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Polymerization Initiated by Particle Contact: A Quiescent State Trigger for Materials Synthesis

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Supporting Information

ABSTRACT: Dispersions of particles onto which reactive groups are bound give rise to inhomogeneous concentrations that may afford fundamentally different chemical behavior compared to the same molecular species dissolved in homogeneous solution. An example is bimolecular reactivity of complementary-functionalized particles, whereby interparticle contact is expected to promote fast kinetics localized to the interface, while exhibiting essentially no reactivity elsewhere. Such materials may exhibit unique properties analogous to blood clotting and thereby be useful in self-healing applications. Here, we demonstrate a radical polymerization reaction whose initiation is controlled by the physical proximity of two complementary co-initiators bound to a substrate and/or polymer beads. Polymerization of the surrounding acrylate monomer only occurs when interfaces functionalized with dimethylaniline encounter interfaces bearing benzoyl peroxide. At the interface of the complementary-functionalized beads, polymerization affords a "clot-like" scaffold of beads and polymer. Interestingly, such a scaffold is only attained when the beads are in a quiescent state. These findings open the way to the design of spatially controlled dual initiator systems and novel self-healing strategies and motifs.

There are fundamental differences in the chemical behavior of reactive groups bound to particles compared to those same constituents in a molecularly dissolved state. One difference stems from the spatial variability of chemical concentration.[1] Whereas molecular solutions are homogeneous everywhere, particle dispersions have nonzero concentrations only where there are particles. These differences are significant for binary particle systems undergoing heterobimolecular reactions.[2] Spatially nonuniform reaction rates are expected for such dispersions, being nonzero only at the contacting interfaces[3] of oppositely functionalized particles. Mass transport characteristics also contribute to chemical behavior differences. Since molecular diffusion alone is sufficient to bring about collision-activated reactivity of homogeneous solutions, reaction rates in these cases are typically insensitive to advection of the medium. In contrast, for reactive constituents bound to particle carriers, the presence (or absence) of bulk fluid motion is important. For example, advection may cause a pair of reacting particles to separate, thus terminating an active chemical transformation. Alternatively, advection may unite a separated pair of complementary-functionalized particles, thereby creating a new zone of reactivity.[4] Emerging from our interests in self-healing applications,[5,6] we have initiated a program of study that aims to exploit the unique characteristics of reactive particles and interfaces in an effort to trigger materials synthesis which depends on the flow state of the dispersing medium. Here, we report our preliminary findings.

Flow,[7] or the lack thereof, is an interesting stimulus that may be useful in triggering damage-induced reactivity for self-healing applications.[8−11] Inspired by the elegant "coagulation cascade"[12] in response to bodily injury, whereby a multitude of activated factors and factor complexes ultimately produce a polymerized fibrin clot and activate surrounding platelets to help seal a wound,[13,14] the recent development of vascularized composites[5,15] motivates the need for analogous behavior in a synthetic context. Blood flow plays various roles in wound healing. Certain aspects, such as platelet adhesion, depend on high blood flow conditions.[16] Other aspects like fibrin deposition take place under low flow conditions.[16] Here, we focus on a quiescent-state trigger for materials synthesis. We sought to develop a system that initiates polymerization only when two interfaces are in intimate and sustained contact. We envision the planar substrates reported here as being analogous to damaged vessel walls, while the polymer beads resemble platelets and the polymerization of monomer mirrors fibrin (Scheme 1).

Scheme 1 shows a radical polymerization reaction initiated by the contact between interfaces functionalized with the complementary co-initiators (e.g., dimethylaniline and benzoyl peroxide). In Scheme 1a, reaction between a functionalized surface and bead results in bead adhesion to the surface by polymer product, similar to clot formation at a damage site. We also explored reaction between complementary beads, specifically investigating the effect of flow (e.g., stationary vs agitated) on polymerization (Scheme 1b). Beads in a quiescent state yield a "clot-like" scaffold composed of beads and polymer product, while no such scaffold is attained when the beads are in flow.

For our first demonstration, we chose to utilize a well-studied co-initiator system involving benzoyl peroxide (**BPO**) and a tertiary amine, namely, dimethylaniline (**DMA**) (Scheme 2).

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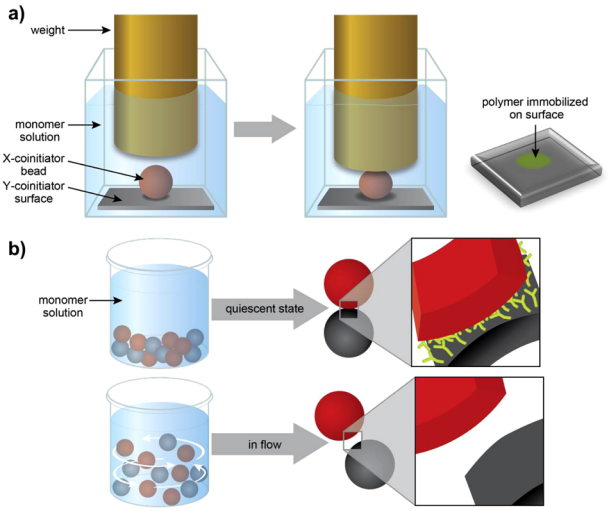
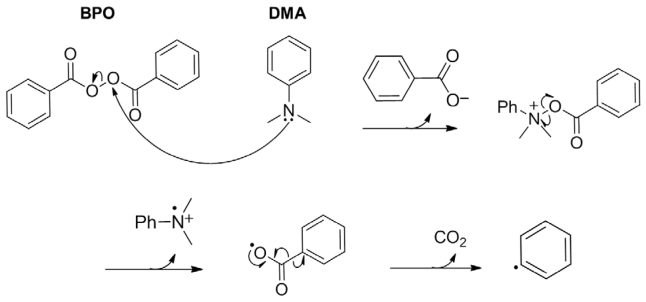
Scheme 1. Contact-Initiated Polymerization Reaction between Complementary-Functionalized: (a) Polymer Bead and Planar Surface and (b) Polymer Beads in a Quiescent State vs Flow



Scheme 2. General Initiation Mechanism for the BPO−DMA System[17]

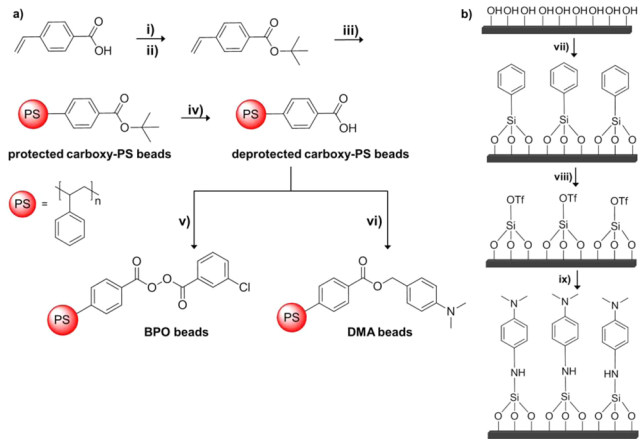


The **BPO-DMA** co-initiator system was first reported by Horner and Schwenk and is extensively used to initiate polymerization of vinyl monomers.[17,18] In spite of its proven utility, the **BPO-DMA** initiation mechanism has been and continues to be debated; however, it is generally accepted that the mechanism involves an S_N2 attack of the peroxide by **DMA**, homolytic cleavage to generate an anilinium radical cation and benzoyl radical, and decarboxylation to generate a phenyl radical, which initiates polymerization.[19−25]

We synthesized functionalized polymer beads with an approximate diameter of 500 μm, which allowed for macroscopic observation of the polymerization reaction. While much research has been devoted to the topic of functionalized polymer particles,[26−32] the incorporation of benzoic acids has not been satisfactorily optimized. To fill this void, we synthesized a styrenic monomer protected with a *tert*-butyl ester group, copolymerized the monomer with styrene using suspension methods, and subsequently removed the *tert*-butyl group using TFA to yield a carboxylic acid modified bead, which was further modified to yield the **BPO** and **DMA** functionalities (Scheme 3a; see Supporting Information (SI)).

The protected styrenic monomer, *tert*-butyl-4-vinylbenzoate, was synthesized using a modified literature procedure[33] (see SI). To yield micron-sized particles, we performed and altered a number of suspension polymerization procedures,[34−40] which afforded ca. 500 μm-sized polydisperse particles. Copolymerization was initiated by addition of benzoyl peroxide to a solution of styrene and *tert*-butyl-4-vinylbenzoate monomers (comonomer ratio 16:1) along with 0.4 mol % ethylene glycol dimethacrylate (EGDMA) as a cross-linker. The *tert*-butoxy group was removed, and the deprotected carboxy-PS particles were functionalized with *meta*-chloroperoxybenzoic acid (**BPO** particles) or 4-dimethylaminopyridine and 4-(dimethyamino)-benzyl alcohol[41] (**DMA** particles) (Scheme 3a). We chose to utilize *m*CPBA for functionalization of the **BPO** beads, as peroxides substituted with electron-withdrawing groups are known to exhibit greater activity in the presence of **DMA**.[24] The functionalized polymer beads were characterized by gel-phase ^{13}C NMR spectroscopy, diffuse reflectance infrared Fourier transform spectroscopy (DRIFTS), and SEM (see SI). To yield a complementary-functionalized surface, silicon wafers were functionalized according to a literature procedure,[42] with the incorporation of *N*,*N*-dimethyl-*p*-phenylenediamine as the aniline (Scheme 3b; see SI).

Scheme 3. Synthesis of (a) BPO- and DMA-Functionalized Polystyrene (PS) Beads and (b) DMA-Functionalized Surface[a]



[a](i) CDI; (ii) *t*-BuOH, DBU; (iii) H_2O, Mowiol, styrene, EGDMA, BPO; (iv) DCM/TFA; (v) mCPBA, DIC; (vi) DMAP, 4-(dimethylamino)benzyl alcohol, DIC; (vii) phenyltrichlorosilane; (viii) triflic acid; (ix) *N*,*N*-dimethyl-*p*-phenylenediamine.

Methyl acrylate (**MA**) was used as a monomer to evaluate the reactivity between complementary interfaces. To investigate the reaction between a functionalized surface and beads, **BPO** beads (ca. 500 μm diameter) were placed on the surface of a **DMA**-functionalized silicon wafer immersed in a solution of neat **MA** at room temperature. A glass stopper was positioned on top of the particles to keep them in contact with the surface. When the stopper was removed after 90 min at room temperature, the **BPO** beads adhered to the surface. After rinsing away unreacted **MA** monomer, the beads were peeled off the surface and the wafer was gently rinsed with water and methanol. A film on the surface was visible to the naked eye.[43] Spectral data collected with confocal Raman microscopy (normalized to the 520 cm^{-1} signal from silicon wafer, Figure S11) exhibited bands from poly(methyl acrylate) (**PMA**, at ca. 1600, 1730, and 3060 cm^{-1}), and optical images of the wafer clearly revealed areas with circular-shaped films imprinted from beads arranged in a pseudohexagonal pattern (Figures 1a,e and S9). Moreover, the **BPO** beads peeled off the surface were also in an approximately hexagonal packing arrangement, held together by **PMA** (Figures 1b, S12, and S18). Two control

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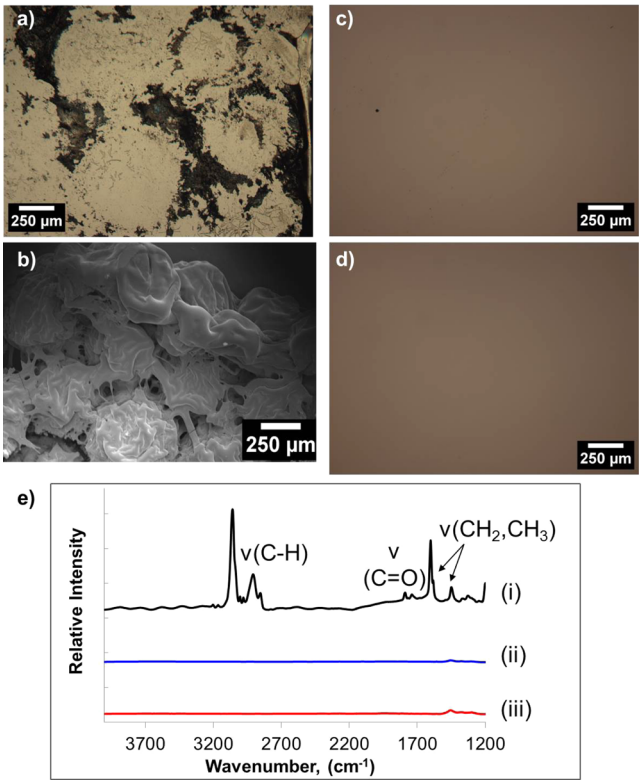

Figure 1. Contact-initiated polymerization reactions: (a) optical image of **DMA** surface after removing beads, (b) SEM image of **BPO** beads removed from surface, optical images of (c) piranha and (d) **DMA** control surfaces after removing beads, and (e) Raman spectra of surfaces after 90 min reaction at rt with **MA**: (i) **DMA** surface + **BPO** beads, (ii) piranha-cleaned surface + **BPO** beads, and (iii) **DMA** surface + carboxy-PS beads (**PMA** signals indicated). Spectra were normalized to the 520 cm^{-1} silicon wafer peak.

experiments were conducted; one with **BPO** beads and a piranha-cleaned wafer, and a second with deprotected carboxy-PS beads (nonfunctionalized) and a **DMA**-functionalized wafer. In both cases, the beads showed no strong adhesion to the surface and were easily removed. Confocal Raman microscopy exhibited no spectroscopic evidence of **PMA**, and optical imaging showed no indication of film formation on the surface (Figure 1c–e). These control experiments demonstrate that physical contact between specifically functionalized surfaces initiates the polymerization reaction.

Given the successful polymerization results from utilizing planar substrates and beads, we tested whether complementary-functionalized beads in a quiescent state bathed in monomer would produce a "clot-like" scaffold composed of beads and **PMA**. For comparison, we also tested agitated suspensions of the beads in solution. Polymerization and scaffold formation in response to sustained contact between functionalized surfaces not only mirrors blood clot formation, but also points the way to a unique strategy for designing flow-dependent healable materials.

Equal amounts of **BPO** and **DMA** beads were placed in a weighing bottle, and neat **MA** was added. The beads were left to sit in a quiescent state (without a weight) or kept suspended by stirring with a magnetic stir bar for a period of 90 min at room temperature. Following the reaction, excess **MA** was removed. The **BPO**–**DMA** beads in a quiescent state formed a "clot-like" scaffold, while the agitated beads were unchanged and remained separated (Figure 2a, experiments i and iv). SEM images of the stationary **BPO**-**DMA** beads demonstrated an

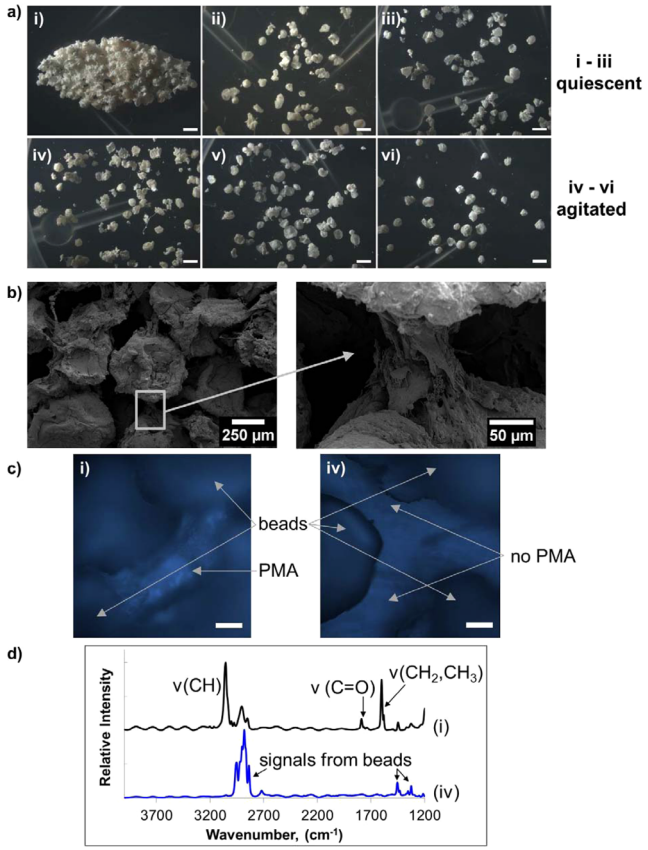

Figure 2. Contact-initiated reactivity between beads: (a) quiescent and agitated experiments (scale bar is 1000 μm) [quiescent: (i) **BPO**-**DMA**, (ii) **BPO**-carboxy-PS, (iii) **DMA**-carboxy-PS; agitated: (iv) **BPO**–**DMA**, (v) **BPO**-carboxy-PS, (vi) **DMA**-carboxy-PS], (b) SEM images of **BPO**-**DMA** quiescent experiment, confocal Raman (c) images (scale bar is 10 μm) and (d) spectra of **BPO** and **DMA** beads after 90 min reaction in **MA** at rt: (i) quiescent state and (iv) agitated (signals from **PMA** and beads indicated).

approximately hexagonal arrangement with nearly all the beads held together by a matrix material (Figure 2b). Spatially resolved spectroscopic evidence from confocal Raman microscopy of the matrix material demonstrated signals indicative of **PMA** (Figure 2c,d).[44] The agitated **BPO**–**DMA** beads, however, were not joined together and did not exhibit signals from **PMA** (Figure 2c,d). Four control experiments were conducted, two with **BPO** and carboxy-PS beads, and two with **DMA** and carboxy-PS beads. A quiescent and agitation experiment was conducted for each pair. After an equivalent reaction time, none of the control experiments yielded beads held together in a scaffold (Figure 2a, experiments ii, iii, v, vi). The control experiments demonstrate the specificity of the **BPO**–**DMA** interaction in initiating the polymerization of **MA**. We note that the **BPO** and **DMA** beads swell in **MA**, and an increase in diameter of approximately 11.0% and 16.5%, respectively, was observed (Table S2, Figure S19). The ability of the beads to swell likely contributes to interbead reactivity.

In summary, we have demonstrated a radical polymerization reaction controlled and initiated by the spatial proximity of complementary co-initiators bound to surfaces and particles. Reaction between complementary beads afforded a "clot-like"

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scaffold composed of polymer and beads akin to the formation of a blood clot at a damaged surface. Clot-like formation was only observed during stationary physical contact. Beads suspended in monomer did not form a scaffold. The proximity and dispersion of the co-initiator species can be controlled, and the resulting bimolecular reactivity is a trigger for polymer synthesis in the quiescent state. These preliminary observations raise several fundamental questions whose understanding will open the way to the design of dual initiator systems for targeted self-healing at damage sites.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b07742.

Experimental details, synthetic procedures, NMR and DRIFTS spectra, confocal Raman microscopy data, SEM images (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Prucker, O.; Rühe, J. *Macromolecules* **1998**, *31*, 602.
(2) Kisailus, D.; Najarian, M.; Weaver, J. C.; Morse, D. E. *Adv. Mater.* **2005**, *17*, 1234.
(3) Kisailus, D.; Truong, Q.; Amemiya, Y.; Weaver, J. C.; Morse, D. E. *Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 5652.
(4) Zhang, J.; Ji, S.; Song, J.; Lodge, T. P.; Macosko, C. W. *Macromolecules* **2010**, *43*, 7617.
(5) Patrick, J. F.; Hart, K. R.; Krull, B. P.; Diesendruck, C. E.; Moore, J. S.; White, S. R.; Sottos, N. R. *Adv. Mater.* **2014**, *26*, 4302.
(6) Diesendruck, C. E.; Sottos, N. R.; Moore, J. S.; White, S. R. *Angew. Chem., Int. Ed.* **2015**, *54*, 10428.
(7) Chen, H.; Fallah, M. A.; Huck, V.; Angerer, J. I.; Reininger, A. J.; Schneider, S. W.; Schneider, M. F.; Alexander-Katz, A. *Nat. Commun.* **2013**, *4*, 1333.
(8) White, S. R.; Moore, J. S.; Sottos, N. R.; Krull, B. P.; Cruz, W. A. S.; Gergely, R. C. R. *Science* **2014**, *344*, 620.
(9) Lopez, J.; Chen, Z.; Wang, C.; Andrews, S. C.; Cui, Y.; Bao, Z. *ACS Appl. Mater. Interfaces* **2016**, *8*, 2318.
(10) Burnworth, M.; Tang, L. M.; Kumpfer, J. R.; Duncan, A. J.; Beyer, F. L.; Fiore, G. L.; Rowan, S. J.; Weder, C. *Nature* **2011**, *472*, 334.
(11) Balazs, A. C.; Emrick, T.; Russell, T. P. *Science* **2006**, *314*, 1107.
(12) Davie, E. W.; Fujikawa, K.; Kisiel, W. *Biochemistry* **1991**, *30*, 10363.
(13) Panteleev, M. A.; Dashkevich, N. M.; Ataullakhanov, F. I. *Thromb. Res.* **2015**, *136*, 699.
(14) Smith, S. A.; Travers, R. J.; Morrissey, J. H. *Crit. Rev. Biochem. Mol. Biol.* **2015**, *50*, 326.
(15) Murphy, E. B.; Wudl, F. *Prog. Polym. Sci.* **2010**, *35*, 223.
(16) Shibeko, A. M.; Lobanova, E. S.; Panteleev, M. A.; Ataullakhanov, F. I. *BMC Syst. Biol.* **2010**, *4*, 5.
(17) Horner, L.; Schwenk, E. *Angew. Chem.* **1949**, *61*, 411.
(18) Horner, L.; Scherf, K. *Justus Liebigs Ann. Chem.* **1951**, *573*, 35.
(19) Imoto, M.; Choe, S. *J. Polym. Sci.* **1955**, *15*, 485.
(20) Meltzer, T. H.; Tobolsky, A. V. *J. Am. Chem. Soc.* **1954**, *76*, 5178.
(21) O'Driscoll, K. F.; Ricchezza, E. N. *Makromol. Chem.* **1961**, *47*, 15.
(22) Sato, T.; Kita, S.; Otsu, T. *Makromol. Chem.* **1975**, *176*, 561.
(23) Sato, T.; Takada, M.; Otsu, T. *Makromol. Chem.* **1971**, *148*, 239.
(24) Swain, C. G.; Stockmayer, W. H.; Clarke, J. T. *J. Am. Chem. Soc.* **1950**, *72*, 5426.
(25) Walling, C.; Indictor, N. *J. Am. Chem. Soc.* **1958**, *80*, 5814.
(26) Breed, D. R.; Thibault, R.; Xie, F.; Wang, Q.; Hawker, C. J.; Pine, D. J. *Langmuir* **2009**, *25*, 4370.
(27) Lunov, O.; Syrovets, T.; Loos, C.; Nienhaus, G. U.; Mailander, V.; Landfester, K.; Rouis, M.; Simmet, T. *ACS Nano* **2011**, *5*, 9648.
(28) Bucsi, A.; Forcada, J.; Gibanel, S.; Heroguez, V.; Fontanille, M.; Gnanou, Y. *Macromolecules* **1998**, *31*, 2087.
(29) Fréchet, J. M. J.; de Smet, M.; Farrall, M. J. *Tetrahedron Lett.* **1979**, *20*, 137.
(30) Stranix, B. R.; Gao, J. P.; Barghi, R.; Salha, J.; Darling, G. D. *J. Org. Chem.* **1997**, *62*, 8987.
(31) Mann, D.; Chattopadhyay, S.; Pargen, S.; Verheijen, M.; Keul, H.; Buskens, P.; M?ller, M. *RSC Adv.* **2014**, *4*, 62878.
(32) Zhang, S.; Zhou, Y.; Nie, W.; Song, L.; Li, J.; Yang, B. *J. Mater. Chem. B* **2013**, *1*, 4331.
(33) Smith, A. B.; Risatti, C. A.; Atasoylu, O.; Bennett, C. S.; Liu, J.; Cheng, H.; TenDyke, K.; Xu, Q. *J. Am. Chem. Soc.* **2011**, *133*, 14042.
(34) Vivaldo-Lima, E.; Wood, P. E.; Hamielec, A. E.; Penlidis, A. *Ind. Eng. Chem. Res.* **1997**, *36*, 939.
(35) Davis, D. A.; Hamilton, A.; Yang, J. L.; Cremar, L. D.; Van Gough, D.; Potisek, S. L.; Ong, M. T.; Braun, P. V.; Martinez, T. J.; White, S. R.; Moore, J. S.; Sottos, N. R. *Nature* **2009**, *459*, 68.
(36) Durie, S.; Jerabek, K.; Mason, C.; Sherrington, D. C. *Macromolecules* **2002**, *35*, 9665.
(37) Toy, P. H.; Reger, T. S.; Garibay, P.; Garno, J. C.; Malikayil, J. A.; Liu, G. Y.; Janda, K. D. *J. Comb. Chem.* **2001**, *3*, 117.
(38) Greig, J. A.; Sherrington, D. C. *Eur. Polym. J.* **1979**, *15*, 867.
(39) Melby, L. R.; Strobach, D. R. *J. Am. Chem. Soc.* **1967**, *89*, 450.
(40) Mendizabal, E.; Castellanosortega, J. R.; Puig, J. E. *Colloids Surf.* **1992**, *63*, 209.
(41) Wiles, C.; Watts, P.; Haswell, S. J. *Tetrahedron Lett.* **2006**, *47*, 5261.
(42) Li, Z. F.; Ruckenstein, E. *Macromolecules* **2002**, *35*, 9506.
(43) We note that partial coverage (ca. 50%) of the DMA surface with BPO beads did result in polymerization and adhesion to the surface; however, close-packing arrangements of beads were not as clearly observed.
(44) The scaffold holding the beads together is likely a combination of polymer formed by initiation between complementary co-initiator beads, as well as polymer chains being grafted to the beads.

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