Homeostatic growth of dynamic covalent polymer network toward ultrafast direct soft lithography

Di Chen¹,², Chujun Ni³, Lulin Xie², Ye Li², Shihong Deng², Qian Zhao²,³*, Tao Xie¹,²,³

Soft lithography is a complementary extension of classical photolithography, which involves a multistep operation that is environmentally unfriendly and intrinsically limited to planar surfaces. Inspired by homeostasis processes in biology, we report a self-growth strategy toward direct soft lithography, bypassing conventional photolithography and its limitations. Our process uses a paraffin swollen light responsive dynamic polymer network. Selective light exposure activates the network locally, causing stress imbalance. This drives the internal redistribution of the paraffin liquid, yielding controllable formation of microstructures. This single-step process is completed in 10 seconds, does not involve any volatile solvents/reactants, and can be adapted to three-dimensional complex surfaces. The living nature of the network further allows sequential growth of hierarchical microstructures. The versatility and efficiency of our approach offer possibilities for future nanotechnologies beyond conventional microfabrication techniques.

INTRODUCTION

Soft lithography plays an essential role in a wide range of modern technologies, including electronics (1), optics (2), and biology (3). It relies on a soft stamp with surface microstructures to realize various operations, such as microcontact printing, micromolding, and microembossing (4–6). Since the surface microstructures on the soft stamp are replicated from a photolithographically defined master, soft lithography can be viewed as an extension of photolithography (4). Photolithography itself has, for several decades, played a dominating role in industrial nanotechnologies due to its high throughput (7). It does, however, suffer from several drawbacks. Its typical process involves three steps: spin-coating of photoresist, light exposure, and development. In this multistep process, a large amount of waste is generated, often involving volatile organic solvents. In addition, the process is intrinsically limited to two-dimensional (2D) flat surfaces, which is a major bottleneck for future devices (8, 9).

We envision that a much more attractive process is to directly grow microstructures on a soft stamp, forgoing entirely the cumbersome spin-coating and development steps in a photolithographic process. For inspiration, we resort to the growth processes in nature. Plants can grow naturally, but this growth mode requires constant intake of nutrients from the soil and is time-consuming. In contrast, certain homeostatic growth (10) can be much more rapid. For instance, when a human body is bitten by a mosquito or hit by a large force, a bump would form immediately on the skin. This rapid process is due to its intrinsic mechanism that simply relies on the redistribution of the surrounding body fluid. We anticipate that a homeostatic process for self-growth of polymers can be potentially effective in addressing the aforementioned issues, simultaneously achieving high speed, high throughput, without generating any waste.

The idea of growing polymer objects has recently gained attention. Polymer networks with dynamic bond equilibrium or living initializing species allow insertion of additional monomers into the network structures (11–14). This process is similar to the plant growth, with monomers playing the role of nutrients. Consequently, the growth speed is likewise limited by the reaction kinetics. In addition, the reaction requires stringent conditions and involves volatile monomers. Dynamically cross-linked hydrogels and organogels can also alter their surface structures by adaptive swelling (15, 16). However, the volatility of the solvent/water makes it difficult to control and intrinsically challenging for high-fidelity growth of microstructures.

RESULTS

To mimic the homeostatic growth without the issues mentioned above, we design a liquid paraffin swollen gel with light responsive dynamic disulfide bonds (17–19) as the cross-linking moiety. The network (Fig. 1A) is formed by thermally polymerizing n-dodecyl acrylate and 2,2′-dithiodiethanol dimethacrylate [10 weight % (wt %) unless otherwise noted]. The obtained solid is then swollen in a liquid paraffin (n-hexadecane, melting temperature of 18°C) containing a photoinitiator. The obtained gel exhibits negligible mass loss below 150°C in its thermogravimetric analysis (fig. S1), confirming the nonvolatility of the paraffin. A comparative gel is synthesized similarly with a cross-linker that contains no disulfide bonds. Upon masked ultraviolet (UV) light exposure (365 nm, 66 mW/cm²) for 1 min, a surface pattern is formed on the dynamic gel (Fig. 1B), in sharp contrast to the nondynamic gel with no pattern formation under the identical condition. The photomask used in obtaining Fig. 1B, along with those used hereafter, is displayed in fig. S2.

Figure 1C illustrates the mechanism of microstructure formation for the dynamic gel. When the polymer network is swollen by the liquid paraffin, the network chains are in a highly stretched state. Spatioselective light exposure activates the dynamic disulfide cross-link bonds locally. This allows the stretched chain segments to relax, as driven by entropic elasticity. Because of the dilution effect of the liquid paraffin, when a disulfide bond reconnects, it is statically more likely to form an intrachain loop instead of the original cross-link. Consequently, the effective cross-linking density is reduced. We note that two other mechanisms displayed in Fig. 1C would also lead to reduction in cross-linking density, namely, the sulfur radicals can be terminated by the radical fragments from the...
photoinitiator, and the physical entanglement may also be reduced during the bond exchange process. A detailed comparative study presented in fig. S3 and related discussion suggests that the first and third mechanisms (i.e., loop formation and reduction in entanglement) play a dominant role. Nevertheless, the localized reduction in cross-linking density would drive the redistribution of the paraffin. Specifically, it would migrate from the nonexposed areas into the exposed areas, forming microstructures as a result. Overall, this self-growth process driven by the internal redistribution of the paraffin closely mimics the homeostatic processes in biology.

Figure 2A illustrates the kinetics of the microstructure formation. For a 200-μm-sized belt pattern, the feature height increases with the light exposure time, reaching a plateau value of 6.8 μm at around 10 s. Reducing the content of the disulfide cross-linker in the network formulation increases both the swelling ratio and the equilibrium feature height (Fig. 2B). The latter can reach 8 μm at 2 wt % cross-linker. Such a correlation is consistent with the mechanism outlined above. For the current material system, further reducing the dynamic cross-linker is prohibited since too much paraffin in the gel tends to weaken its mechanical properties (fig. S4). However, extension to other material systems in the future offers opportunities for improvement.

The gel thickness also has a slight influence on the feature height (fig. S4). We choose 1-mm-thick gels containing 10 wt % cross-linker for further investigation presented hereafter. With this gel, the equilibrium aspect ratio is found to increase with the reduction of feature size, reaching 0.25 for a feature size of 0.75 μm. Higher aspect ratios are expected for smaller features. In reality, however, significant reduction below 0.75 μm is prohibited for the current experimental setup since it would approach the diffraction limit of the UV light used. This study focuses mainly on establishing the photopatterning method using conventional photomasking techniques. In principle, further reduction of the achievable feature size is possible if more advanced photolithographic methods involving much shorter wavelength is used. For instance, the extreme UV (λ = 13.5 nm) lithography used in the chip manufacturing industry can achieve sub–20-nm features. However, the effect of shorter wavelength light on the dynamic bond exchange would require further investigation in the future. Figure 2D shows that different patterns can be obtained by simply altering the mask. In particular, the second image represents a dipped pattern obtained by light-induced growth of the surroundings around the dip features. Figure 2E illustrates a more complex array of cylinders fabricated using the identical process of single light exposure. The structure patterning can also be conducted with multiple light exposure. Starting from a featureless surface (Fig. 2F), line patterns of different orientations can be sequentially written onto the surface using the same photomask oriented at different angles. In general, the patterned gels are very stable at room temperature. Nondetectable change in weight or surface pattern can be found after keeping under ambient conditions for 1 week. However, the hexadecane can be removed by heating under 100°C for 24 hours (i.e., drying). Such a drying step erases the

Fig. 1. Light induced homeostatic growth on the gel surface. (A) Precursors of dynamic and nondynamic liquid paraffin gels. (B) Surface profiles for the dynamic (left) and nondynamic (right) gels. (C) Molecular mechanism for the growth process.
surface features (fig. S6), but the exact same surface features reappear upon reswelling in hexadecane.

We next use a commercial projector light (405 nm) as a more flexible digital mask to control the homeostatic growth. In this setup (Fig. 3A), multiple arbitrary light patterns can be generated by computer control. At its maximum light intensity of 5 mW/cm², the feature height grows (Fig. 3B) in a similar way to the UV light (Fig. 2A) but at a much slower rate. At 15-min light exposure, an equilibrium height of 22 μm is obtained for a belt pattern of 400-μm line width. A stepped pattern (Fig. 3C) can be generated by controlling spatially the exposure time. The digital light control allows creating more sophisticated patterns, including the ridge arrays of different heights (Fig. 3D) and ridge-valley arrays (Fig. 3E). Figure 3F illustrates that the homeostatic growth mechanism offers an unusual opportunity to dynamically manipulate the surface features. Starting from a line pattern, light exposure in the valleys between the line features induces structure growth accordingly. As the ridges grow in the valleys, the original line-ridge height continues to decrease to the extent that the ridges and valleys reverse. When the light exposure is switched to the original line ridge, the process is reversed. These interesting observations are the direct consequence of the internal redistribution of the paraffin. They represent versatilities beyond conventional light-patterned hydrogels (20, 21). Our material system uses a photoinitiator to trigger the disulfide exchange. In principle, disulfide bond exchange can also be directly triggered by UV, but it would demand a much higher light intensity or a much longer exposure time. Specifically, for the digital light (405 nm) used in our work, no surface pattern is formed without the photoinitiator (fig. S7). In contrast, with the photoinitiator, the gel can still be repeatedly patterned as shown in Fig. 3F.

Combining the digital and physical masks allows simultaneous control of the structure growth at both the macroscopic and microscopic scales. The result is the generation of physical mask–determined microstructures at locations defined by the digital light (Fig. 4A). Using this method, a diverse set of structural colored images are created using the same physical mask (Fig. 4B). Our approach of creating structural colored patterns is notably simpler and more flexible than existing methods (22, 23). Since the homeostatic growth mechanism does not require a spin-coating of a photoresist layer as conventional photolithography does, it can be, in principle, applied to complex nonplanar surfaces. Figure 4C demonstrates that multiscale features can be written onto the surface of a 3D complex object. Here, the hollow egg made of the dynamic gel is obtained using a 3D printed sacrificial mold. Two vertical curved regions are exposed to UV light with different masks, the blue squared region with a dotted microarray of 80 μm in diameter and yellow squared region with a millimeter-sized flower. The patterned dot array in the blue area is difficult to identify but is clearly visible in its optical microscopic image. In particular, the local curved contour is reflected in the surface profile. The macroscopic flower, while visible in the close-up

---

**Fig. 2. Controlling factors for the surface patterning.** (A) Impacts of exposure time on feature height. (B) Impact of cross-linking density on feature height and swelling ratio. (C) The aspect ratios of the microstructures at different feature sizes. (D) Surface profiles of a belt pattern (feature size, 0.75 μm; shown in fig. S5) and a dipped array. (E) Optical image of a cylindrical pattern and related profile. (F) Sequentially patterning process by rotating the same photomask.
Fig. 3. Digital mask based homeostatic patterning. (A) The experimental setup. (B) Impact of exposure time on feature height. (C) A stepped pattern (inset image) with its surface profile. (D) Ridge arrays of different heights and the corresponding surface profile of the rectangular area marked in red. (E) A ridge-valley array pattern (inset image) with the orthogonal surface profiles corresponding to the directions of the red and blue arrows. (F) Dynamic manipulation of the valley-ridge patterns and the corresponding surface profiles.

Fig. 4. Multiscale control of micropatterning by combining the digital and physical masks. (A) The process of combining the digital and physical masks (left) and the surface profile of a microstructured array confined in a macroscopic flower pattern (right). (B) Diverse structural colored patterns obtained using an identical physical mask (feature size, 2 μm) with additional digital light control by the projector. (C) Patterning on a 3D object with complex surface contours. Photo Credit: Chujun Ni, Zhejiang University.
view, becomes difficult for imaging under optical microscope. This is a direct reflection of the macroscopic curvature that makes it difficult to achieve optical focusing. Nevertheless, its existence is verified with an interferometer.

**DISCUSSION**

Our microfabrication method is distinctively different from soft lithography and conventional photolithography, although we use them as the closest references for introducing our homeostatic growth of microstructures. We believe that the direct growth of microstructures on a soft material is complementary to both those techniques. Its simple one-step process ensures its low cost, high speed, and high throughput, without requiring high-cost equipment. Its unique ability to dynamically manipulate surface microstructures in situ can be further explored for various engineering devices. Being adaptable to 3D complex surfaces is another unique attribute beyond classical microfabrication methods. The general principle can be expanded to a wide variety of dynamic polymers to satisfy the needs of different applications.

**MATERIALS AND METHODS**

**Materials**

The 2,2’-dithiodiethanol (98%) and methacryloyl chloride (98%) were purchased from D&B Biotechnology Co. and J&K Technology Co., respectively. Triethylamine (99.5%), dodecyl acrylate (90%), and N,N’-dimethyl aniline (99%) were all purchased from Aladdin Reagent Company. Dichloromethane (99.5%) was acquired from Sinopharm Chemical Reagent Company. Benzoyl peroxide (99%) and ethylene glycol dimethacrylate (98%) were obtained from Sigma-Aldrich. n-hexadecane (98%) was purchased from Macklin Biochemical Technology Company. Anhydrous magnesium sulfate (98%) and the photoinitiator [phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide, 2 mg/ml] were acquired from TCI chemicals. All chemicals were used as received. All the photomasks were custom-made by Suzhou Mask Optoelectronics Company and Shenzhen Luwei Photoelectric Company.

**Synthesis of 2,2’-dithiodiethanol dimethacrylate cross-linker**

The cross-linker was synthesized according to the procedure reported in the literature (24). Specifically, 2.0 g of 2,2’-dithiodiethanol was dispersed in 30 ml of dichloromethane, and 5.4 ml of triethylamine was added to make a clear solution. After cooling to 10°C, 3.14 ml of methacryloyl chloride was gradually introduced into the solution using a syringe. The reaction was allowed to proceed for 24 hours at room temperature under magnetic stirring. Afterward, the solid by-product was removed by filtration. The obtained filtrate was washed successively using a saturated sodium bicarbonate water solution, deionized water, and a saturated sodium chloride water solution. Anhydrous magnesium sulfate was introduced into the obtained solution to absorb water. Afterward, it was removed by filtration. The final product was obtained by volatilizing the solvent.

**Gel synthesis**

For a gel with 10 wt % cross-linker, 1.0 g of dodecyl acrylate, 100 mg of disulfide cross-linker, and 20 mg of benzoyl peroxide were mixed and stirred for an hour at 50°C. After cooling to room temperature, 20 µl of N,N’-dimethyl aniline was added, and the obtained solution was transferred to a mold. After 24 hours, a cross-linked solid polymer was obtained. The polymer was swollen in n-hexadecane with a dissolved photoinitiator [phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide, 2 mg/ml] to obtain a liquid paraffin gel. The gels with different disulfide bond densities were synthesized similarly except the amount of disulfide cross-linker was adjusted accordingly. A reference nondynamic paraffin gel was synthesized by replacing the disulfide cross-linker with 10 mg of ethylene glycol dimethacrylate.

**Surface patterning procedure**

For patterning via a physical mask, the gel was covered with a photomask and directly exposed under the UV light. For digital patterning, the light patterns were controlled by a computer and projected onto the gel surface through a projector. For the combined digital-physical patterning, the digital light was projected onto the gel sample covered by a physical photomask.

**Patterning on 3D objects**

The 3D egg was made by molding using a water-dissolvable sacrificial 3D printed mold (25). The obtained 3D egg was swollen in n-hexadecane with a dissolved photoinitiator [phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide, 2 mg/ml] to obtain a liquid paraffin gel. Two different regions of the gel were light-patterned using physical masks.

**Characterization**

The UV light source was IntelliRay 600 by Uvitron. The projector used for digital masking was made by Xianlin Company. Mechanical properties were tested using an Instron 5944 machine. Thermogravimetric analysis was performed using Thermal Gravimetric Analyzer (TGA) (STA 449F3 by Netzsch). Surface patterns were characterized by white light interferometer (NT9100 by Veeco) and scanning electron microscope (SU-3500 by Hitachi). The swelling ratio of a gel was calculated as 100% × (Mf − M0)/M0, where M0 was the mass of the dry polymer and Mf was the mass of the gel after reaching its swelling equilibrium.

**SUPPLEMENTARY MATERIALS**

Supplementary material for this article is available at https://science.org/doi/10.1126/sciadv.abj3760.

**REFERENCES AND NOTES**

1. J. A. Rogers, R. G. Nuzzo, Recent progress in soft lithography. Mater. Today 8, 50–56 (2005).
2. Y. Xia, E. Kim, X. Zhao, J. A. Rogers, M. Prentiss, G. M. Whitesides, Complex optical surfaces formed by replica molding against elastomeric masters. Science 273, 347–349 (1996).
3. G. M. Whitesides, E. Ostuni, S. Takayama, X. Jiang, D. E. Ingber, Soft lithography in biology and biochemistry. Annu. Rev. Biomed. Eng. 3, 335–373 (2001).
4. Y. Xia, G. M. Whitesides, Soft Lithography. Angew. Chem. Int. Ed. 37, 550–575 (1998).
5. X. Gao, X. Yan, X. Yao, L. Xu, K. Zhang, J. Zhang, B. Yang, L. Jiang, The dry-style antifogging properties of mosquito compound eyes and artificial analogues prepared so soft lithography. Adv. Mater. 19, 2213–2217 (2007).
6. S. Yu, H. Cho, J. P. Hong, H. Park, J. C. Jolly, H. S. Kang, J. H. Lee, J. Kim, S. H. Lee, A. S. Lee, S. M. Hong, C. Park, S. Yang, C. M. Koo, Shaping micro-clusters via inverse jamming and topographic close-packing of microbombs. Nat. Commun. 8, 721 (2017).
7. C. G. Willson, R. A. Dammel, A. Reiser, Photore sist materials: A historical perspective. Prog. SPIE 3051, 28–41 (1997).
8. S. Xu, Z. Yan, K. Jiang, W. Huang, H. Fu, J. Kim, Z. Wei, M. Flavin, J. McCracken, R. Wang, A. Badea, Y. Liu, D. Xiao, G. Zhou, J. Lee, H. U. Chung, H. Cheng, W. Ren, A. Banks, X. Li, U. Paik, R. G. Nuzzo, Y. Huang, Y. Zhang, J. A. Rogers, Assembly of micro/nanomaterials into complex, three-dimensional architectures by compressive buckling. Science 347, 154–159 (2015).
9. Y. Kim, H. Yuk, R. Zhao, S. A. Chester, X. Zhao, Printing ferromagnetic domains for unthethered fast-transforming soft materials. Nature 558, 274–279 (2018).
10. M. M. Lerch, A. Grinthal, J. Aizenberg, Viewpoint: Homeostasis as inspiration-toward interactive materials. Adv. Mater. 32, 1905554 (2020).
11. J. Cuthbert, A. Beziau, E. Gottlieb, L. Fu, R. Yuan, A. C. Balazs, T. Kowalewski, K. Matyjaszewski, Transformable materials: Structurally tailored and engineered macromolecular (STEM) gels by controlled radical polymerization. Macromolecules 51, 3808–3817 (2018).

12. M. Chen, Y. Gu, A. Singh, M. Zhong, A. M. Jordan, S. Biswas, L. T. J. Korley, A. C. Balazs, J. A. Johnson, Living additive manufacturing: Transformation of parent gels into diversely functionalized daughter gels made possible by visible light photoredox catalysis. ACS Cent. Sci. 3, 124–134 (2017).

13. L. Xue, X. Xiong, B. P. Krishnan, F. Puza, S. Wang, Y. Zheng, J. Cui, Light-regulated growth from dynamic swollen substrates for making rough surfaces. Nat. Commun. 11, 963 (2020).

14. T. Matsuda, R. Kawakami, R. Namba, T. Nakajima, J. Gong, Mechanoresponsive self-growing hydrogels inspired by muscle training. Science 363, 504–508 (2019).

15. B. D. Fairbanks, S. P. Singh, C. N. Bowman, K. S. Anseth, Photodegradable, photoadaptable hydrogels via radical-mediated disulfide fragmentation reaction. Macromolecules 44, 2444–2450 (2011).

16. F. Fan, C. Liu, S. Wang, J. Lv, W. Li, Y. Fu, H. Xu, Swelling-induced 3D photopatterning on a diselenide-containing elastomer. J. Mater. Chem. C 7, 10777–10782 (2019).

17. B. T. Michal, C. A. Jaye, E. J. Spencer, S. J. Rowan, Inherently photohealable and thermal shape-memory polydisulfide networks. ACS Macro Lett. 2, 694–699 (2013).

18. X. Du, J. Li, A. Welle, L. Li, W. Feng, P. A. Levkin, Reversible and rewritable surface functionalization and patterning via photodynamic disulfide exchange. Adv. Mater. 27, 4997–5001 (2015).

19. G. Deng, F. Li, H. Yu, F. Liu, C. Liu, W. Sun, H. Jiang, Y. Chen, Dynamic hydrogels with an environmental adaptive self-healing ability and dual responsive sol-gel transitions. ACS Macro Lett. 1, 275–279 (2012).

20. L. Huang, R. Jiang, J. Wu, J. Song, H. Bai, B. Li, Q. Zhao, T. Xie, Ultrafast digital printing toward 4D shape changing materials. Adv. Mater. 29, 1605390 (2017).

21. J. Kim, J. A. Hanna, M. Byun, C. D. Santangelo, R. C. Hayward, Designing responsive buckled surfaces by halftone gel lithography. Science 335, 1201–1205 (2012).

22. H. S. Kang, J. C. Jolly, H. Cho, A. Kalpattu, X. A. Zhang, S. Yang, Three-dimensional photoengraving of monolithic, multifaceted metasurfaces. Adv. Mater. 33, 2005454 (2021).

23. W. Fan, J. Zeng, Q. Gan, D. Ji, H. Song, W. Liu, L. Shi, L. Wu, Iridescence-controlled and flexibly tunable retroreflective structural color film for smart displays. Sci. Adv. 5, eaaw7355 (2019).

24. Y. Huang, R. Sun, Q. Luo, Y. Wang, K. Zhang, X. Deng, W. Zhu, X. Li, Z. Shen, In situ fabrication of paclitaxel-loaded core-crosslinked micelles via thiol-ene “click” chemistry for reduction-responsive drug release. J. Polym. Sci. Pol. Chem. 54, 99–107 (2016).

25. S. Deng, J. Wu, M. D. Dickey, Q. Zhao, T. Xie, Rapid open-air digital light 3D printing of thermoplastic polymer. Adv. Mater. 31, 1903970 (2019).

Acknowledgments: We thank Z. Fang and Y. Shi for helping with the digital projector. We also thank L. Chen for assistance on surface characterization with the technical support by State Key Laboratory of modern optical instruments. Funding: National Natural Science Foundation of China grant U20A6001 (to Q.Z.), National Natural Science Foundation of China grant 52033009 (to T.X.). Start-up funding of Ningbo Research Institute of Zhejiang University grant 202012320193 (to D.C.). Author contributions: Q.Z. and T.X. conceived and supervised the project. D.C. designed and performed the experiments with assistance from C.N., L.X., and Y.L. C.N. and S.D. printed the 3D sacrificial mold. D.C., Q.Z., and T.X. analyzed data and wrote the manuscript. All authors participated in the discussion. Competing interests: The authors declare that they have no competing interests. Data and materials availability: All data needed to evaluate the conclusions in the paper are present in the paper and/or the Supplementary Materials.

Submitted 28 March 2021
Accepted 26 August 2021
Published 20 October 2021
10.1126/sciadv.abi7360

Citation: D. Chen, C. Ni, L. Xie, Y. Li, S. Deng, Q. Zhao, T. Xie, Homeostatic growth of dynamic covalent polymer network toward ultrafast direct soft lithography. Sci. Adv. 7, eabi7360 (2021).