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Chemical Programming of Solubilizing, Nonequilibrium Active Droplets

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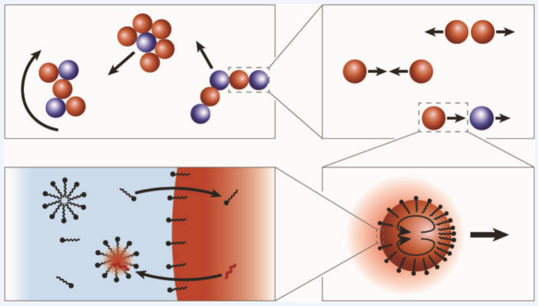

CONSPECTUS: The multifunctionality and resilience of living systems has inspired an explosion of interest in creating materials with life-like properties. Just as life persists out-of-equilibrium, we too should try to design materials that are thermodynamically unstable but can be harnessed to achieve desirable, adaptive behaviors. Studying minimalistic chemical systems that exhibit relatively simple emergent behaviors, such as motility, communication, or self-organization, can provide insight into fundamental principles which may enable the design of more complex and life-like synthetic materials in the future.

Emulsions, which are composed of liquid droplets dispersed in another immiscible fluid phase, have emerged as fascinating chemically minimal materials in which to study nonequilibrium, life-like properties. As covered in this Account, our group has focused on studying oil-in-water emulsions, specifically those which destabilize by solubilization, a process wherein oil is released into the continuous phase over time to create gradients of oil-filled micelles. These chemical gradients can create interfacial tension gradients that lead to droplet self-propulsion as well as mediate communication between neighboring oil droplets. As such, oil-in-water emulsions present an interesting platform for studying active matter. However, despite being chemically minimal with sometimes as few as three chemicals (oil, water, and a surfactant), emulsions present surprising complexity across the molecular to macroscale. Fundamental processes governing their active behavior, such as micelle-mediated interfacial transport, are still not well understood. This complexity is compounded by the challenges of studying systems out-of-equilibrium which typically require new analytical methods and may break our intuition derived from equilibrium thermodynamics.

In this Account, we highlight our group's efforts toward developing chemical frameworks for understanding active and interactive oil-in-water emulsions. How do the chemical properties and physical spatial organization of the oil, water, and surfactant combine to yield colloidal-scale active properties? Our group tackles this question by employing systematic studies of active behavior working across the chemical space of oils and surfactants to link molecular structure to active behavior. The Account begins with an introduction to the self-propulsion of single, isolated droplets and how by applying biases, such as with a gravitational field or interfacially adsorbed particles, drop speeds can be manipulated. Next, we illustrate that some droplets can be attractive, as well as self-propulsive/repulsive, which does not fall in line with the current understanding of the impact of oil-filled micelle gradients on interfacial tensions. The mechanisms by which oil-filled micelles influence interfacial tensions of nonequilibrium interfaces is poorly understood and requires deeper molecular understanding. Regardless, we extend our knowledge of droplet motility to design emulsions with nonreciprocal predator−prey interactions and describe the dynamic self-organization that arises from the combination of reciprocal and nonreciprocal interactions between droplets. Finally, we highlight our group's progress toward answering key chemical questions surrounding nonequilibrium processes in emulsions that remain to be answered. We hope that our progress in understanding the chemical principles governing the dynamic nonequilibrium properties of oil-in-water droplets can help inform research in tangential research areas such as cell biology and origins of life.

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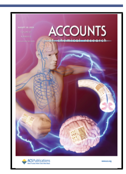

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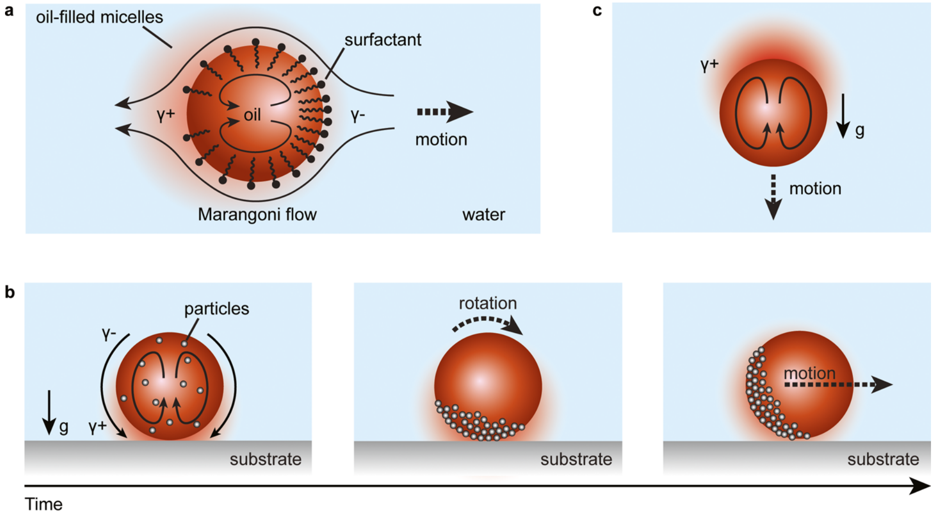

Figure 1. Self-propulsion of isolated droplets. (a) Scheme of the proposed mechanism for droplet self-propulsion. An oil droplet undergoing micellar solubilization emits oil-filled micelles, and spontaneous symmetry breaking can result in an interfacial tension gradient (denoted by $\gamma+$ and $\gamma-$ for high and low interfacial tension, respectively). The interfacial tension gradients cause Marangoni flow which propels the droplet forward. The motion is self-sustaining under conditions of appropriate Péclet number.[20] The surfactant is not drawn to scale proportionally with the droplet. (b) Schematic showing how particles adsorbed to a solubilizing droplet interface can enhance droplet motility.[4] Particles dispersed within a nonmotile, solubilizing oil droplet over time adsorb to the interface. Marangoni flow, which is induced by symmetry breaking in the solubilized oil gradients by the substrate, packs the adsorbed particles into a cap. The cap rotates, breaking lateral symmetry, and results in droplet lateral motion. (c) A self-propelled droplet settling under the effects of gravity (g) experiences both Marangoni and gravitational forces, the combination of which affects the speed and trajectory the droplet takes as it settles.[21] Panel b adapted with permission from ref 4. Copyright 2021 Royal Society of Chemistry. Panel c adapted with permission from ref 21. Copyright 2023 American Physical Society.

repulsive behavior is hypothesized to arise from a kinetic balance of molecular and micellar solubilization pathways.

- Meredith, C. H.; Moerman, P. G.; Groenewold, J.; Chiu, Y.-J.; Kegel, W. K.; van Blaaderen, A.; Zarzar, L. D. Predator−Prey Interactions between Droplets Driven by Non-Reciprocal Oil Exchange. *Nat. Chem.* **2020**, *12*, 1136−1142.[2] *Oil droplets with different compositions exhibit chasing behavior. This nonreciprocal interaction arises from net oil transport between solubilizing droplets to create a source−sink pair and leads to droplet self-organization.*
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- Cheon, S. I.; Silva, L. B. C.; Khair, A. S.; Zarzar, L. D. Interfacially-Adsorbed Particles Enhance the Self-Propulsion of Oil Droplets in Aqueous Surfactant. *Soft Matter* **2021**, *17*, 6742−6750.[4] *Adding hydrophobic particles to an oil droplet which adsorb to its interface can dramatically increase swimming speeds; in some cases, particles cause inactive droplets to become active. Particles are hypothesized to modify behavior by introducing anisotropy in the droplet structure.*

■ INTRODUCTION

Understanding how to design and control nonequilibrium systems that convert chemical energy into motion is critical for the development of adaptive and multifunctional life-like synthetic materials.[5] One class of dynamic materials that has attracted considerable interest is active colloidal swimmers. Microscale swimmers dissipate energy as mechanical work, thus breaking detailed balance. An example of a living active swimmer in nature is bacteria, which consume adenosine triphosphate to swim using flagella.[6] Active colloids are chemically minimal systems which similarly yield motility from chemical reactions or chemical gradients. There are many different types of active colloids, such as solid catalytic bimetallic nanorods and polymeric microrobots, which have been examined extensively.[7−12] Liquid microdroplets can also be active and are sometimes called swimming or self-propelled droplets; in many cases, active droplets not only are motile but also can chemically interact with each other. The rudimentary droplet "life-like" behavior was actually noted as early as 1892 by Otto Bütschli who studied oil-in-water droplets as protocellular components.[13] However, this knowledge was seemingly lost until a century later when self-propelled droplets were theoretically proposed in 1994 independent of Bütschli's work.[14] Several experimental examples of self-propelled swimmers followed.[15−17] This later work primarily focused on the hydrodynamics and mass transport involved in droplet motion. Systematic exploration of the role of the molecular composition on the properties of active droplets has emerged more recently, revealing the relatively unexplored chemical complexity that orchestrates droplet self-propulsion, interactions, and self-organization.

In this Account, we discuss the progress our group has made toward understanding the chemical principles governing active behaviors of oil-in-water emulsions.[1−4,18−25] As chemists, we are interested in developing a chemo-mechanical framework that connects the chemical makeup of emulsions to behaviors such as droplet self-propulsion and communication. Our research often adopts a systematic exploration strategy,

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sampling across the chemical space of oils and surfactants to identify the role of different components in generating active motion and droplet interactions, including repulsion, attraction, nonreciprocal interactions, and collective organization. We build upon this intuition to develop a more complete picture of the nonequilibrium molecular processes in emulsions and apply this understanding to design active droplet systems with higher order complexity.

THE CURRENT PICTURE OF SELF-PROPELLED DROPLETS

Emulsions consist of liquid droplets dispersed in another immiscible liquid continuous phase, often with an interfacial stabilizer such as a surfactant. Most emulsions are out-of-equilibrium and undergo processes such as coalescence, Ostwald ripening, etc.[26,27] With addition of an emulsifying agent, such as a surfactant that decreases interfacial tension and reduces coalescence, emulsion droplets can persist for days to years.[27] Active droplets may be "fueled" and become motile by several mechanisms, including interfacial reactions,[28−30] externally applied fields,[31] or solubilization.[16] These processes can create gradients across the drop surface which in turn lead to interfacial tension gradients and self-propulsion via Marangoni flow.

We focus here on active droplets driven by solubilization. Considering oil-in-water droplets, oil is solubilized from the droplet into the aqueous phase by micelles, which are self-assembled surfactant aggregates that form above the critical micelle concentration (CMC). But how does solubilization generate the requisite interfacial tension gradient for self-propulsion? One hypothesis is that the surfactants in the oil-filled micelles are more tightly "bound" and thus less available to saturate the droplet interface, leading to an increase in interfacial tension.[32−34] Similarly, a decrease in the CMC in the presence of solubilized oil would decrease the concentration of surfactant monomers and increase interfacial tension. As such, spontaneous symmetry breaking in the released cloud of solubilized oil creates a gradient of oil-filled micelles across the drop surface and generates an interfacial tension gradient that leads to Marangoni flow (Figure 1a). Provided that advective surfactant transport is fast relative to diffusion (e.g., a sufficiently large Péclet number),[35] there is positive feedback that enables an isotropic droplet to continuously self-propel without any applied field; drops with a low Péclet number quickly re-establish a symmetric chemical environment via diffusion and have no self-propulsion. These conceptual frameworks are useful to intuit many (but not all) of the observed active droplet behaviors, but our understanding is far from complete. For instance, it is not a given that solubilization will lead to interfacial tension gradients; e.g., we have observed that bromoalkane oil drops are not active in any concentration of the nonionic surfactant Tween 20 despite solubilizing at a considerable rate. We have also reported solubilizing droplets that appear to have their interfacial tension *lowered* in the presence of solubilized oil.[1] Though we may not precisely know the molecular mechanisms by which interfacial tension gradients are generated, we do know that interfacial tension gradients are present as evidenced by the convective flows in and around the droplet.

ASYMMETRY IN ISOLATED SELF-PROPELLED DROPLETS

For a colloid to move, it must experience tangential stress arising from some form of asymmetry. Manipulating the source and direction of the asymmetry can provide routes to control the speed, direction, and efficiency of colloid motility. Compared to other widely studied colloidal swimmers, such as catalytic Janus particles wherein motion is derived from intrinsic asymmetry in the particle,[7] an isotropic, single-phase droplet necessitates symmetry breaking of some other source for motility. For many self-propelled droplets, the symmetry breaking can happen spontaneously and become self-sustaining through positive feedback provided the ratio of advective transport to diffusive transport (Péclet number) is sufficiently high. For a solubilizing droplet near a solid surface, the wall can break symmetry, sometimes leading to droplet levitation.[32,33,36] We have also studied two additional cases where symmetry breaking occurs: solubilizing droplets with particle-laden interfaces and droplet gravitational settling.

Asymmetrically Adsorbed Particles Enhance Droplet Motility

We discovered that a simple approach to enhancing droplet speed is adding interfacially adsorbed particles (Figure 1b).[4] Hydrophobic silica particles are dispersed inside oil and emulsified in aqueous surfactant to produce droplets. Symmetry breaking from the substrate initially leads to some Marangoni flow from top to bottom of the droplet. As particles adsorb to the interface over time, this flow packs the particles into a cap at the drop's bottom pole. An inhomogeneous particle distribution results in spontaneous cap rotation and lateral Marangoni force which propels the droplet sideways. Cap size is controlled by the particle concentration, and the speed of the droplet correlates with the cap's surface coverage. Peak drop speeds are reached when the cap coats about half of the drop surface. While the mechanism of how the adsorbed particles enhance the drop motility is not fully understood, we presume a key aspect involves the cap's introduction of additional asymmetry across the interface. The precise mechanism is likely more complicated; particles and surfactants stabilize interfaces by different mechanisms (interfacial displacement and reduction in interfacial tensions, respectively),[37,38] and when both particles and surfactants are present at an interface, there can be complex interactions between them.[39,40] Regardless, the general effect is robust, with enhancements in drop speeds observed for a wide array of oils and surfactants (both nonionic and ionic).[4] For example, adding particles to bromohexadecane droplets in 0.5 wt % Triton X-100 produced swimming speeds of nearly 100 μm/s, whereas the drops without particles did not self-propel. Perhaps future work on the observed properties of the active droplets may provide some insight into the physiochemical properties of liquid interfaces when both surfactants and particles are present.

Active Droplets under the Effect of Gravity

We have explored how symmetry breaking due to gravitational settling of dense, active droplets can influence droplet speed and directional motion.[21] We expect alignment between the Marangoni force of a self-propelled droplet and the gravitational force (Figure 1c). We were interested whether this force alignment increases droplet settling speed. We measured the settling speed of bromodecane droplets of varying diameter in both low (0.01 wt %) and high (3 wt %) Triton X-100

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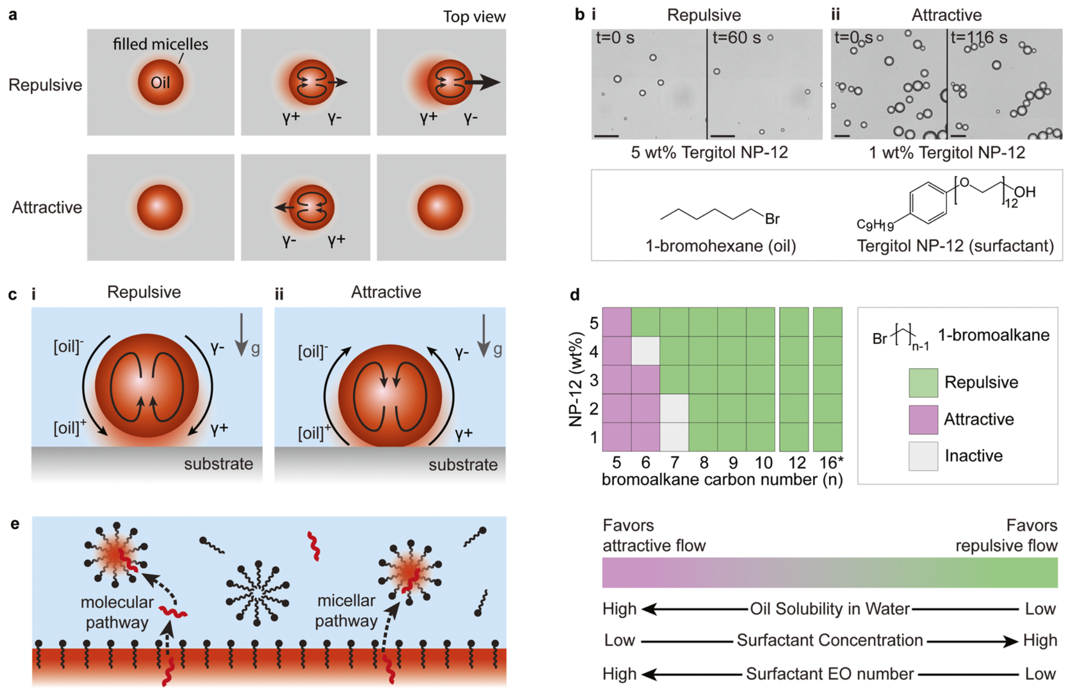

Figure 2. Droplets can be repulsive or attractive. (a) For repulsive droplets, filled micelles are chemorepellents, leading to positive feedback and sustained self-propulsion. For attractive droplets, filled micelles are chemoattractants, so droplets experience a self-restoring force and have no lateral motion. (b) 1-Bromohexane droplets (b-i) repel in 5 wt % Tergitol NP-12 and (b-ii) attract in 1 wt % Tergitol NP-12. Scale, 50 μm. (c-i) Repulsive droplets exhibit increased interfacial tension in the presence of oil-filled micelles, resulting in flow from the top to bottom of the droplet. Sometimes, droplets levitate. (c-ii) Attractive droplets exhibit reduced interfacial tension in the presence of oil-filled micelles, resulting in flow from the bottom to top of the droplet. (d) Repulsive/attractive/inactive behavior is dependent on the bromoalkane carbon number (n) and surfactant composition. n = 16* has an asterisk (*) because it is an iodoalkane, not a bromoalkane. (e) Two proposed transport pathways for solubilization into micelles. The kinetic balance of these solubilization pathways might affect the interfacial tension. Panels b−d adapted with permission from ref 1. Copyright 2022 John Wiley and Sons.

surfactant concentrations (CMC = 0.02 wt %). We compared the observed settling speed to the Hadamard−Rybczynski (HR) prediction for the settling of liquid droplets in an immiscible medium without Marangoni stresses. Droplets with no self-propulsion in a dish environment (i.e., low Triton X-100 concentrations) settled slightly slower than the HR prediction regardless of droplet size; this is also typical for bubbles in the presence of surfactant and is expected.[41−43] In contrast, droplets which were self-propelled in a dish, with radii between 10 and 40 μm, had increased settling speeds with up to a 4-fold enhancement for the smallest droplets. However, at larger diameters, gravity dominated and contributions in settling speed from the Marangoni force disappeared. In some cases, we observed decorrelated droplet trajectories due to lateral forces from the Marangoni flow; this chaotic settling became more pronounced for small droplets where the Marangoni force dominated over the gravitational force.

■ PAIRWISE DROPLET INTERACTIONS

Attractive Droplets

There are many reported cases of solubilizing, self-propelled single emulsion droplets of various composition.[20,33] However, as noted previously, there is uncertainty around the mechanism by which the interfacial tensions are altered for these solubilizing, nonequilibrium interfaces. We wondered, if the interfacial tension can be increased by the products of solubilization in some situations, is it also possible that interfacial tension is *decreased* in others? We set out to try to find such a situation.[1] Consider a droplet wherein interfacial tension is decreased by the products of solubilization: that droplet would be "attracted" to higher concentrations of oil. Even if the droplet was perturbed, it would be attracted to the oil-filled micelles which it emits, thus experiencing a self-restoring force and no motility (Figure 2a). Unfortunately, droplet nonmotility is the norm rather than exception, so searching for nonmotile droplets was not going to be very useful. However, if two such droplets were to drift into each other's vicinity, we would expect them to be attracted to each other. This gave us something to look for: situations where oil droplets experienced short-range chemo-attractive interactions.

In our initial search for attractive droplets, we chose to focus on the bromo-n-alkane oil droplets as a model droplet system since their water solubility can be tuned with the alkyl chain length and many of them are denser than water which is experimentally convenient. Starting with 1-bromohexane in the nonionic nonylphenylethoxylate surfactant Tergitol NP-12 (CMC = 0.0085 wt %), we found that droplets in 5 wt % Tergitol NP-12 were mutually repulsive as expected (Figure 2b-i). However, simply lowering the Tergitol NP-12 concentration to 1 wt % caused the same droplets to become mutually attractive (Figure 2b-ii). This same transition from repulsive to attractive behavior was observed for droplets composed of different oils (1-bromooctane and 1-bromopentane) in the same surfactant, 2 wt % Tergitol NP-12. Inspection of the flows around single, isolated repulsive and attractive droplets from the side profile matched expectation, where repulsive droplets pumped fluid from top to bottom (toward the substrate; Figure 2c-i) while attractive droplets pumped fluid from bottom to top (away from the substrate;

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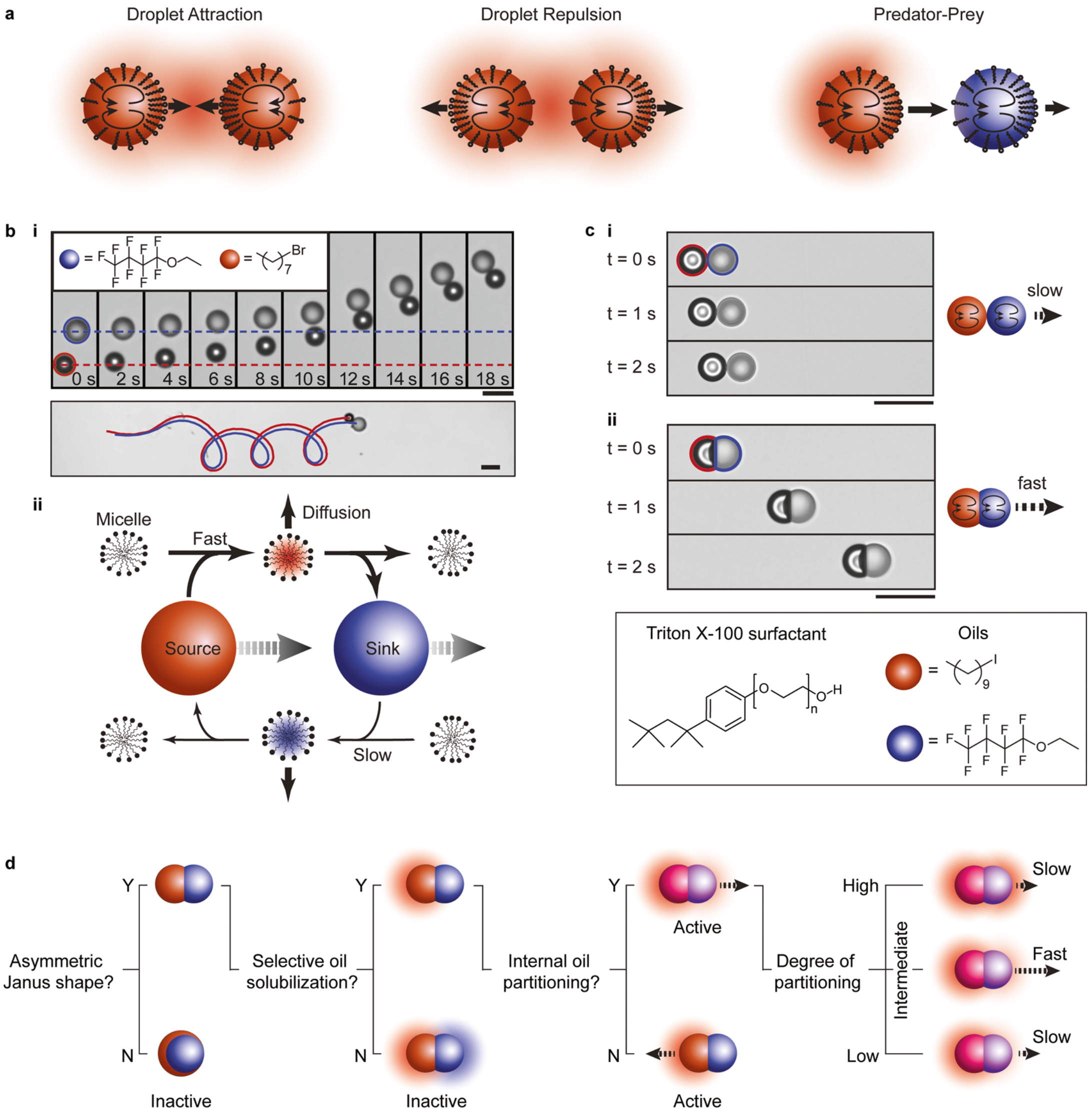

Figure 3. Interactions between droplets are mediated by oil transport and exchange. (a) Two droplets can have reciprocal (attractive/repulsive) or nonreciprocal (predator−prey) interactions. (b) Predator−prey behavior in active oil droplets. (b-i) A 1-bromooctane droplet (red) chases an ethoxynonafluorobutane (EFB) droplet (blue). (b-ii) Schematic of the source−sink framework governing drop chasing. (c) Comparison of predator−prey single emulsion drops and Janus droplets of the same oil composition. (c-i) A 1-iododecane predator droplet chases an EFB prey droplet. (c-ii) A Janus droplet composed of 1-iododecane and EFB swims over an order-of-magnitude faster than the predator−prey type single droplets. (d) Decision tree outlining how different characteristics of a Janus droplet impact active behavior. All scale bars are 100 μm. Panels b−d adapted with permission from refs 2 and 3. Copyright 2020 Springer Nature and 2022 Elsevier.

Figure 2c-ii). We expect the concentration of oil-filled micelles to be higher near the substrate where diffusion is limited; we thus inferred a relationship between the concentration gradients of oil-filled micelles and the interfacial tension gradients for both the repulsive and attractive droplets.

To try to gain insight into the mechanism governing the change in interfacial tensions, we searched for qualitative trends in the relationship between droplet behavior (i.e., attractive vs repulsive vs inactivity with no discernible interfacial flows) and different points in compositional chemical space (i.e., variation in the oil, surfactant molecule, and surfactant concentration). Screening across the bromo-*n*-alkanes ($n = 5-16$), the Tergitol NP series of surfactants (with average number of headgroup ethylene oxide repeat units from 9 to 30), and surfactant concentration (1−5 wt %), we observed the following trends: attractive flow was favored for lower carbon number oils, larger surfactant headgroups, and lower surfactant concentrations (Figure 2d). Droplets could show inactivity for conditions in the intermediate regime between attractive and repulsive conditions. Interestingly, the conditions which favor attractive vs repulsive behavior correlated to those in which solubilization favors the molecular vs micellar pathway, respectively (Figure 2d). In the molecular pathway, oil molecules diffuse into the continuous phase and are subsequently taken up into micelles, while in the micellar pathway, oil is directly incorporated into micelles at the liquid−liquid interface (Figure 2e). The molecular pathway would be favored for oil having higher water solubility (low carbon number), larger surfactant headgroups (which discourages micelles approaching the interface due to sterics) and lower surfactant concentrations (i.e., fewer micelles). An interesting hypothesis that follows is that a kinetic balance between these two transport processes influences the droplet's interfacial composition and interfacial tension. To the best of

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our knowledge there is currently no analytical method to directly characterize the solubilization mechanism for a droplet *in situ*. Indirect strategies based on solubilization rates have been reported and are useful for making inferences about the solubilization mechanism.[44,45] However, it is challenging to glean rigorous insights using these methods due to the many interconnected phenomena (advection, surfactant partitioning into the droplet,[24,25] etc.) occurring in active droplets. New tools and methods to investigate how out-of-equilibrium interfacial transport impacts liquid–liquid interfaces are needed to draw conclusions.

Net Oil Transport between Source–Sink Droplets Drives Nonreciprocal Interactions

By creating gradients, modifying gradients, and exchanging chemicals, droplets can "communicate". This "communication" can lead to simple, pairwise reciprocal interactions as discussed in prior, wherein solubilizing droplets can attract or repel depending on whether the products of solubilization lower or raise interfacial tension, respectively. However, in nature, we also observe examples of pairwise nonreciprocal interactions between species such as predator–prey behavior;[46−48] this nonreciprocity defies action–reaction symmetry and can only occur in nonequilibrium situations.[49,50] Developing the ability to create droplets systems that combine attractive, repulsive, and chasing interactions presents an exciting opportunity to study collective behavior and experimentally test theories that have been developed in this field of active colloids.[49,51,52] So, how can we also go about designing nonreciprocal chemotactic droplets (Figure 3a)?

Upon mixing two populations of droplets, 1-bromooctane and ethoxynonafluorobutane (EFB) in 0.5 wt % Triton X-100 surfactant, we noticed something surprising: the 1-bromooctane droplets were attracted to EFB, while EFB droplets were repelled by bromooctane. This appeared to be an example of a "predator–prey" nonreciprocal interaction (Figure 3b-i).[2] To understand the underlying chemomechanical mechanism, we considered the transport kinetics between droplets and the continuous phase and the thermodynamics of mixing. While the two oils are fully miscible, only the 1-bromooctane droplet was solubilized into the Triton X-100. Thus, the gradients driving motion were composed of solubilized bromooctane. When we placed a high number density of the two types of droplets together in proximity, the EFB droplets' refractive index (initially n = 1.28) steadily increased while the 1-bromooctane droplets' refractive index (n = 1.45) remained fairly constant, indicating that EFB absorbed 1-bromooctane. These two oils thus form a source–sink pair that facilitates chasing: bromooctane is the source of chemorepellent oil, while EFB is the sink for the chemorepellent. Favorable free energy of mixing of the two oils coupled with asymmetric transport kinetics enables the formation of the source–sink pair. Both droplets move away from high concentrations of the chemorepellent, leading to a sustained chase (Figure 3b-ii).

Chasing occurs for many different oils, and the oil chemical structures need not be so dissimilar. For example, 1-iodoheptane chases 1-iodohexane. Alkanes also exhibit chasing but are less dense than water so are not as experimentally convenient to study compared to haloalkanes. When we characterized the chasing interactions between droplets composed of different oil pairs, we found that oils of both the lowest (n = 4−6) and highest (n = 12 and 16) carbon numbers tended to be prey, whereas intermediate (n = 7−10) carbon numbers tended to be predators. There was also a nonmonotonic relationship between solubilization rate and carbon number. Thus, solubilization rates alone did not dictate predator or prey. Interestingly, the tendency of a droplet to be predator or prey aligned with our expectation of whether an oil should primarily solubilize via the molecular or micellar pathway (Figure 2d). The two oils also had to have some degree of miscibility (even a few volume percent) to facilitate the oil exchange in order to generate chasing. Changing the surfactant was useful in modifying the direction of the oil transport and hence direction of the chase. These observations highlight how the predator–prey behavior not only is influenced by the direction and rate of oil transport between droplets but also is likely affected by the oil solubilization transport pathway which appears to influence the interfacial tensions.

Motile, Biphasic Source–Sink Janus Droplets

In predator–prey single emulsion droplets, motility depends on micelle-mediated oil transfer through the water. We wondered how adding an oil–oil interface between source and sink across which molecules can directly partition, such as in a biphasic Janus droplet, would influence swimming speed. To investigate swimming Janus droplet behavior, we began by testing Janus droplets containing a pair of oils that exhibit predator–prey behavior: 1-iododecane and EFB.[3] While not fully miscible, these oils have a few volume percent solubility in each other. The 1-iododecane and EFB source–sink pair moved over an order of magnitude faster when in a Janus droplet compared to single emulsions (about 200 μm/s versus 13 μm/s in 0.5 wt % Triton X-100) (Figure 3c). The Janus drop propulsion efficiency, defined as the ratio of swimming speed to loss rate of oil via solubilization, was also about 14 times higher than the predator–prey single emulsion droplets. Testing Janus droplets containing many different combinations of oils in Triton X-100, we observed that the degree of oil partitioning between the two compartments, oil solubilization rates, and Janus droplet shape were important factors controlling droplet speed. The fastest Janus droplets that we prepared moved up to 3−4 body lengths per second (∼350 μm/s).

The impact of each of these factors affecting drop speed is summarized in an empirical decision tree (Figure 3d). First, an asymmetric Janus shape is required for fast motion. Second, one oil should be preferentially solubilized. Third, oil partitioning across the oil–oil interface is critical, influencing both the speed and the swimming direction. Oil combinations with an intermediate degree of oil partitioning (≈2−6 vol %) demonstrate fast swimming. Since the source oil can solubilize out of both compartments in the Janus drop, we imagine that there is continuous net transfer of the source oil into the sink compartment as the drop swims. Oil combinations which have very low degree of mutual solubility may exhibit "reverse" swimming, where the solubilizing predator is in the lead, prey at the rear, to maximize the advection of empty micelles to the droplet interface. Generally, factors which increase asymmetry in the chemical environment contribute to droplet motility; however asymmetry in droplet shape (Janus morphology) alone is not enough to generate motion, and the two oil compartments must cooperatively exchange molecules to generate motion.

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■ SELF-ORGANIZATION OF INTERACTING ACTIVE DROPLETS

Emergent behavior and organization in multibody systems such as swarming insects, traffic jams, or schools of fish result from nonequilibrium, distance-dependent coupling between group constituents that is often nonreciprocal. This dynamic self-organization under nonequilibrium conditions contrasts with the self-assembly of static structures that form at equilibrium. As our group has demonstrated,[1,2] active droplet mixtures can exhibit both reciprocal (attractive/repulsive) and nonreciprocal (predator−prey) behaviors, making these systems ripe for studying emergent self-organization phenomena. Indeed, when we increased the number density of droplets in a predator−prey system, we found that droplets not only formed chasing dimers but also could self-organize into larger clusters each with their own characteristic dynamics, such as translational motion, rotation, run and tumble behavior, etc. (Figure 4a). Droplet clusters influenced one another via longer-range solute-mediated interactions. Varying the number density and relative diameters of the predator−prey droplets as well as the surfactant molecule produced a range of self-organized structures which spontaneously assembled and disassembled over their lifetimes (Figure 4b).[53] The droplet dynamics were well-described using a minimal model composed of chemotactic interactions and steric repulsions.

Active Janus droplets[3] also exhibited self-organization. Janus droplets slowed down and reoriented when encountering the "exhaust trails" (solubilized oil) of other droplets (Figure 4c); this behavior has been observed in other active droplets[54] and is reminiscent of trail-mediated interactions in living systems such as ants and bacteria.[55] When the number density of droplets increased, the Janus droplets formed clusters of typically 3 to 5 droplets which rotated clockwise or counterclockwise depending on symmetry (Figure 4d). We suspect these clusters form a vortex which cooperatively pumps fresh surfactant solution toward the cluster and solubilized oil away from the cluster. We also demonstrated use of a near-infrared laser to induce temperature-directed motion and orientation of Janus droplets; the effects of temperature can be complex, as temperature impacts solubilization rates, interfacial tensions, and degree of oil mixing[56] (Figure 4e).

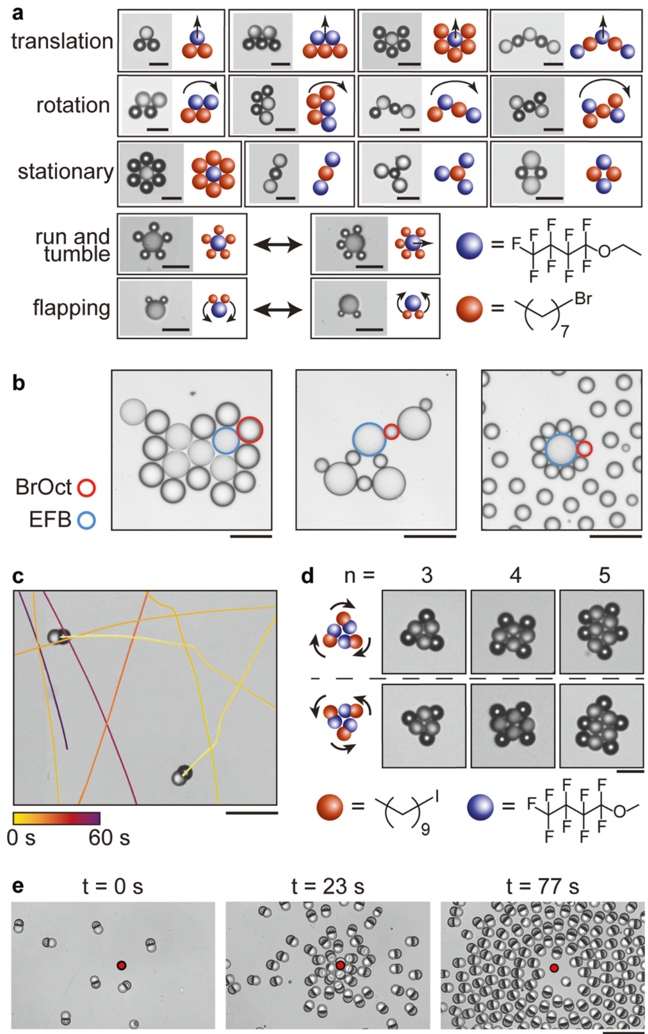

Figure 4. Self-organization of interacting active droplets. (a) Self-organization of predator−prey droplets in 0.5 wt % Triton X-100. Red droplets (predators) are 1-bromooctane (BrOct) and blue droplets (prey) are ethoxynonafluorobutane (EFB). Scale, 100 μm. (b) Varying number density and diameter of BrOct and EFB drops produces a range of self-organized structures. Scale, 100 μm. (c) Janus droplets of 1-iododecane and EFB in 0.5 wt % Triton X-100 slow down and reorient when encountering the exhaust trails of other droplets. Scale, 250 μm. Trail color corresponds to age. (d) Spinning clusters of Janus droplets of 1-iododecane (red) and methoxyperfluorobutane (blue) in 0.5 wt % Triton X-100. Scale, 100 μm. (e) 1-iododecane/EFB Janus droplets in 0.5 wt % Triton X-100 exposed to a near-IR laser, focused on the red dot. The laser heats the solution locally, attracting droplets that organize radially. Scale, 250 μm. Panels a and c−e adapted with permission from refs 2 and 3. Copyright 2020 Springer Nature and 2022 Elsevier.

■ LINKING MOLECULAR-SCALE PROCESSES TO COLLOIDAL-SCALE BEHAVIOR

As chemists, our observation that oil-filled micelles can increase, decrease, or have no impact on interfacial tension compared to empty micelles at surfactant concentrations far above the CMC was puzzling to us.[1] The underlying chemical cause is nonobvious, especially when considering that simply lowering the surfactant concentration while keeping all else constant can flip a droplet's behavior from repulsive (increased interfacial tensions) to attractive (decreased interfacial tensions). In general, characterizing nonequilibrium fluid interfaces can be challenging, but it seems we have much more to learn. Employing emerging spectroscopic methods that can provide some information about the molecular structures of the micelles or the interfaces may provide valuable insights.

Oil-Filling of Micelles Affects Water Structure

Elucidating the structure of the oil-filled versus empty micelle might provide insight about the structure of the surfactant-laden oil interface as it undergoes solubilization. We used Raman multivariate curve resolution (MCR) spectroscopy, which probes the degree of hydrophobic hydration, to gain insight about the oil and water structure within oil-filled micelles.[22] Raman MCR is an emerging technique used to detect changes in solvent structure upon addition of a solute. When micelles were filled with oil, we found that the amount of water solvating the micelle (referred to as "perturbed water") decreased; this change is evidenced by a decrease in the MCR area corresponding to perturbed water (Figure 5a). Testing alkanes of varying chain length, we found that shorter chain alkanes displaced more water than long chain alkanes in

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Acc. Chem. Res. 2024, 57, 2372−2382

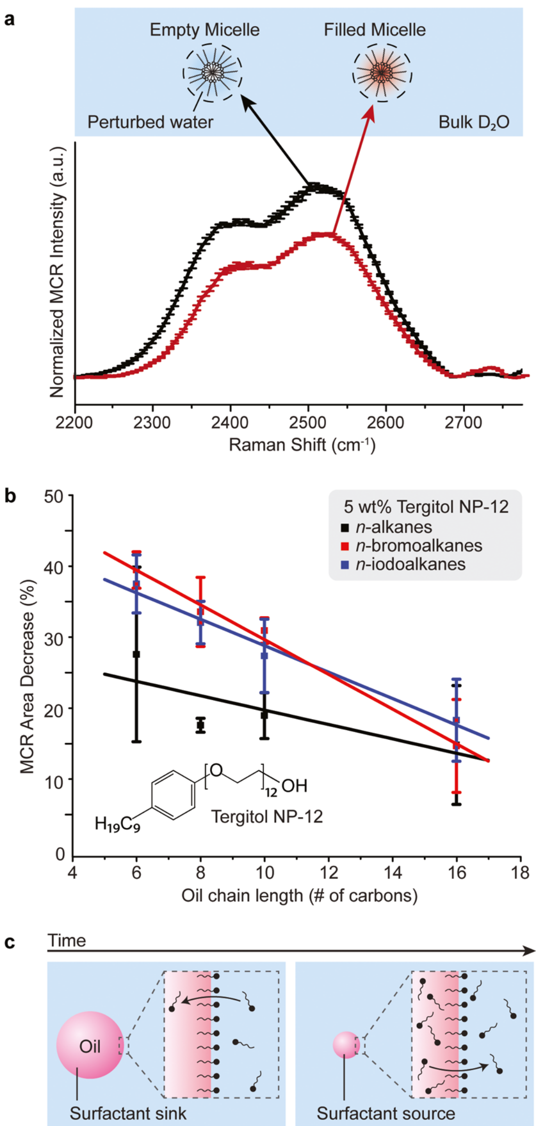

Figure 5. Molecular processes in emulsions. (a) Raman MCR resolves differences in water structure for a solution of empty Tergitol NP-12 micelles (black curve) and Tergitol NP-12 micelles filled with hexane (red curve). The area decrease corresponds to displacement of perturbed water from the micelle upon hexane solubilization. (b) MCR area decrease for various oils when filling Tergitol NP-12 micelles. (c) An oil droplet is a surfactant sink at early times as it partitions surfactant then becomes a surfactant source as it loses volume via solubilization. Panels a and b adapted from ref 22.

micelles of Tergitol NP-12 (Figure 5b). For short chain oils, the surfactant pi–hydrogen interaction disappeared in the Raman MCR spectrum, implying that oil displaced the water around the aromatic group of the surfactant and penetrated further into the hydrophilic region of the micelle. Short chain alkanes are more readily soluble than long chain alkanes in PEG 200 (which has a similar structure to the headgroup of the alkylphenol ethoxylate Tergitol NP-12) so this observation seems reasonable. Trends in the impact of oil-filling on water structure were similar for micelles of Makon TD-12 and sodium dodecyl sulfate. The insights into how the micelle structure depends on oil and surfactant chemistries are likely mirrored in the structure of the bulk oil–water interface. However, further investigation is required to understand how these molecular structures are related to the apparent interfacial tensions.

Nonequilibrium Surfactant Partitioning

Discussion up to this point has assumed that droplets produce chemical gradients via oil solubilization which leads to droplet chemotaxis. However, especially when using nonionic surfactants, the surfactant itself can also partition into the oil. Surfactant partitioning between oil and water has been studied extensively at equilibrium.[57,58] We were curious as to what degree, and over what time scales, nonionic surfactant would transfer from the aqueous phase into a nonequilibrium solubilizing oil droplet. In this scenario, the droplet has a finite lifetime and disappears at equilibrium, so the system cannot be described by an equilibrium partition coefficient. How should we think about partitioning in an out-of-equilibrium droplet? What impact does this partitioning have on the droplet activity (Figure 5c)?

Using quantitative mass spectrometry, we found that on short time scales (minutes) nonionic surfactants indeed partition into microscale droplets to significant concentrations; for example, the concentration of Tergitol NP-9 inside a tetrachloroethylene droplet was 22% w/v when the aqueous concentration was only 0.2% w/v.[25] The surfactant concentration in the droplet plateaued to a steady state that remained constant for the duration of analysis (2 h). The droplet solubilized during that time, slowly losing volume. Surfactant that goes in must eventually come out, and interestingly, at longer times (hours) we observed that droplets' release of the accumulated surfactant could lead to the evolution of ultralow interfacial tension.

Clearly, a solubilizing oil droplet can accumulate notably high concentrations of nonionic surfactant, in some cases much higher than the water, yielding nonequilibrium apparent partition coefficients, $K_{app} = C_o/C_w \gg 1$. In this sense, droplets can act as a surfactant sink at early times but then switch to a source at long times as surfactant is released during solubilization. Both surfactant uptake and surfactant release generate surfactant concentration gradients. We imagine the possibility that when the droplet acts as a surfactant sink, the local environment around the droplet is depleted of surfactant monomers causing the droplet to seek regions with higher surfactant concentration; when the droplet acts as a source, self-propulsion may be suppressed as the droplet experiences a restoring force toward its own emitted surfactant cloud. However, the role of partitioning-induced gradients in active drop motion remains to be explored. Nevertheless, we have observed that nonequilibrium surfactant partitioning can lead to surprising droplet dynamics such as sessile oil droplets that dewet from hydrophobic substrates,[24] oscillating oil-in-water droplets,[59] and other behaviors which are currently under investigation within our group.

■ CONCLUSION

Emulsions are one class of nonequilibrium materials which exhibit life-like dynamics such as active motion, communication between actors, and self-organization. Although active droplets have been studied extensively from a physical perspective, our group has been largely interested in how the chemistry of droplets impacts behavior and nonequilibrium properties. The ability to generate reciprocal and nonreciprocal interactions between droplets presents an opportunity to

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design self-organization and collective behaviors if we can understand how to chemically manipulate these interactions. Although the observations of droplet activity and interactions are robust, there are many remaining fundamental questions about the properties of fluid interfaces under nonequilibrium conditions. Much work remains to explore how chemical processes at the molecular scale impact colloidal-scale active, out-of-equilibrium behavior. In the future, we envision using this fundamental chemical knowledge to guide the construction of controllable active droplets for applications that require life-like adaptive behavior. These might include designing droplet microsensors,[60−62] employing droplet "vacuum cleaners" to sequester environmental pollutants,[63−66] modeling collective behaviors in biology,[53,67−69] drug/cargo delivery,[70−72] and engineering self-propelled protocells for biomedicine.[73−75] We also expect that studying the nonequilibrium properties of chemically minimal nonequilibrium droplets will help spur new advances in understanding more chemically complex multiphase systems including biomolecular condensates in cell biology[76−78] or chemically fueled protocells in origin-of-life theory.[79−81]

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CRediT: **Kueyoung E. Kim** conceptualization, visualization, writing-original draft, writing-review & editing. **Rebecca V. Balaj** conceptualization, visualization, writing-original draft, writing-review & editing. **Lauren D. Zarzar** conceptualization, visualization, writing-review & editing.

Notes

The authors declare no competing financial interest.

Biographies

Kueyoung Kim is an undergraduate majoring in chemistry at The Pennsylvania State University. His research focuses on the role of nonequilibrium liquid−liquid partitioning in oil-in-water emulsions.

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Lauren Zarzar earned bachelor's degrees in chemistry and economics at the University of Pennsylvania and earned a Ph.D. at Harvard University in the Department of Chemistry and Chemical Biology under the supervision of Joanna Aizenberg. She completed postdoctoral training at the Massachusetts Institute of Technology in the group of Timothy Swager. She has been a faculty member at The Pennsylvania State University since 2016, where her group studies complex fluids, nonequilibrium soft matter, laser synthesis, and microscale optics.

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