DOI: 10.1002/ange.201304333

Smart Materials

A Self-Powered Polymeric Material that Responds Autonomously and Continuously to Fleeting Stimuli**

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We describe herein the design of a polymeric material that performs a macroscopic function continuously once exposed to a specific stimulus, even when the stimulus is no longer present. The material is self-powered, requires no reagents from solution, operates autonomously, and converts chemical energy into a mechanical response. Thus, the design offers a combination of attributes that are not available currently in smart polymeric materials.[1]

To demonstrate these capabilities we prepared a modified TentaGel microsphere that is capable of initiating the pumping of fluid surrounding the microsphere (the macroscopic response),[2] even after the applied signal (UV light, a model stimulus) has been removed (Figure 1). The microsphere provides this continuous pumping response through networks of reactions that occur on the surface of, and perhaps within, the microsphere.[3] These chemical reactions enable not only selective responses to UV light, but also a means to propagate the response, even when the light is removed, which is a level of control that is analogous—in the regulated behavior—to externally controlled polymerization reactions.[4] The consequence of this network of reactions is the continuous production of small-molecule products that generate a gradient as they diffuse away from the microsphere (Figure 1). This gradient then induces movement of the surrounding fluid towards the microsphere (the pumping response).

On the molecular level, the ability of the material to continue performing its function arises from a self-propagating autoinductive reaction[5] that uses reagents, which are incorporated directly onto the polymer (see reagent **2**, which is grafted onto a 300 μm diameter TentaGel microsphere; Figure 1 and Scheme 1 a). This self-propagating autoinductive reaction amplifies the gradient of products, which is similar to

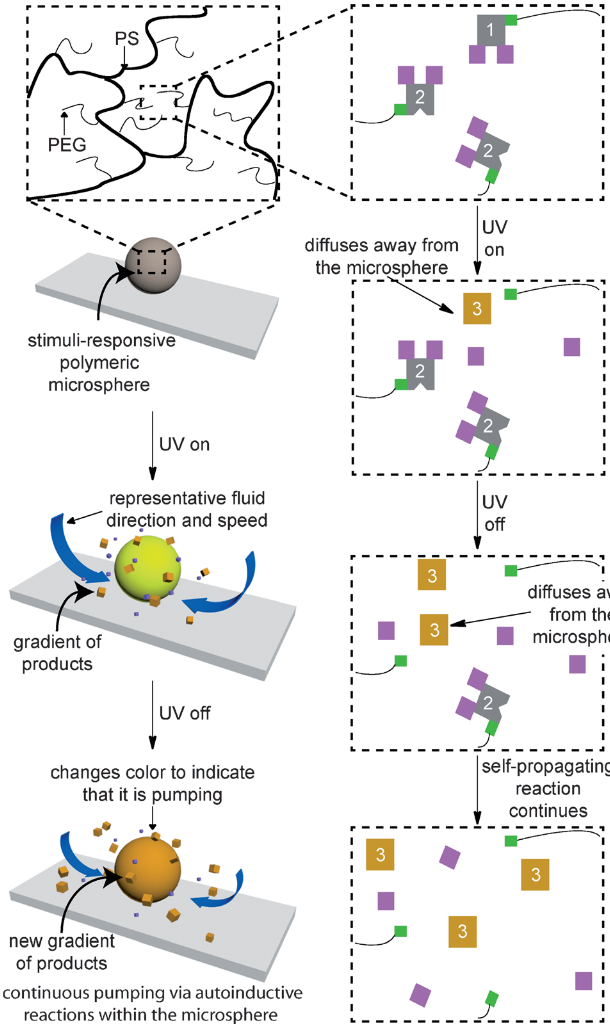

Figure 1. Schematic representation of a polymer microsphere pump that induces the movement of fluid surrounding the pump in response to a specific stimulus, even after the stimulus has been removed. The left-hand column provides a view of the macroscopic pumping response, while the dotted box at the top of the column depicts the composition of the microsphere; PEG refers to poly(ethylene glycol) and PS refers to poly(styrene). The blue arrows represent the direction of fluid movement, and the size of the arrows illustrates an approximation of the relative magnitude of fluid flow when the signal is present or absent. The right-hand column provides a schematic view of the reactions occurring in the microsphere. When the UV light is off, a self-propagating reaction (using reagent **2**, Scheme 1) enables the microsphere to continue generating a concentration gradient of products that drive the pumping response. The purple squares represent signal transduction reagents that translate the reaction of reagent **1** (Scheme 1) with UV light to initiation of the self-propagating reaction. These signal-transduction reagents also perpetuate the self-propagating reaction with **2**. The by-product of **1** and **2** (i.e., **3**) is yellow/orange in color and, thus, turns the microsphere from colorless to yellow to orange over the course of the pumping response.

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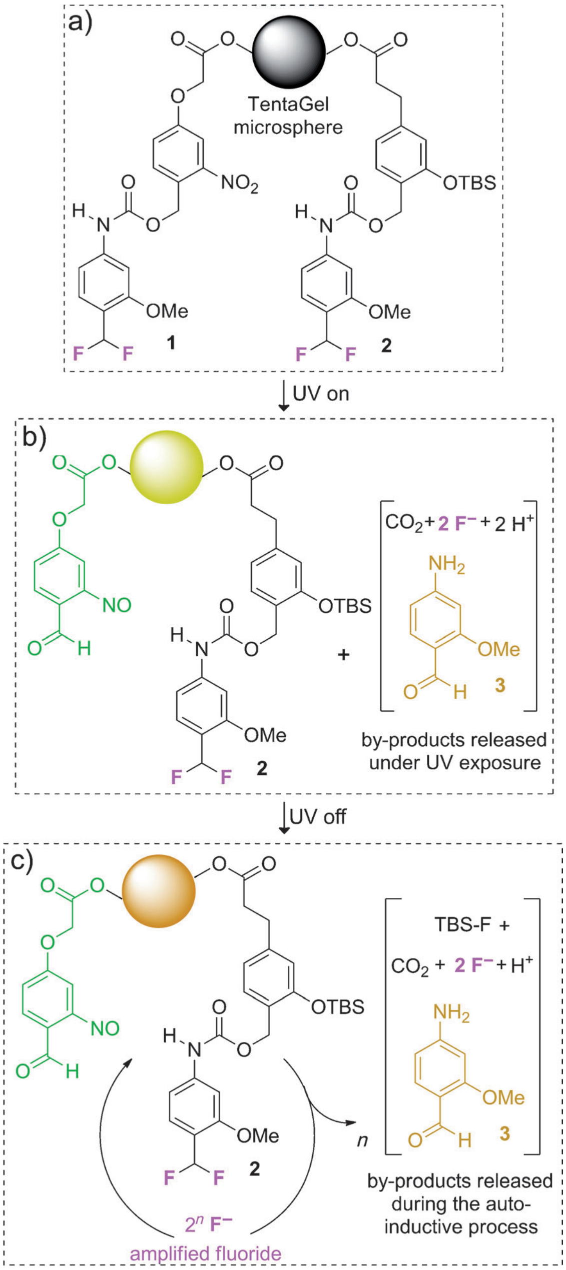
[**] This work was supported by the NSF (CHE-1150969), the Air Force Office of Scientific Research (FA9550-10-1-0509), and in part by the Department of the Defense, Defense Threat Reduction Agency (HDTRA1-13-1-0039). Additional support was provided by the Penn State MRSEC (DMR-0820404) and Louis Martarano. S.T.P. acknowledges support from the Alfred P. Sloan Research Fellows Program. We thank Gregory G. Lewis for assistance in preparing the supporting videos and Figure 1.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201304333.



Scheme 1. Structures and reactions of reagents **1** and **2** that are grafted onto a 300 μm diameter TentaGel microsphere. The structures are color-coded to match the schematic depiction in Figure 1. a) A microsphere that contains a 1:1 ratio of **1** and **2**. b) Exposure of this microsphere to UV light causes the activity-based detection reagent (**1**) to release fluoride, compound **3**, and protons.[11] c) The released fluoride then reacts with **2** to initiate a self-propagating reaction that amplifies fluoride, **3**, and protons.[11] The gradient of these small molecules causes fluid movement around the microsphere (i.e., pumping).[12] The notation "*n*" refers to the number of cycles of the autoinductive reaction in (c). TBS = *tert*-butyldimethylsilyl.

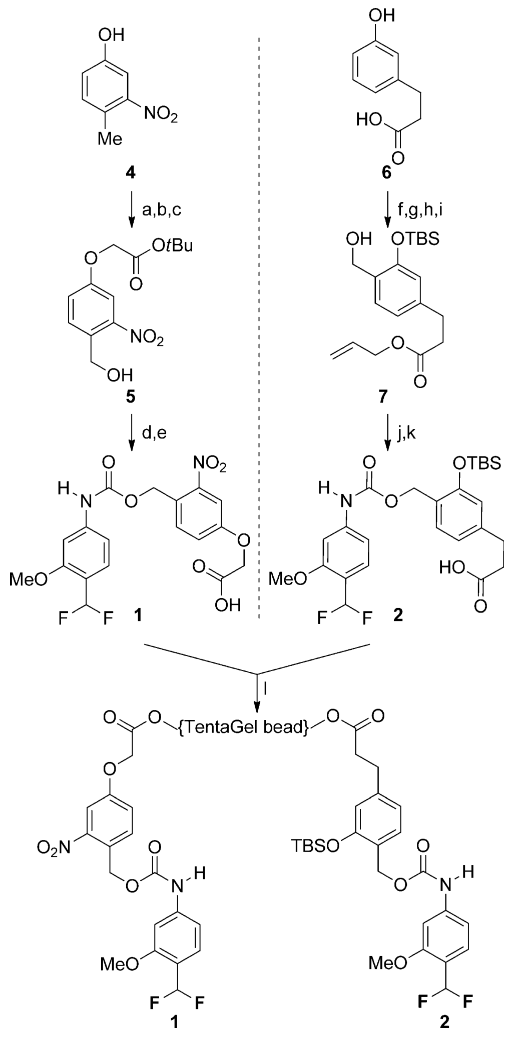
the behavior of pumps based on signal-induced depolymerization reactions.[2b]

The microsphere also contains an activity-based detection reagent[6] (e.g., reagent **1** in Figure 1 and Scheme 1 a) that detects a predefined stimulus through reaction of a specific functionality with the stimulus. In principle, this activity-based detection reagent can be exchanged with other functionalities to create modular materials that respond to a variety of fleeting stimuli.[6]

Reagent **1** in Scheme 1 a is designed to respond to light with wavelengths of 254 nm to 365 nm[7] and release two equivalents of fluoride, carbon dioxide, 4-aminobenzaldehyde derivative **3**, and two protons (Scheme 1 b). The released fluoride is a signal transduction reagent (represented by the purple squares in Figure 1) that translates the detection event into the initiation of a self-propagating reaction. This self-propagating reaction involves reagent **2**, which responds to one equivalent of fluoride and releases two additional equivalents of fluoride as well as more of **3** and a proton.[5,8] The released fluoride is then available to react with additional equivalents of **2** to continue amplifying the quantity of fluoride, **3**, and protons in the microsphere until all of **2** has been consumed (see Scheme 1 c and the two boxes on the bottom right in Figure 1). This self-propagating autoinductive reaction enables the continuous response of the material, even when the stimulus is removed, since the self-propagating reaction generates and amplifies an ion gradient and a small-molecule gradient (Figure 1 and Scheme 1 c) that induce movement of the surrounding fluid.[2]

The modified TentaGel microsphere was prepared as depicted in Scheme 2, where both the activity-based detection reagent (**1**) and the self-propagating reagent (**2**) were grafted to the polymeric bead in a presumed 1:1 ratio under 2,4,6-mesitylenesulfonyl-3-nitro-1,2,4-triazolide (MSNT) mediated esterification conditions.[9] We chose a 1:1 ratio of reagents **1** and **2** to ensure that the beads contained sufficient quantities of both reagents to sustain the two halves of the reaction network, which is particularly important since approximately 40–60 % of the reactions occur on the surface of the microsphere[3] where diffusion could interfere with the signal transduction and autoinductive processes. Two control microspheres were also prepared by analogous reactions, one containing 100 % of **1** and the other 100 % of **2**.

Before testing whether the microsphere containing both **1** and **2** was capable of "remembering" its predefined stimulus, we first conducted control experiments to determine whether the microspheres that contain **2** were capable of supporting the autoinductive, self-propagating reaction. Thus, treatment of these colorless microspheres with 2 mM cesium fluoride in 10:4:1 2-propanol/water/pyridine for 3 h yielded dark yellow/orange microspheres (the color of **3**) (Figure 2 a,b). The color change was caused by **3** being released into solution, a fact that was confirmed by injecting an aliquot of the reaction mixture into an HPLC connected to a mass spectrometer (LCMS; see Figures S1 and S2 in the Supporting Information). We quantified the time-dependent intensity of the yellow/orange colorimetric response by photographing the beads over time (Figure 2 b) and by using image-processing software to measure the intensity of the color in the digital images.[5,8] The change in color over time reflects the extent of completion of the autoinductive reaction and provides a visual indication that the material is performing its function (i.e., pumping, see below).[10] The resulting sigmoidal response curves derived from the intensity of this color are consistent with an autoinductive reaction (Figure 2 c).[5,8]



Scheme 2. Functionalization of a 300 μm diameter TentaGel microsphere with a 1:1 ratio of the activity-based detection reagent (**1**) and the reagent that causes the autoinductive, self-propagating reaction (**2**). Reagents and conditions: a) *tert*-butyl bromoacetate, K_2CO_3 (quant.); b) NBS, AIBN; c) $AgNO_3$ (26% over 2 steps); d) 1. 4-(difluoromethyl)-3-methoxybenzoic acid, $(COCl)_2$, DMF; 2. NaN_3; 3. 100°C, **5** (50%); e) TMSOTf, TEA (58%); f) imidazole, DMAP, TBSCl (87%); g) CH_3OCHCl_2, $TiCl_4$; h) $(COCl)_2$, allyl alcohol, DMF; i) $NaBH_4$ (9% over 3 steps); j) 1. 4-(difluoromethyl)-3-methoxybenzoic acid, $(COCl)_2$, DMF; 2. NaN_3; 3. 100°C, **7** (96%); k) $[Pd(PPh_3)_4]$, pyrrolidine (77%); l) MSNT, methyl imidazole, TentaGel-OH. NBS = *N*-bromosuccinimide, AIBN = 2,2′-azobisisobutyronitrile, TMS = trimethylsilyl, Tf = trifluoromethanesulfonyl, TEA = triethylamine, DMAP = 4-dimethylaminopyridine.

We further verified the autoinductive behavior of **2** by exposing microspheres containing only **2** to substoichiometric quantities of added fluoride relative to the loading level of the TentaGel microsphere. Regardless of the quantity of fluoride used to initiate the autoinductive reaction, all the microspheres provided equal levels of color over time, which is the expected result for a self-propagating reaction. As expected for an autoinductive reaction, the time to reach completion when the microspheres are exposed to lower quantities of fluoride is longer than when the microspheres are exposed to higher quantities of fluoride (Figure 2c).

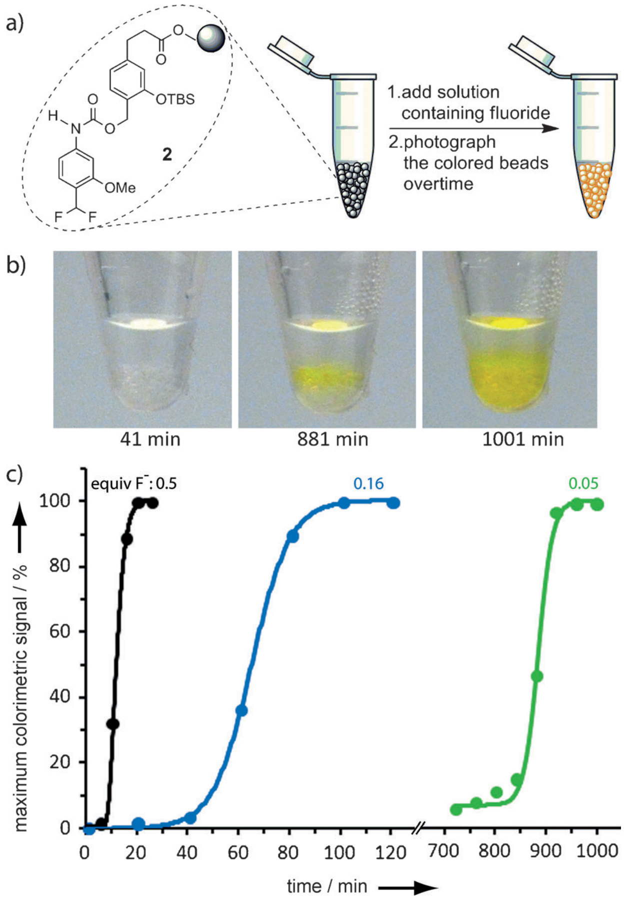


Figure 2. Colorimetric response of a TentaGel microsphere that contained 100% of **2**. a) The procedure for testing the autoinductive, self-propagating reaction that is mediated by **2**. The product of the autoinductive reaction is **3** (Scheme 1c), which turns the microspheres a yellow/orange color (b). c) This color reflects the extent of the autoinductive reaction,[5,8] and can be quantified by photographing the microspheres and by using image-processing software to measure the intensity of color. Exposure of the microspheres to substoichiometric quantities of fluoride (relative to the loading level of the microspheres) reveals sigmoidal kinetics characteristic of autoinductive reactions.[5,8] Note that the scale of the *x*-axis changes after the break.

We also performed a control experiment on microspheres containing only **1**. In this experiment, we tested the ability of **1** to respond to UV light when the microspheres were exposed for 40 min to light with a wavelength of 365 nm. As expected, the microspheres turned a bright yellow/orange color, which is indicative of the formation of 4-amino-2-methoxybenzaldehyde (**3**), a fact that was verified by LCMS analysis (see Figure S3 in the Supporting Information).

Overall, these two sets of control experiments performed on microspheres containing only **1** or **2** demonstrate that reagents **1** and **2** are capable of performing their individual functions on a molecular level when grafted to the microspheres. We next tested whether they were capable of imparting a macroscopic response to the microspheres by measuring whether they could induce pumping of the surrounding fluid. The experiment involved placing the microspheres on a glass slide that was immersed in 10:4:1 2-

propanol/water/pyridine in a closed system and then exposing the microspheres to UV light.

When microspheres containing 100% of **1** were exposed to light with a wavelength of 365 nm, the surrounding fluid displayed directional movement towards the microsphere, as reflected by the movement of 2 μm diameter amine-functionalized polystyrene tracer particles towards the microsphere with an average speed of $4.5 \pm 0.5\ \mu m\,s^{-1}$ (see Video S1 in the Supporting Information and Figure 3 (blue data)).[13] This directional fluid movement (i.e., pumping) can be turned on and off repeatedly by switching on and off the UV light. In contrast, when microspheres containing 100% of **2** were exposed to light with a wavelength of 365 nm for 20 min, no directional fluid movement was observed and no switching behavior was established (orange data, Figure 3a; see also Video S2 in the Supporting Information).

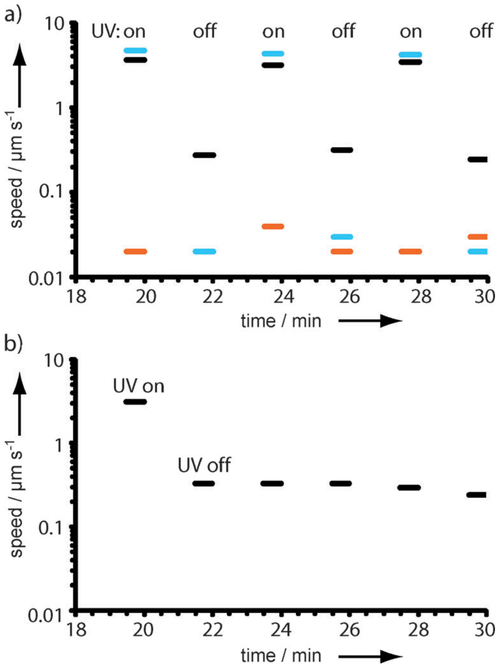


Figure 3. Average pumping speeds resulting from TentaGel microspheres exposed to light with a wavelength of 365 nm. a) The pumping action can be switched on and off for a microsphere functionalized with **1** only (blue data), whereas no pumping is observed for microspheres functionalized with only **2** (orange data). In contrast, the pumping speed can be varied for microspheres functionalized with both **1** and **2** by turning on and off the UV light (black data). The pumping speeds reflect the averages of measurements acquired over 30 s intervals that span the length of the data bars. b) Continuous pumping is also possible using microspheres functionalized with **1** and **2** once the microspheres are exposed to UV light for 20 min. For both (a) and (b), the average pumping speeds were obtained by tracking the distance that 30 tracer beads traveled over time. Error bars associated with these measurements are included in complementary standard scale data point graphs in Figures S4 and S5 in the Supporting Information. In brief: for speeds below $1\ \mu m\,s^{-1}$ the error bars are approximately the thickness of the data bars in (a) and (b).

Clearly only **1**, as anticipated, is capable of responding to the stimulus (UV light) and inducing a macroscopic response from the materials. However, **1** alone does not enable the microsphere to “remember” the applied stimulus when the UV light is removed. For that capability, we introduced **2** to the microsphere to complete the designed network of reactions (Figure 1 and Scheme 1). First, we established a baseline pumping speed for the microspheres containing a 1:1 ratio of **1** and **2** when exposed for 20 min to light with a wavelength of 365 nm. In this experiment, directional fluid movement was observed once again, albeit at a reduced speed of $3.5 \pm 0.5\ \mu m\,s^{-1}$ (see Video S3 in the Supporting Information) compared with the microsphere that contained 100% of **1** ($4.5 \pm 0.5\ \mu m\,s^{-1}$). This reduced pumping speed is to be expected, since the microspheres containing approximately equal quantities of **1** and **2** have less of **1** to react with the UV light than the microspheres containing 100% of **1**.

Next, we cycled the UV light on and off, which yielded persistent fluid pumping during the off cycles for the microspheres containing **1** and **2** (unlike the microsphere containing only 100% of **1**), with an average pumping speed when the light was off of $0.28 \pm 0.07\ \mu m\,s^{-1}$ (black data, Figure 3a; see also Video S3 in the Supporting Information). This $0.28 \pm 0.07\ \mu m\,s^{-1}$ pumping speed arises from the autoinductive reaction mediated by **2**, which is a slower chemical reaction (Figure 2c) than the direct photochemical reaction of **1** when the UV light is turned on.[7]

Perhaps more revealing about the behavior of the microspheres containing **1** and **2** is their ability to respond continuously when they are exposed only once to the stimulus, rather than periodically (Figure 3b). Specifically, when microspheres that contain a 1:1 ratio of **1** and **2** are exposed to light with a wavelength of 365 nm for 20 min, and then the light is removed, the average pumping speed drops from $3.2 \pm 0.3\ \mu m\,s^{-1}$ to $0.33 \pm 0.08\ \mu m\,s^{-1}$ and maintains that speed for approximately 8 min, at which point the pumping speed begins to decrease, likely as a result of the consumption of **2** in the microspheres.[14]

These combined data demonstrate that pumping speeds can be modulated by periodic exposure of the material to its predefined stimulus. More importantly, these results show that the microspheres continue pumping even when the signal is removed, which is an unusual capability in the context of stimuli-responsive materials, and one that is achieved by building into the material the capacity for a self-propagating reaction.

In conclusion, we have described a new approach for creating smart, stimuli-responsive materials that are capable of remembering when they were exposed to a stimulus, even when the stimulus is no longer present. The proof-of-concept application is a plastic microsphere-based fluidic pump, which is capable of pumping the fluid surrounding the microsphere in response to UV light, as well as continuous pumping even when the UV light is removed. The microsphere provides this continuous pumping without using reagents supplied in solution and without intervention by the user. Moreover, the pumping speed can be altered if the signal is present or absent, and the microsphere reveals that it is responding to the signal by turning a yellow/orange color (Figure 2), the intensity of which loosely correlates with the remaining lifetime of the pump (i.e., the quantity of **2** that has been consumed). This level of autonomous function extends beyond existing smart materials,[1] where closely related examples include materials that have a memory for their original shape,[15] or have the ability to perpetuate an oscillatory response to an applied signal by using reagents from the surroundings.[16]

The particular application of a fluidic pump may prove useful in a variety of contexts, ranging from collecting and concentrating select agents, to biological sensing, to directing flow in microfluidic devices in response to specific signals. Efforts are underway to expand the scope of this autoinductive approach that enables continuous responses,[17] and to create other types of stimuli-responsive pumps with improved response rates and duration of pumping. Parameters to explore in this context include varying the shape,[18] size, loading capacity, and porosity of the polymeric material, as well as the ratio of reagents grafted to the polymer. More broadly, the chemical concepts described herein may enable the preparation of other types of stimuli-responsive polymeric materials that perform continuous, macroscopic operations, other than pumping, when exposed to a fleeting signal.

Received: May 20, 2013
Published online: August 12, 2013

Keywords: amplification · autocatalysis · autoinduction · nanomotors · smart materials

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[1] a) J. M. Spruell, C. J. Hawker, *Chem. Sci.* **2011**, *2*, 18–26; b) I. R. Epstein, V. K. Vanag, A. C. Balazs, O. Kuksenok, P. Dayal, A. Bhattacharya, *Acc. Chem. Res.* **2012**, *45*, 2160–2168; c) M. A. C. Stuart, W. T. S. Huck, J. Genzer, M. Müller, C. Ober, M. Stamm, G. B. Sukhorukov, I. Szleifer, V. V. Tsukruk, M. Urban, F. Winnik, S. Zauscher, I. Luzinov, S. Minko, *Nat. Mater.* **2010**, *9*, 101–113.

[2] a) D. J. Laser, J. G. Santiago, *J. Micromech. Microeng.* **2004**, *14*, R35–R64; b) H. Zhang, K. Yeung, J. S. Robbins, R. A. Pavlick, M. Wu, R. Liu, A. Sen, S. T. Phillips, *Angew. Chem.* **2012**, *124*, 2450–2454; *Angew. Chem. Int. Ed.* **2012**, *51*, 2400–2404; c) S. T. Chang, E. Beaumont, D. N. Petsev, O. D. Velev, *Lab Chip* **2008**, *8*, 117–124; d) S. T. Chang, V. N. Paunov, D. N. Petsev, O. D. Velev, *Nat. Mater.* **2007**, *6*, 235–240; e) T. R. Kline, W. F. Paxton, Y. Wang, D. Velegol, T. E. Mallouk, A. Sen, *J. Am. Chem. Soc.* **2005**, *127*, 17150–17151; f) W. F. Paxton, P. T. Baker, T. R. Kline, Y. Wang, T. E. Mallouk, A. Sen, *J. Am. Chem. Soc.* **2006**, *128*, 14881–14888; g) Y. Hong, M. Diaz, U. M. Córdova-Figueroa, A. Sen, *Adv. Funct. Mater.* **2010**, *20*, 1568–1576; h) V. Yadav, H. Zhang, R. Pavlick, A. Sen, *J. Am. Chem. Soc.* **2012**, *134*, 15688–15691.

[3] S. R. McAlpine, S. L. Schreiber, *Chem. Eur. J.* **1999**, *5*, 3528–3532.

[4] a) F. A. Leibfarth, K. M. Mattson, B. P. Fors, H. A. Collins, C. J. Hawker, *Angew. Chem.* **2013**, *125*, 210–222; *Angew. Chem. Int. Ed.* **2013**, *52*, 199–210; b) B. M. Neilson, C. W. Bielawski, *Chem. Commun.* **2013**, *49*, 5453–5455.

[5] M. S. Baker, S. T. Phillips, *J. Am. Chem. Soc.* **2011**, *133*, 5170–5173.

[6] D.-G. Cho, J. L. Sessler, *Chem. Soc. Rev.* **2009**, *38*, 1647–1662.

[7] a) Y. V. Il'ichev, M. A. Schwörer, J. Wirz, *J. Am. Chem. Soc.* **2004**, *126*, 4581–4595; b) C. G. Bochet, *J. Chem. Soc. Perkin Trans. 1* **2002**, 125–142.

[8] M. S. Baker, S. T. Phillips, *Org. Biomol. Chem.* **2012**, *10*, 3595–3599.

[9] X. Jorba, F. Albericio, A. Grandas, W. Bannwarth, E. Giralt, *Tetrahedron Lett.* **1990**, *31*, 1915–1918.

[10] We demonstrated this relationship between color and extent of reaction in a previous solution-phase study (see Refs [5] and [8]).

[11] The protons generated during the photochemical reaction likely exist predominantly as pyridinium ions.

[12] The pumping mechanism is currently under detailed investigation.

[13] Note: to ensure that we measured the maximum sustainable directional movement of the fluid, the measurements were made after about 19 min of exposure to UV light. Also, the microspheres did not move during the pumping experiments. Their density is higher than the surrounding solvent, therefore they remained on the surface of the glass slide in the test chamber.

[14] The standard deviation indicated for the pumping speed $(0.33 \pm 0.08)\ \mu\text{m}\,\text{s}^{-1}$ is the largest standard deviation value obtained for the five speeds over the pumping range of 20 min to 30 min indicated in Figure 3 b, which happens to be the first data point after the UV light is removed.

[15] a) A. Lendlein, H. Jiang, O. Jünger, R. Langer, *Nature* **2005**, *434*, 879–882; b) L. Sun, W. M. Huang, Z. Ding, Y. Zhao, C. C. Wang, H. Purnawali, C. Tang, *Mater. Des.* **2012**, *33*, 577–640; c) Y. Liu, H. Lv, X. Lan, J. Leng, S. Du, *Compos. Sci. Technol.* **2009**, *69*, 2064–2068; d) X. Luo, P. T. Mather, *ACS Macro Lett.* **2013**, *2*, 152–156; e) A. Lendlein, S. Kelch, *Angew. Chem.* **2002**, *114*, 2138–2162; *Angew. Chem. Int. Ed.* **2002**, *41*, 2034–2057.

[16] a) R. Yoshida, *Adv. Mater.* **2010**, *22*, 3463–3483; b) A. Kaminaga, V. K. Vanag, I. R. Epstein, *Angew. Chem.* **2006**, *118*, 3159–3161; *Angew. Chem. Int. Ed.* **2006**, *45*, 3087–3089; c) S. Shinohara, T. Seki, T. Sakai, R. Yoshida, Y. Takeoka, *Angew. Chem.* **2008**, *120*, 9179–9183; *Angew. Chem. Int. Ed.* **2008**, *47*, 9039–9043; d) L. Kuhnert, *Nature* **1986**, *319*, 393–394.

[17] a) K. Yeung, K. M. Schmid, S. T. Phillips, *Chem. Commun.* **2013**, *49*, 394–396; b) H. Mohapatra, K. M. Schmid, S. T. Phillips, *Chem. Commun.* **2012**, *48*, 3018–3020; c) R. Perry-Feigenbaum, E. Sella, D. Shabat, *Chem. Eur. J.* **2011**, *17*, 12123–12128; d) E. Sella, R. Weinstain, R. Erez, N. Z. Burns, P. S. Baran, D. Shabat, *Chem. Commun.* **2010**, *46*, 6575–6577; e) P. Scrimin, L. J. Prins, *Chem. Soc. Rev.* **2011**, *40*, 4488–4505.

[18] S. G. Jang, D. J. Audus, D. Klinger, D. V. Krogstad, B. J. Kim, A. Cameron, S.-W. Kim, K. T. Delaney, S.-M. Hur, K. L. Killops, G. H. Fredrickson, E. J. Kramer, C. J. Hawker, *J. Am. Chem. Soc.* **2013**, *135*, 6649–6657.