# Digital Optofluidics: LED-Gated Transport and Fusion of Microliter-Sized Organic Droplets for Chemical Synthesis

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S *Supporting Information*

ABSTRACT: Microdroplet-based organic syntheses have been developed as a valuable alternative to traditional bulk-based methods. However, unlike their water counterparts, organic microdroplets can prove challenging to manipulate. Here, we describe the first optical manipulation of discrete, nanoliter- to microliter-sized apolar droplets floating on a liquid surface to induce on-demand droplet fusion for organic synthesis. We demonstrate droplet transport on centimeter-scale distances at speeds of 0.1 to 1 mm·s^{-1} with well-programmable, sequential or parallel, fusion events. Because our strategy is compatible with most usual hydrocarbon solvents, such droplets can be used as microcompartments for reagents. Organic reactions readily occur upon droplet fusion, as demonstrated with an ene reaction. With an LED as the sole power source, and without any fabrication step, optical setup, pump or electrode implementation, our method provides a robust and versatile way to place digital organic chemistry under optical control.
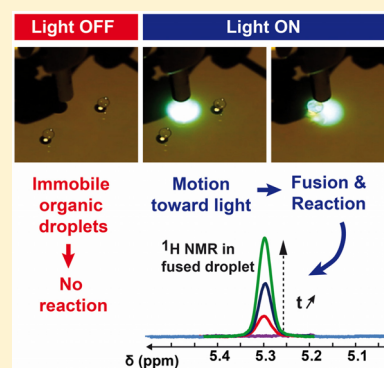
INTRODUCTION

Because compartmentalization leads to higher yields and selectivity thanks to the improved management of parameters such as heat dissipation, diffusion length, and surface-to-volume ratios, a particular focus of microfluidics[1] has recently been placed on performing organic-phase reactions in reduced volumes,[2,3] and especially in discrete droplets.[4−10] Droplet-based microfluidics in enclosed micrometer channels has successfully been applied to various organic reactions but still faces challenges such as overcoming channel clogging, contamination through the channel walls, and solvent compatibility issues. A channel-free alternative consists of manipulating discrete droplets using an electrode array by exploiting electrowetting on dielectric (EWOD) effects[11,12] on solid[13,14] or liquid[15] substrates, but this requires precise electrode addressing and it is limited to sufficiently large and polar droplets, although recent developments have widened the scope of EWOD application.[16,17] Digital optofluidics, digital microfluidics under optical control, would allow for the contactless control of organic droplets with great spatiotemporal precision, enhanced flexibility, and reduced contamination.[18] Optical manipulation of organic droplets has been achieved on solid substrates bearing photosensitive chemical functions,[18−20] but only short-range movements can be achieved and applications to organic synthesis have yet to be demonstrated. Elaborate droplet manipulations have been performed by applying light patterns to control EWOD or dielectrophoretic effects, but such approaches have been limited to polar droplets and they have never been used to induce organic reactions.[21−23] Here, we describe the first method to

manipulate discrete organic droplets optically, including those made of apolar material, to induce droplet fusion and perform organic synthesis. Our strategy relies on the creation of light-induced surface tension gradients that generate Marangoni flows able to transport droplets floating on a free liquid surface. The underlying phenomenon is reminiscent of the thermocapillary effect, where gradients in surface tension are due to temperature gradients.[24−26] In fact, lasers have been used to generate a local increase in temperature (i.e., a decrease in interfacial tension for the usual systems) that led to Marangoni flows away from the laser.[27,28] Here, the light-induced Marangoni flows are due to the isomerization of a light-responsive surfactant that creates an increase in surface tension over the illuminated area, resulting in surface flows transporting droplets toward the light spot. This approach, where droplets are attracted to a light spot, is especially well suited for the fusion of floating organic droplets, regardless of their polarity. Our actuation method is particularly flexible and technically straightforward because it does not rely on electrodes, lasers, pumps, or any microfabrication step.

RESULTS AND DISCUSSION

Figure 1 shows our experimental setup. Floating microliter-sized organic droplets were deposited on a photoresponsive aqueous solution created by dissolving AzoTAB, an azobenzene trimethylammonium bromide surfactant able to undergo
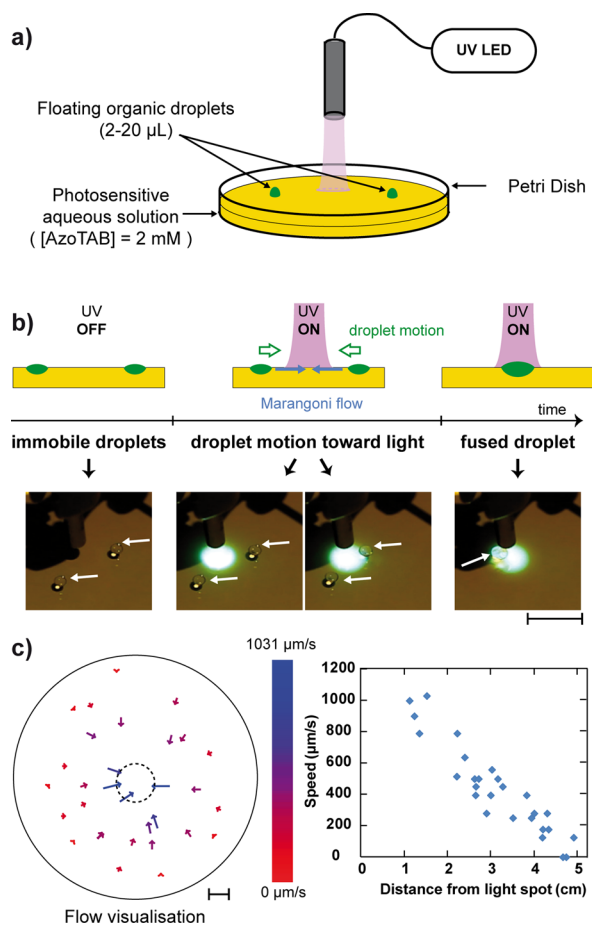
Figure 1. LED-gated Marangoni flow for the transport and fusion of floating droplets. (a) Experimental setup. (b) Schematic representation (top) and images (bottom) of two 3 µL oleic acid droplets (white arrows) immobile without light (left, t = −1 min), moving toward the illuminated spot (middle, t = 0 and 30 s), and finally fusing under light (right, t = 77 s). Droplets are transported by the LED-gated Marangoni flow at the water/air interface. (c) Surface flow velocity profile (left) and radial flow rate at different positions as a function of the distance from the light spot (right). All scale bars are 1 cm.

trans−cis isomerization upon UV illumination (Supporting Information Figures S1−S3).[29] A light guide connected to an LED emitting at 365 nm was placed about 1 cm above the water surface to provide the light stimulus (Figure 1a). In the absence of light, the lens-shaped droplets remained immobile (Figure 1b, top). Upon UV illumination, droplet motion toward the light spot was immediately visible. In the presence of more than one droplet, droplet fusion was systematically observed under the light spot. For instance, two discrete 3 µL oleic acid droplets were deposited 1.2 cm apart (Figure 1b, bottom). As soon as the UV stimulus was applied, both droplets started to move toward the illuminated area, and 77 s later, the two droplets merged under the light spot (Supporting Information Movie S1). Much smaller nanoliter-sized droplets were also successfully transported toward the light spot and fused together (Supporting Information Movie S2). Droplet motion in each of these cases was brought about by the UV-triggered Marangoni flow at the free interface. Because UV illumination caused a trans−cis isomerization leading to a higher surface tension at the water/air interface under the UV spot,[30] it generated a surface tension gradient that in turn resulted in surface flow toward the light source at the water/air free interface.[31]

Visualization of the flow profile with solid tracers showed the marked radial symmetry of the profile (Figure 1c, left), in agreement with light-induced Marangoni flows.[31,32] The velocity was at its highest value in the vicinity of the light source, reaching a speed of about 1 mm·s⁻¹, and decreased in a nearly linear fashion as the distance to the light source increased (Figure 1c, right). Applying blue light after a short UV stimulus led to the opposite profile, with the surface flowing away from the light spot (Supporting Information Figure S4 and Movie S3). This can in part be attributed to the blue-light-triggered cis−trans isomerization that leads to a decrease in surface tension under the light spot. Droplets floating on this surface were repelled. Similar droplet repulsion upon illumination was reported in experiments relying on lasers to produce temperature gradients by locally heating a solution, resulting in a lower surface tension over the illuminated area for usual liquids. In such cases, droplet motion was explained by the thermocapillary effect.[24−28] In contrast, with our setup, droplets were systematically attracted to the UV light spot by following the light-induced Marangoni flows at the air/water interface. An interesting situation arose when the droplet entered the illuminated area because the oil/water interfacial tension was also photodependent. Indeed, the partial UV illumination of the droplet created a surface tension gradient along its interface with water. In the absence of free surface flows, this gradient should induce droplet motion away from the UV light spot as a result of the chromocapillary effect.[29] In our experiments, droplets always kept moving toward the center of the light spot, showing that Marangoni flows at the free air/water interface were strong enough to overcome this additional force. As a result, light-induced Marangoni flows could be harnessed for unsupervised droplet attraction to light. This feature greatly enhanced the flexibility of our method because (i) the droplets did not need to be continuously illuminated to be moved; (ii) actuation was performed from and over long distances; (iii) motion was achieved with droplets ranging from nanoliter to microliter volumes; and (iv) several droplets were transported simultaneously until their fusion.

We then tailored the light-induced surface flows to tune droplet motion. This required adjusting the surface tension gradients according to the desired droplet motion. For instance, a cylindrical optical lens was used to generate a light sheet and therefore obtain a rectangular light pattern (Figure 2a). By placing pairs of oleic acid droplets in suitable mirror positions, it was possible to trigger, upon UV illumination, droplet motion along parallel trajectories toward the illuminated area. Once the droplets were under the light source, the fusion of the paired droplets was consistently observed. Instead of changing the geometry of the static light spot, the surface flow was also dynamically adjusted by simply using a mobile UV illumination source (Figure 2b, top). A droplet was deposited on the water surface and placed under the UV illumination source in the outer region of the light spot. The droplet could be transported along a complex pathway, several tens of centimeters long, by adequately moving the light source along a predefined trajectory (Figure 2b, bottom and Supporting Information Movie S4). Droplets could be carried on straight lines at maximum speeds that increased from 100 to 500 µm·s⁻¹ as the volume of the droplet decreased from 10 to 2 µL (Supporting Information Figure S5), which might be explained by a decrease
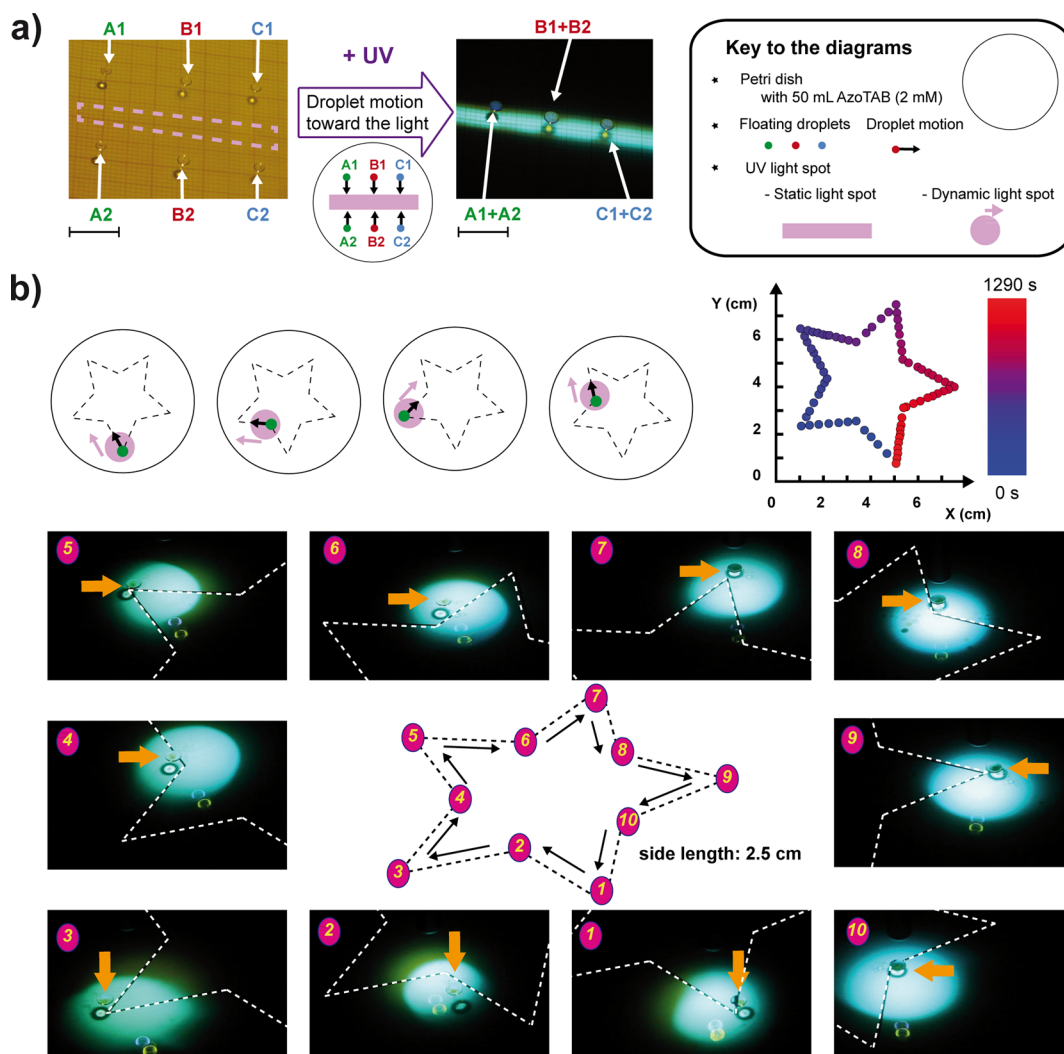
Figure 2. Light stimulation patterns for a broad range of droplet manipulations. (a) The application of a rectangular illumination pattern induces parallel motion of three pairs of 3 μL oleic acid droplets initially immobile without light (left image). Droplets fuse in a pairwise fashion in the illuminated area (right image). Scale bars are 1 cm. (b) A circular light spot is moved along a star-shaped pathway (top schemes) to transport a 6 μL oleic acid droplet. The top-right diagram shows the position of the droplet as a function of time. The lower panel shows time-lapse images of the droplet (orange arrow) at 10 different positions along the star-shaped pathway (dashed lines).

in the drag force exerted by the immersed portion of the droplet. Note that although the droplet speed strongly decreased at the tips of the star, it was possible to have the droplet perform sharp turns. The fidelity of the droplet trajectory was tested on several designs (Supporting Information Figure S6 and Movies S5−S7), establishing, among other features, the possibility to perform curved trajectories and to transport the droplet several times over the same position. Interestingly, we were able to reuse the same photoresponsive solution over many experiments, provided that we regularly regenerated a *trans*-AzoTAB solution, by simply placing the Petri dish under a blue-light source for several minutes. The liquid surface used in our setup is therefore easily reconfigurable by simply applying a new light pattern. As a result, droplet motion can also be tailored.

Another interesting feature of our strategy was the attraction of droplets toward the light source. We then tested the possibility to actuate multiple droplets and obtain sequential fusion events. The first approach consisted of placing droplets at different distances from a center droplet. In this case, UV illumination on the center droplet resulted in the motion of all

droplets toward the light spot accompanied by sequential fusion events when two droplets came into contact (Figure 3a, left and Supporting Information Movie S8). The order in which droplets fused correlated with their initial distance to the center droplet (Figure 3a, right). Because of the surface flow profile at water/air interface (Figure 1c), the time to fusion sharply increased with an increase in the distance to the light spot. This simple approach is reliable yet limited to a few (three to five) well-distributed droplets within a 2 cm region around the target droplet.

For a more robust multidroplet fusion operation, we used a dynamic light source moving at constant speed along a straight path. Five droplets were distributed along the path prior to UV illumination. The light spot was then placed over the first droplet and used to transport the first droplet at 255 μm·s^{-1} toward the next droplet, inducing successive fusion events at regular time intervals (Figure 3b and Supporting Information Movie S9). Because each target droplet is strongly attracted by the light spot at short distances, the droplet usually fused to the transported droplet at a slightly shifted location compared to its initial position (Figure 3b, left). Interestingly, the time to fusion
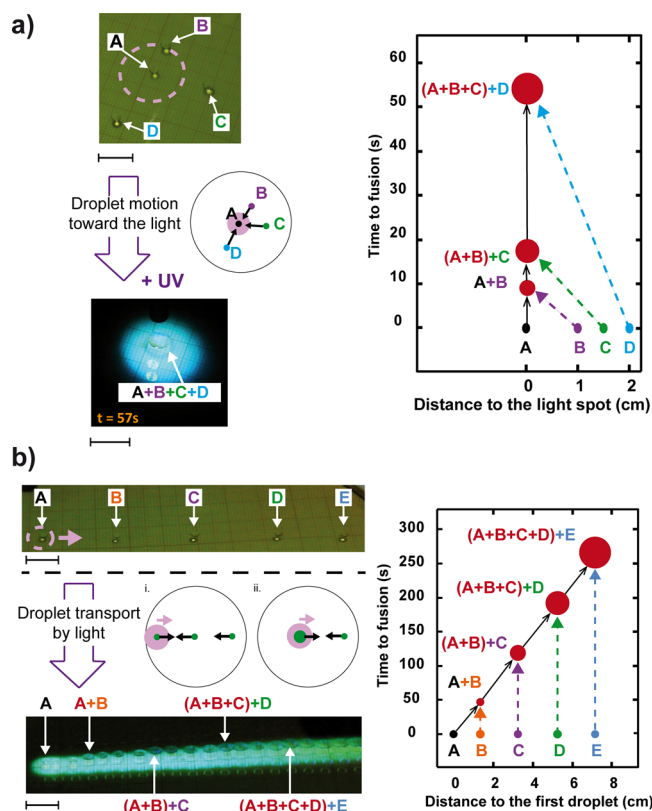
a)

b)

Figure 3. Multidroplet manipulation for sequential fusion events. (a) Three 3 μL oleic acid droplets (B−D) are placed at different distances from a center droplet (A). The application of a static circular spot triggers the motion of B−D droplets toward droplet A, leading to sequential fusion events. The upper and lower images show the droplets before illumination and after the fusion of all droplets, respectively. The right diagram shows the initial positions of droplets A−D and the time required for each fusion event (red disks, with an area proportional to the fused droplet size). (b) Five 3 μL oleic acid droplets are distributed along a straight line. A dynamic light spot moving at 255 μm·s^{-1} transports droplet A and induces sequential fusion events. The upper and lower images show the droplets before illumination and a superposition of images of the droplet transportation, where fusion events are indicated by a white arrow. The right diagram shows the initial positions of droplets A−E and the time required for each fusion event (red disk, with an area proportional to the fused droplet size). All scale bars are 1 cm.

was mainly controlled by the speed of the light source (Figure 3b, right).

To demonstrate the possibility to induce an organic synthesis by the LED-gated fusion of two droplets containing reagents, we selected toluene as a solvent to perform an ene reaction[33−35] between diethyl azodicarboxylate (compound **1**, enophile) and ß-pinene (compound **2**, ene) to create a C−N bond and generate compound **3** (Figure 4a). Two 10 μL droplets of each compound were deposited on the water surface. Without light, droplets were immobile and adopted a lens shape with higher spreading in the case of **2**. The application of UV light induced the immediate attraction of both droplets toward the light spot (Figure 4b). Right after droplet fusion, we turned off the light to avoid possible UV-induced perturbation of the droplet content, we placed a lid on the Petri dish to limit evaporation, and we followed the reaction by ¹H NMR (300 MHz) in d_8-toluene (Figure 4c). Note that we did not detect any characteristic peak of AzoTAB in any
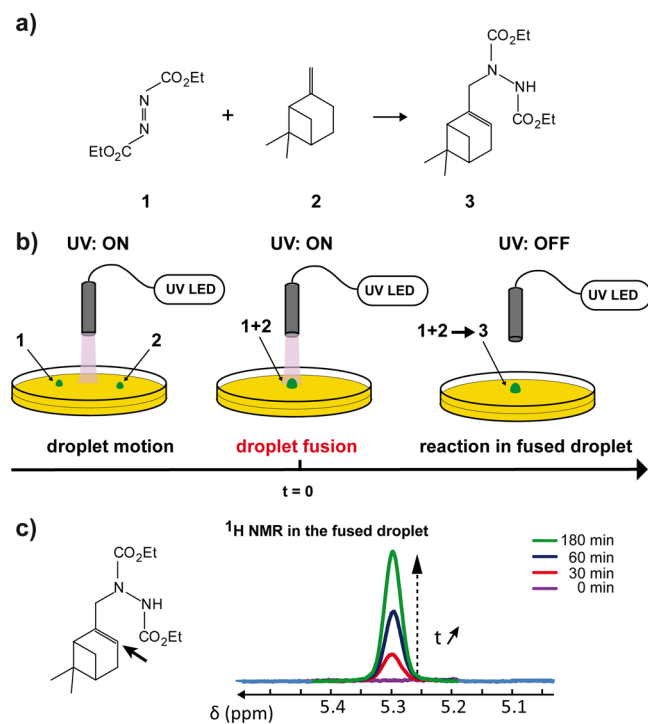
a)

b)

c)

Figure 4. Digital optofluidics for organic chemical reaction. (a) Diethylazo-dicarboxylate (compound **1**) reacts with ß-pinene (compound **2**) in toluene at room temperature to give compound **3**. (b) UV light is applied to trigger the motion of a 10 μL droplet of **1** in toluene (2 M) and a 10 μL droplet of **2** in d_8-toluene (2 M) toward the illuminated area. UV light is turned off right after droplet fusion. (c) ¹H NMR spectra (300 MHz) of droplets 1 and 2 before fusion (left panels) and of the fused droplet for different reaction times (right panel). The broad peak is attributed to the vinyl proton of compound **3** as indicated by the black arrow.

droplet, before or after fusion, showing that AzoTAB remained in the water phase and did not contaminate the toluene droplets containing reagents and products. In the 5.1−5.5 ppm range, droplet 1 (respectively 2) did not display any peak because it contained compound **1** (respectively **2**). Interestingly, in the fused droplet, a marked change in the NMR spectrum was observed as the reaction time increased. A broad peak at 5.3 ppm specific to product **3** appeared and increased with time. By comparing the product **3** peak integration to the compound **2** peak integration over time, we found that about 70% conversation was reached after 180 min (Supporting Information Figures S7−S8). In our study, the mixing obtained upon droplet fusion was clearly sufficient to allow for the organic reaction to proceed efficiently. Note that a mixing step can easily be added following droplet fusion by moving the fused droplet along the surface to homogenize the droplet contents.[25] To our knowledge, our results constitute the first demonstration of a successful light-gated organic reaction in toluene.

■ CONCLUSIONS

Simple LED stimulation on a water/air interface was used to manipulate discrete nanoliter- to microliter-sized apolar droplets optically with great precision, control their fusion, and induce organic synthesis in fused droplets for the first time. This expands the optical toolbox for the control of microfluidic operations achieved by LED illumination.[18,36] Because of the

relative stability of *cis*-AzoTAB, our solution needs to be regenerated after a few experiments. This regeneration step can be suppressed by using tailored azobenzene surfactants with a fast thermal relaxation rate. The absence of any contact with solid substrates during droplet manipulation is a striking feature that limits contamination issues and enlarges solvent compatibilities. Floating droplets have limitations, such as sensitivity to ambient air flows, dust particles, vibrations, and solvent evaporation, which can be easily solved by straightforward technical improvements (e.g., by using a UV-transparent lid or by working under a saturated atmosphere). The isothermal nature of the actuation is an additional advantage over classical optical actuation methods relying on highly focused lasers. For reactions requiring higher temperatures to proceed at reasonable rates, the whole setup should be heated to avoid potentially disruptive thermocapillary flows produced by localized heat sources. The useful temperature range is limited by the evaporation of droplets as well as by the temperature dependence of the surface tension because the surface tension gradients need to remain sufficiently large to trigger satisfactory droplet motion. Our digital optofluidic approach allows both sequential and parallel organic reactions in microreactors, paving the way to screening operations and multistep syntheses under sole optical control. Our robust method, which does not require any laser, electrode, pump nor fabrication step, is inexpensive, highly flexible and readily implementable in any standard research environment.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental section, Figures S1–S8, and legends of Movies S1–S9. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

D.B. designed the work with contributions from A.V.-M. A.V.-M. performed all experiments. D.B. and A.V.-M. analyzed the data and wrote the paper.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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