be varied greatly by changing the film thickness and the intersurface separation. The fact that the hydrogel patterns observed here have the same length scale (~$3H$) as in the PDMS elastomeric films of different cross-link densities[24,25,27] indeed supports the theoretical expectation[26,28,29] that the lateral length scale does not depend on the elastic properties of the film. Thus, the elastic contact induced patterning can work with a wide variety of soft materials because of its underlying physics which makes the pattern length scale largely independent of the material properties.

Conclusions

In summary, we have shown elastic contact induced instability and its control for micropatterning of hydrogel films by a novel soft lithography, elastic contact lithography (ECL). The patterns are formed directly in the solid phase with a one-step process. Various complex patterns such as an array of femtoliter beakers, doubly periodic channels, and aligned columns are generated in hydrogel films from a single stamp consisting only of parallel channels. The elastic contact lithography is quite distinct from the imprint lithography-based methods that aim for a *negative* replica of the stamp under high pressure and plastic deformations. In fact, the initial contact of the stamp in ECL generates a *positive* replica of the stamp, which can be further modulated to the shapes uncorrelated to the stamp topography by movement of the stamp. Elastic instability induced patterning is also rather general in that the soft solids like hydrogels can be readily patterned by this method, regardless of their radiation curing properties. Elastic contact lithography can thus further develop into a simple, flexible, rapid, and low-cost method suitable for large area patterning with the use of techniques, allowing precise positioning and movement of the stamp and the film. Further variants could include multiple layered films and coated stamps for enhanced flexibility. This “do-it-yourself” method requires no special lithography facilities and can thus be particularly useful to the researches who routinely require hydrogel patterned surfaces as substrates, templates, stamps, and molds for rapid prototyping and experiments, for example, in confined chemistry phenomena, microfluidics, and biological applications. The method has the advantage of patterning under gentle conditions, without excessive pressure, temperature, radiation, and chemical treatments, and thus may be especially suitable for applications involving structured hydrogels such as gels with embedded biomaterials and cells in tissue engineering.

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