Chemoadaptive Polymeric Assemblies by Integrated Chemical Feedback in Self-Assembled Synthetic Protocells

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ABSTRACT: The design and chemical synthesis of artificial material objects which can mimic the functions of living cells is an important ongoing scientific endeavor. A key challenge necessary for fulfilling the criteria for a system to be living currently regards evolution, which is derived from adaptivity. Integrated chemical loops capable of feedback control are required to achieve chemical systems which exhibit adaptivity. To explore this, we present an integrated, two-component orthogonal chemical process involving reversible addition–fragmentation chain transfer (RAFT) based polymerization-induced self-assembly (PISA) and a copper-catalyzed azide–alkyne click (CuAAC) coupling reaction. The chemical processes are linked through electron transfer from the activated chain-transfer agent (CTA) to the dormant Cu(II) precatalyst. We show that combining these complementary chemistries in a single reaction pot resulted in two primary outcomes: (i) simplification of the PISA process to synthesize the macro-CTA in situ from available nonamphiphilic components and (ii) routes to complexity and adaptation involving population dynamics, morphologies, and dissipative phenomena observed during in situ microscopy analysis.

INTRODUCTION

Living systems are out of thermodynamic equilibrium physicochemical systems which, using chemistry, (a) handle information, (b) perform metabolism, (c) reproduce, and (d) evolve.¹ In natural life on Earth (the only instance of life we know so far) these qualities are expressed with biochemistry. The “elementary units of life”, cells, are compartmentalized physicochemical systems whose internal components are separated by a semipermeable membrane from their outside environment.² They rely on the continuous consumption of energy and matter to maintain their integrity and autonomous operation.³ Within the cell complex exquisitely staged and interconnected reactions, such as metabolic processes, allow them to exhibit functions associated with extant life.⁴ It is widely considered that modern cells which today behave according to highly optimized and exceptionally complex processes originated from primitive objects, albeit with simplified internal functions.⁵

Given this complexity of naturally occurring life, the design and synthesis of artificial physicochemical systems which can mimic the functions of living cells is a long-held scientific goal.⁶ To this end, protocell models including giant unilamellar vesicles formed of molecular amphiphiles⁷ or coacervate-based systems^{8,9} assembled with presynthesized biologically based proteins or amphiphilic components have been observed to exhibit a range of interesting life-mimic behaviors. However, key problems in the emergence of life remain. These include the ex-novo construction of a membrane to encapsulate reaction media which prevents bulk diffusion of dilute reaction products, known

as the “concentration problem” and the construction of chemically powered mechanisms which enable the evolution of system complexity.

These problems can be addressed by using synthetic chemistry to produce block copolymer vesicles which possess a membrane-encapsulated interior lumen.¹⁰ In this context, polymerization-induced self-assembly (PISA) has emerged as an effective one-pot method to produce microscale self-assembled block copolymer vesicles in aqueous solution.^{11,12} The chemical synthesis of protocells with an encapsulating semipermeable and tunable membrane from an initially isotropic and homogeneous medium through PISA offers a plausible autonomous mechanism for the formation of such essential structures.^{10,13} As such, PISA offers a chemical route to obtain these structures, which is not offered by the typically used methods to synthesize protocells and vesicles, by the exogenous delivery of amphiphiles to the media using techniques such as solvent-switch or extrusion.^{14–16} Indeed, PISA provides a route to increase chemical system complexity using external energy and fuel by producing amphiphiles during the polymerization reaction through a far-from-equilibrium process as reagents

Received: June 4, 2021

Published: August 20, 2021

Figure 1. Chemically integrated CuAAC and photo-RAFT polymerization reaction. (a) Photographs of the reaction mixture at the initial ($T = 0$) and final ($T = 4$ h) stages of the click-PISA reaction. (b) Overlaid GPC (Normalized RI signal) traces displaying the shift in retention time of PEG-*b*-PAN during the click-PISA reaction. (c) Cartoon depicting the proposed click-PISA process based on ^1H NMR and GPC data.

are consumed and the resulting assemblies become dynamic in morphology and structure.¹⁷ Our group has shown that under excitation, giant vesicular objects can undergo cyclic growth-collapse “phoenix” behavior,^{17,18} dynamic merging¹⁹ or division,²⁰ or rearrange their internal structure²¹ as the result of maintaining this consumption of energy. But can we go deeper in the laboratory search for simpler origins?

PISA usually requires presynthesized macro-chain-transfer agents (macro-CTA) as a hydrophilic block and to control polymerization of the hydrophobic block.¹² Simplifying this supplied component would further align us to the concept of evolving complexity satisfying the primary function (b). In this article, we show that the chemical simplification of the initial macro-CTA can be achieved by integrating two chemical reactions connected by using the radicals in reversible addition-fragmentation chain-transfer (RAFT) based PISA to reduce a precatalyst for an orthogonal copper-catalyzed azide-alkyne click (CuAAC) reaction.²² The high reaction rate, atom economy and chemo-selectivity makes the CuAAC reaction an ideal candidate for integration with other chemical processes, while avoiding the catastrophic effects of the so-called “arithmetic demon” associated with cascade syntheses which plague origin of life scenarios.²³ An integrated CuAAC/living radical polymerization process was first reported 13 years ago by Geng and Haddleton et al. through coupling atom transfer radical polymerization (ATRP) with the CuAAC, for the in situ functionalization of monomers featuring pendant alkynyl groups.²⁴ Similar CuAAC-ATRP integrated processes have since been applied to synthesize block copolymers²⁵ and protein-polymer hybrid amphiphiles²⁶ in situ. The activation of a Cu(II) precatalyst by photoexcitation of a RAFT CTA under iniferter conditions to produce block copolymers (BCPs) inspired our strategy,²⁷ though no approaches have been integrated with PISA to date.

A hitherto unaddressed challenge for bringing synthesized and self-assembled objects closer to “living mimics” involves adaptivity, which requires at least two integrated feedback loops.²⁸ The system made of the click-PISA (RAFT polymerization and CuAAC coupling reaction) introduced in this paper indeed also provides chemical realizations for feedback mechanisms in adaptive control theory (Supplementary Scheme 1), which are absent from previous approaches using presynthesized macro-CTA reagents. The reaction occurs in a well-mixed one-pot, thus allowing its consideration in analogy to natural scenarios for self-organized systems. Macromolecular amphiphiles are produced which dissipatively self-assemble into giant microscale structures under the constant input of activating light energy. The behaviors of the self-assembled

microscale objects were studied as the system is pushed far-from-equilibrium by photoirradiation within a fluorescence microscope. The larger gap in chemical complexity between the starting reagents and products due to using these simpler components is compensated by the consumption of energy through the integrated reaction cycles. For this reason, the objects produced in this study exhibit a high sensitivity to the energetic environment compared to objects formed by non-chemically integrated approaches^{17,18} and therefore morphological and population evolution occur over much shorter time scales. Changes in the chemical and (through osmotic and defect-generated processes) physical state of the system, driven by the external input of energy, provide routes to complex behavior starting with simple nonamphiphilic components.

RESULTS

Integrated Chemical Processes of the CuAAC and RAFT Polymerization. The integration of RAFT polymerization and CuAAC occurred by electron transfer reduction of the Cu(II), N,N,N',N',N''-pentamethyldiethylenetriamine (PMDTA) to the active Cu(I)PMDTA CuAAC catalyst from the activated CTA molecule. Evidence of this was observed during the aqueous PISA process, as the reaction solution changes from a deep blue at $T = 0$, to a green/brown color during the click-PISA reaction (Figure 1a). UV-vis analysis of a solution of CTA with Cu(II)PMDTA showed that the absorption in the green region ($\lambda = 542\text{--}545$ nm) of the visible spectrum decreased by 15% over 100 min irradiation within the reactor (Figure S1), as reduction of the Cu metal center increases transmission in the green region of the spectrum. These early results encouraged us to further study the integrated click chemistry and RAFT-PISA process.

Proton NMR analysis of the click-PISA reaction showed the CuAAC product was formed before polymerization of acrylonitrile (AN) occurred, to produce the assemblies comprising $\text{PEG}_{44}\text{-b-PAN}_{23}$ (Figure S2a-d). This is supported by GPC data, where no significant shift in molecular weight was observed until 1 h after initiation (Figure 1b). Consistent with previous literature,²⁵ we propose the RAFT-PISA mechanism to occur through a two-stage process (Figure 1c). Initial photo-initiated reduction of Cu(II)PMDTA consumes the generated radicals to produce the active Cu(I)PMDTA catalyst which initiates the CuAAC reaction. Subsequently, RAFT polymerization of AN can occur to produce the self-assembling amphiphiles through dissipative processes. GPC analysis of an identical reaction conducted without the presence of CuSO_4 showed no shift in molecular weight of the $\text{PEG}_{44}\text{-alkyne}$ after 4 h irradiation with blue light (Figure S3).

Scheme 1. Proposed Mechanism of the Chemically Integrated CuAAC Coupling and PISA Reaction, with Displayed Chemical Structures of the Reagents and Products^a

^aThe process is intrinsically interconnected by multiple loops which act across varying time scales.

Scheme 1 shows the processes and proposed mechanism of the integrated CuAAC and RAFT-PISA reaction based on the characterization data, with labeled feedstock reagents. The reduction of Cu(II)[PMDTA] by the photoactivated CTA molecule occurs rapidly, initially preventing the RAFT polymerization of AN. The Cu(I)[PMDTA] complex rapidly catalyzes the CuAAC reaction, producing the macro-CTA product. As a result, the macro-CTA is produced before RAFT polymerization of AN occurs (Figure S 2d), generating microscale assemblies through PISA. We observed that the color of the solution postreaction slowly changed from green to blue after the reaction mixture was exposed to air over 24 h, which we attributed to the oxidation of Cu(I)[PMDTA] to Cu(II)[PMDTA] . The integrated chemical reaction loops presented in

Scheme 1 provide a route to chemically controlled feedback similar to those in adaptive control engineering (Scheme S1). Reduction of the Cu(II)[PMDTA] complex scavenges the photogenerated radicals and so competes with the living radical polymerization and subsequent PISA, acting as a control inhibitor. Once a critical threshold of reduced Cu(I)[PMDTA] complex is formed in solution, the PISA reaction can occur. The PISA and resulting phase-separation²⁹ generates the self-organization of the structures during blue light irradiation and causes a variety of behaviors which will be discussed in the forthcoming sections.

Self-Assembled Objects Produced by the Click-PISA Reaction. The click-PISA process (Figure 2a, b) produced spherical nano- to microscale assemblies observed by electron

Figure 2. Evolution of PEG-*b*-PAN microscale assemblies during the integrated click-PISA reaction in aqueous solution. Cartoon depicting the PISA process in the microscope (a) before and (b) after illumination. (c) Cryo-SEM image of an exemplary PEG-*b*-PAN object. (d) Optical image of PEG-*b*-PAN objects prior to microscopy analysis. (e) Optical image of PEG-*b*-PAN objects following 1 h in situ analysis (from Supplementary Video 1). (f) Graph displaying the change in diameter of an exemplary object measured using optical microscopy images during in situ analysis. Scale bars = 50 and 1 μm (optical images and insets, respectively) and 200 nm (SEM image).

(Figure 2c) and optical (Figure 2d,e) microscopy. The spherical structures produced have a strong optical contrast, which we attribute to the high Cu concentration within the membrane and contents of the objects (Figure 2d, e). A broad distribution of object sizes was observed by analysis of bright-field optical images, with measured average object radii of 0.96 μm , PDI = 1.3 following 4 h of polymerization (Figure S4a). DLS analysis of the colloidal solution showed a broad range of object sizes from hundreds of nanometers to multiple microns with a maximum intensity particle diameter 562 nm, and PDI = 0.48 (Figure S5). The object size measured by DLS is smaller than that measured from optical images due to the contribution of submicron scale structures which cannot be resolved by the optical microscope.

The trithiocarbonate CTA is activated by both UV and blue light (maximum absorption observed at $\lambda = 345$ and 440 nm, respectively), as determined by UV-vis analysis (Figure S6). Continued reaction of monomer and CuAAC reagents with the constant input of blue light energy kept the system in a state driven far-from-equilibrium. Two primary populations of self-assembling objects emerge during in situ analysis, framboidal objects and vesicles (Figure 2e, Supplementary Video 1). It was observed that objects increased in diameter under irradiation as the internal reagents are consumed, presumably by intake (“drinking”) of the reaction media due to osmotic pressure differences. Analysis of individual objects allowed for the increase in diameter to be visualized (Figure 2f). An initial and rapid increase in size was observed over 10 min, until a critical diameter was reached, after which slow growth continues (Figure 2f). The average object radii increased from 0.96 μm , PDI = 1.3 (prior to irradiation) to 1.1 μm , PDI = 1.3 following 1 h analysis (Figure S4a, b). The modest increase in the average measured object diameter can be attributed to the large existing population in the submicron scale range detected by DLS (Figure S5) increasing in size during analysis and then becoming detectable by optical microscopy. This is supported by over 90% of the detected objects which possessed a radius between 0.98

and 1.78 μm after 1 h analysis within the microscope (Figure S7).

Individual vesicular objects were observed to reach a maximum sustainable diameter before collapsing into a small droplet (Supplementary Video 1, Figure S8), which is possibly due to the objects reaching a critical surface tension across the membrane which results in the implosion of the object.^{17,18} Fluorescence microscopy and cryogenic SEM analysis of the objects postirradiation was conducted (Figure S9 and Figure S10). The objects analyzed by cryo-SEM were not observed to be spherical, which we attribute to the intense energy input causing the structures to distort and form higher energy nonequilibrium conformations. A band of higher fluorescence intensity around the periphery of the objects was observed, indicative of a polymer rich membrane encapsulating an interior lumen (Figure S8). To be used as a control, assemblies were produced by an analogous protocol using a presynthesized analog of the macro-CTA which yielded irregular 1D aggregates (Figure S11 and Figure S12a–c) as seen during optical microscopy analysis. The difference in the evolution of structures when using presynthesized macro-CTA to when the macro-CTA is synthesized in situ by the CuAAC has two likely contributions. First, there may be a small degree of homopolymerization of AN which will increase hydrophobic volume fraction and favor the formation of low-curvature structures such as vesicles. Second, the CuAAC will decrease the interfacial energy between the membrane and aqueous solution in situ by increasing the PEG grafting density.

During in situ analysis the click-PISA reaction is most active within the field-of-view where the light is most intense. Objects at the periphery of the field-of-view are of similar morphology to those initially observed prior to microscopy analysis (Figure 2d, e). Continued reagent consumption drives an increase in population of the self-assembled objects with time (Figure S13, Supplementary Video 1) through the formation of new objects and photoinduced osmotic pressure gradients drive object

Figure 3. Chemotaxis of objects during in situ microscopy analysis toward the center of highest light intensity. (a) Cartoon depicting the proposed mechanism for object motion by chemotaxis based on surface deformation of objects. (b) Segmented image displaying tracked object trajectories within the field-of-view (denoted by the white arrows) from [Supplementary Video 1](#) toward the center of highest intensity within the beam over 1 h. (c) Plot showing the distance between a tracked object and the center of light intensity and corresponding velocity with time.

chemotaxis to within the field-of-view. Close observation of the population growth curve shows a stuttered population increase in a stepwise manner ([Figure S13](#)) with a variable population growth rate and acceleration. The shape of the population growth curve ([Figure S13](#)) is similar to that exhibited by synchronous population growths of bacteria induced by periodic changes in substrate supply and depletion.³⁰ This similarity can be rationalized by the flux of Cu(II) causing periodic inhibition of RAFT polymerization as the reduction of Cu(II) to Cu(I) consumes polymerization radicals. By changing the minimum detected object radii it was determined that self-assembled objects $<1.26 \mu\text{m}$ in radius were the primary contributor to the observed population growth ([Figure S7](#)), which can be attributed to the nanoscale population of objects increasing their size during irradiation to become resolvable by the optical microscope. Control experiments without the presence of copper catalyst yielded limited population growth ([Figure S14a–c](#)), which is expected without the generation of macro-CTA amphiphiles to produce new self-assembled structures. Population growth of the self-assembled objects was observed by transmission imaging in the absence of blue light stimulation ([Figure S15a–c](#), [Figure S16](#)), which may be explained by the white light used to obtain the transmission images being still somewhat capable of activating the CTA molecules to an extent. These objects were not observed to evolve morphologically as the necessary energy input (in the form of blue light) was not present ([Figure S15a–c](#)).

Rapid Chemotaxis and Dye-Influenced Assembly Behavior. The movement of objects toward the center of the beam has previously been attributed to membrane instabilities causing Marangoni-induced motion.¹⁷ This is due to the rate of photo-RAFT reaction varying across the self-assembled structure which induces membrane deformations to propel the structures through the solution ([Figure 3a](#)). Bright-field optical images following 1 h analysis showed a tendency for objects to gather in a specific region of the field-of-view ([Figure 2e](#), [Supplementary Video 1](#)). Tracking of object paths using the inbuilt trackmate function within ImageJ³¹ revealed the relatively direct pathway of the object's movement to the center of the beam intensity ([Figure 3b](#)), at an average velocity of $0.13 \mu\text{m}/\text{min}$. The consistent reduction in distance ([Figure 3c](#)) between the object and the region of highest light intensity suggests that the movements are photoinduced, rather than due to thermal convection currents. This is further supported by

control experiments without blue light irradiation, in which the objects are not observed to migrate to a specific location within the field-of-view ([Figure S15b](#), [Figure S17](#)). As light irradiation is limited to a beam $800 \mu\text{m}$ in diameter, spot-heating may contribute to the observed chemotaxis. The temperature of the illuminated sample surface was analyzed using an infrared camera ([Figure S18a, b](#)) and showed a temperature variation over the sample of $0.1\text{--}0.2^\circ\text{C}$ which is not so significant to drive object chemotaxis. To further identify the role of the chemical reaction regarding the observed motion, we conducted another experiment in which polystyrene (PS) beads of $3.7 \pm 0.3 \mu\text{m}$ in diameter were subjected to an identical protocol in a mixture of monomer, alkyne-functionalized PEG and Cu[PMDTA] ([Figure S19a–e](#)). The PS beads were observed to move randomly, presumably with Brownian motion ([Figure S19c](#)), and the object tracks did not display a trajectory toward the area of highest light intensity ([Figure S19d](#)). Additionally, the PS bead population and distribution remained consistent across the field-of-view during the experiment ([Figure S19b, e](#)).

Fluorescent objects were prepared by copolymerization of a small proportion of Rhodamine B and Nile Blue-labeled monomers (1.7×10^{-5} wt %) with AN. The choice of dye-labeled monomer influenced the obtained morphologies, despite the low loading amounts. Rhodamine B-labeled objects were observed to form giant vesicles during blue light illumination, demonstrated by a higher fluorescence intensity around the objects peripheries ([Figure 4a–c](#), [Figure S20ai, ii](#)). Objects produced by copolymerization with nile blue-functionalized monomers exhibited multicompartimentalized structures ([Figure 4d–f](#), [Figure S20bi, ii](#)). We attribute this to the difference in hydrophilicity of the dye molecules, as Rhodamine B has a relatively higher hydrophilicity in comparison to Nile Blue, which in turn will influence the hydrophobicity of the membrane.

Objects labeled with Rhodamine B grew into giant vesicle structures until a critical diameter was reached, after which the vesicles collapsed into small droplets which exhibited 100% brighter fluorescence signals ([Figure 4ci–iii](#), [Figure S21a](#), [Supplementary Video 2](#)), due to the local increase in concentration of the fluorescent dye confined within the object). This behavior was previously observed^{17,18} in the absence of dye-labeled monomer for individual objects ([Figure S8](#)) and was observed to be prevalent in the presence of Rhodamine B-labeled monomers. The measured reduction in

Figure 4. Evolution of PEG-*b*-PAN object morphology during microscopy analysis. (a) Fluorescence microscopy images of rhodamine B-labeled objects at $T =$ (i) 0, (ii) 30, and (iii) 60 min. (b) Cartoon schematic of the growth-collapse process. (c) Magnified fluorescence image of a giant vesicle (i) before ($T = 27.4$ min) and (ii) after ($T = 27.5$ min) collapse with corresponding fluorescence intensity traces (iii). (d) Fluorescence microscopy images of Nile Blue-labeled objects which form multicompartmental structures and subsequently undergo crowding at $T =$ (i) 0, (ii) 30, (iii) and 60 min. (e) Cartoon schematic of the framboidal object growth process. (f) Magnified segments of fluorescence images at $T =$ (i) 0 and (ii) 60 min with relative fluorescence intensity traces (iii). Scale bars = 10 μm .

object diameter was 80% (Figure S21b). The mechanism by which this occurs can be related to the already reported examples,^{17,18} where a critical membrane tension is reached across the giant vesicle and induces vesicle cavitation and rupture, causing parts from the interior lumen to be ejected. In contrast with previous reports, however, now there is little observed regrowth of the vesicle after its collapse (Figure S21b). Previously observed behaviors relied on the presence of an external photocatalyst to provide the radicals for RAFT polymerization of methacrylate monomers.^{17,19} The slow polymerization of AN in this system can be reasonably offered as the explanation for the lack of regrowth observed in this study.

Interestingly, copolymerization of Nile Blue with AN did not result in “phoenix” behavior.¹⁹ The initially spherical objects transformed into multicompartmentalized structures, whose internal compartments were separated by an internal membrane (Figure 4di–iii,e). These multicompartment structures were distorted from their original spherical shape, as the energy provided by the excitation light drives the structures far-from-thermodynamic equilibrium during growth (Figure 4diii) and therefore from their spherical shapes. The fluorescence intensity increased during irradiation within the microscope (Figure 4diii,

fi–iii), which can be attributed to concentration of the dye molecules increasing within the membrane during phase separation.

DISCUSSION

The integration of the CuAAC reaction and RAFT-PISA resulted in the evolution of BCP assemblies when driven out of equilibrium under blue light irradiation. The PEG-*b*-PAN objects increase in size and population numbers and exhibit chemotaxis-driven crowding to the spot with highest light intensity. This behavior has previously been observed over periods of 14 h.^{17,18} In contrast, in this investigation we observed massive object chemotaxis within 1 h of microscopy analysis, which suggests that there is a greater anisotropy across the object membranes during irradiation. Unlike in the case where presynthesized macro-CTAs are provided to the PISA reaction, objects produced by click-PISA have additional contributions to the stability of the membrane, based on the rate of the CuAAC reaction (Scheme 2).

Within the illuminated area, the CuAAC reaction between azide-CTA and PEG-alkyne contributes to the stability of the membrane, as the PEG chains grafted to the membrane will

Scheme 2. Cartoon Schematic of the Integrated Processes in the Click-PISA Reaction^a

^aThe processes of initiation, CuAAC reaction, RAFT polymerization, and PISA of giant microscale objects are linked through integrated feedback loops related to the reduction of the CuAAC Cu(II) precatalyst by the activated CTA molecule.

shield the hydrophobic PAN from high energy interactions with the aqueous media.^{10,16,32} Further polymerization of AN will destabilize the membrane as the comprising BCPs increase in amphiphilicity and hydrophobic volume fraction. In response to these two influences, further rearrangement of the macromolecules (self-assembly) occurs to minimize the surface energy which, then, changes the morphology (Figure 4a–f). Remarkably, these contributions can be mapped to a feedback system consisting of integrated feedback loops (Scheme 2, Supplementary Scheme 2). This is a far from trivial system, controlled by the RAFT-PISA process which led to object growth until collapse, multicompartmentalization, and en-mass chemotaxis under the far-from-equilibrium conditions induced by light irradiation within the microscope. Self-assembly acts as positive feedback to the RAFT polymerization because phase-separation increases the local monomer concentration in the vicinity of the CTA functional groups.³³ The reduction of the Cu(II)-PMDETA precatalyst by electron abstraction from the RAFT polymerization to activate the CuAAC reaction drives a negative feedback loop. Remarkably, this system comprising positive and negative feedback has the same topological structure as the canonical system for describing adaptation in control engineering.^{28,34} This provides a potential mechanism toward chemical adaptivity, where the degree of adaptation in the system to external inputs is dependent on the relative rates of the associated chemical and physical processes.

SUMMARY AND CONCLUSIONS

The one-pot chemically integrated click-PISA reaction generates self-assembled objects through a dissipative far-from-equilibrium reaction, while being derived from simpler parts than in standard PISA thanks to the complementary catalytic processes. We observe complex behavior in terms of morphological evolution and population growth, alongside ensemble behaviors in response to light stimulation, namely chemotactic-driven

crowding. By jointly using principles of systems chemistry and adaptive control and using nonamphiphilic simple components, we synthesized objects capable of complex collective behaviors. These are observed as the photodriven click-PISA process in the fluorescence microscope pushes the system far-from-equilibrium. Changing the external input patterns “forces” the system’s dynamic response properties, thus demonstrating this approach as a design (with control) of adaptive populations of colloidal objects. This work can ultimately lead toward dissipative materials or synthetic models of natural population phenomena inspired by processes already exhibited by extant life and involving adaptation.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acscentsci.1c00681>.

Experimental details and methods, materials and morphological characterization (PDF)

Video S1: Video of a click-PISA sample undergoing blue light illumination cycles over 1 h, obtained from bright-field optical images (MPG)

Video S2: Video of a click-PISA sample labeled with Rhodamine B-functionalized monomers undergoing blue light illumination cycles over 1 h, obtained from fluorescence images (MPG)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

S.P. would like to thank Drs. Chenyu Lin, Sai Krishna Katla, and Gong Cheng for useful scientific discussions. S.P. thanks Dr. Alec Pawling for help with the image analysis and Matlab code. This work was funded by Repsol, S.A., Spain. The funders had no role in the study design, data collection, and analysis, decision to publish, or preparation of the manuscript. Parts of this work were performed at the Center for Nanoscale Systems (CNS), a member of the National Nanotechnology Coordinated Infrastructure Network (NNCI), which is supported by the National Science Foundation under NSF award no. 1541959. CNS is part of Harvard University.

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