Computational Design of Microscopic Swimmers and Capsules: From Directed Motion to Collective Behavior

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Systems of motile microscopic particles often exhibit behaviors that resemble those of living microorganisms, including cooperative motion, self-organization, and adaptability to changing environments. Using mesoscale computational modeling, we design synthetic microswimmers and microcapsules that undergo controllable, self-propelled motion in solution. Stimuli-responsive hydrogels are used to actuate the microswimmers and to enable their navigation and chemotaxing behavior. The self-propelled motion of microcapsules on solid surfaces is achieved by the release of encapsulated solutes that alter the surface adhesiveness. These signaling solutes also enable interactions among multiple microcapsules that lead to complex, cooperative behavior. Our findings provide guidelines for creating microscopic devices and machines able to autonomously move and mimic the communication and chemotaxis of biological microorganisms.

Keywords: microswimmers, microcapsules, self-propulsion, self-organization, collective motion, computational modeling, mesoscale methods

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1. Introduction

Whether it is the swarming behavior of *Proteus mirabilis* during the colonization of agar surfaces [1] or the fertilization of an ovum by spermatozoa [2], in almost all biological systems, life and survival are ultimately dependent on the motility of unicellular microorganisms. Over a long evolutionary period, microorganisms have developed unique and effective methods to move in complex environments [3]. They are able to sense and distinguish different chemical and mechanical signals and navigate along their gradients [4, 5]. Mediated by molecular signaling mechanisms, microorganisms can self-organize to form colonies that exhibit sophisticated cooperative and social behaviors critical for the colonies' survival [6, 7]. Such coordinated behaviors are considered to have laid the foundation for the evolution of multicellular organisms [7].

Over the last several decades, researchers have been exploring various approaches to create microscopic synthetic systems that can mimic specific aspects of the complex behaviors that are attributed to unicellular microorganism [8-11]. Analogous motile and intelligent microrobots have enormous potential for applications in biomedical assays, tissue engineering studies, nano-manufacturing and other fields in which direct access and complex manipulations with micrometer and nanometer sized objects are required [12-15]. Furthermore, understanding the behavior of such synthetic "microbes" provides researchers with important insights into the underlying physics that enable microorganisms to move and perform other physiological functions in their native environments [16].

A range of synthetic microscopic swimmers that can effectively self-propel in a viscous fluid have been successfully created over recent years [17-22]. Some of these swimmers elegantly mimic the mechanics of microorganisms found in nature, such as the flagella-like gold and nickel based nanowire swimmers [23]. Other swimmers innovatively exploit engineering and hydrodynamic principles, such as the acoustically powered bubble swimmers [24]. Stimuli-sensitive polymeric materials [25] are especially attractive for designing biomimetic microswimmers. Their use enables direct external control over the swimmer motion and provides an effective means for incorporating self-regulating behavior and autonomous sensory functions into devices. Among stimuli-sensitive materials, hydrogels that are chemomechanical transducers [26] are of high interest due to their biocompatibility [27]. When exposed to external stimuli, such as changes in electric/magnetic fields, pH levels, temperature, light intensity, and salinity, these materials exhibit large and reversible mechanical deformations [28]. As such, hydrogel-based swimmers are particularly interesting for *in vivo* biomedical applications.

In the first part of this article, we describe our computational efforts to design microswimmers that utilize hydrogels for actuation or swimming control. We discuss how to design a simple, yet efficient microscopic swimmer that is made of a bi-layered hydrogel sheet that generates large amplitude, out-of-plane bending when exposed to an appropriate external stimulus [29]. We then discuss how such responsive, bending materials can be utilized to construct a synthetic microswimmer that can navigate in a microfluidic environment [30]. Furthermore, we describe how stimuli-sensitive microgels integrated with catalytic swimmers

yield a system in which the pH level sets the distribution of swimmers in space [31], thereby mimicking chemotaxing behavior of microorganisms [32].

In the second part of the article, we focus on modeling synthetic microcapsules in order to design cell-like objects, or “artificial cells”, that can undergo autonomous motion on solid surfaces. Microcapsules synthesized via the layer-by-layer (LbL) approach [33-35] or “polymersomes” [36-39] are attractive candidates for artificial cells since these objects can be tailored to exhibit a range of biomimetic, cell-like functionality [33]. The shells of the LbL microcapsules are sufficiently robust to act as a protective barrier, and adequately permeable for the controlled exchange of reagents with an external solution [40]. Furthermore, the permselectivity of the shells can be readily tuned [38, 39, 41-43]. By functionalizing the shell’s outer surface, these microcapsules can bind to an underlying substrate [38]. Moreover, the LbL microcapsules can encapsulate and release various nanoparticles [41-43]. There is also experimental evidence [44, 45] that if the released nanoparticles become bound to an underlying surface, they would be effective at regulating the capsules’ motion on this surface. In particular, a small fraction of adsorbed “sticky” nanoparticles were found to be highly effective at retarding and even arresting the fluid-driven motion of the colloids over the surface [44].

In these studies of cell-like systems, we describe our efforts to design a mechano-responsive capsule that releases nanoparticles under an applied force and then undergoes self-propelled motion [46]. We also discuss how the introduction of biomimetic feedback loops into the system can drive the collective behavior of multiple capsules [47-49]. Furthermore, we describe how patterned substrates can be used to guide the motion of the capsules, and thus, enable these micro-carriers to perform valuable functions in microfluidic devices [50].

The overarching, unifying theme of these different studies is the use of new computational models to design systems that can undergo controllable, self-propelled motion. Notably, all the systems described below undergo dissipative processes, harnessing energy from the environment to perform the autonomous motion. The development of models for dissipative systems is still in its infancy and the work described below can serve as a springboard for new avenues of exploration.

2. Swimming in viscous fluid

Responsive polymeric materials, such as hydrogels, can be used to directly convert chemical energy into mechanical work and, therefore, are attractive for designing functional microscopic devices. We use computer simulations to probe how hydrogels can be employed as actuators to design autonomous self-propelling microswimmers. We focus on designing a “simple” microswimmer that features a design that can be readily implemented experimentally. Responsive hydrogels can be used not only as an “engine” driving swimmer propulsion in a viscous fluid, but also as sensory elements that facilitates swimmer navigation. We, therefore, examine how environmentally-sensitive components can be integrated in a microswimmer to direct its motion to a specific target, or, for micrometer-sized catalytic swimmers, to control swimmer aggregation in space, mimicking bacteria chemotaxis.

2.1 Self-propelling microgel swimmer

Swimming at the microscale is drastically different from the swimming we are all familiar with in the macroscopic world [17]. At the microscale realm, swimming is characterized by a low-Reynolds-number environment. It means that in this inertia-less world viscous forces dominate the swimmer motion, and the swimmer has to generate time-irreversible kinematics in order to propel itself forward through the fluid. This phenomenon is highlighted by the famous Purcell's scallop theorem [51] which states that reciprocal motion cannot lead to propulsion in a low Reynolds number environment. Microorganisms use different means to overcome this limitation including beating and rotating flexible flagella, surface waves, and complex shape changes [16]. In synthetic micrometer-sized systems that lack the complex biomolecular machinery of living microorganisms, generating non-reciprocal self-propelling motion is a challenging task.

We use dissipative particle dynamics (DPD) [52-55] to design a synthetic self-propelling hydrogel microswimmer [29] that can rapidly move through a viscous fluid when exposed to a periodic stimulus, triggering the gel to expand or contract. The swimmer which is modeled using a mesoscale polymer network model [56, 57] has an X-shaped geometry and is comprised of two hydrogel sheets that are permanently bonded together (Fig. 1a-b). These two polymeric layers have identical material properties but exhibit different sensitivities to external stimuli. While one layer responds to the external stimulus by swelling the other layer remains passive. In the presence of a periodic outside stimulus the microscopic Janus X-shaped structure, which is submerged in viscous solvent exhibits complex dynamics. The swimmer first experiences rapid expansion due to the swelling of the responsive layer. After this, as a result of the mismatch in stresses in each of the two polymeric layers an internal bending moment develops and the swimmer arms start to bend out-of-plane until the swimmer reach its new equilibrium shape. Removal of the external stimulus causes the stresses in the gel network to relax, resulting in a contraction of the expanded swimmer arms. This is followed by a slow straightening of the swimmer. The aforementioned microswimmer deformations are illustrated in Fig. 1b.

In this study the swimmer is actuated using a 50% duty cycle with a period T . The illustrated geometrical shape changes repeat periodically with each application of the external stimulus. These periodical changes, in turn, lead to a forward motion of the swimmer through the solvent. Figure 1c shows the center-of-mass trajectory of the swimmer as a function of time. In this figure the highlighted regions represent the portion of time during which the external stimulus is applied. When the stimulus is applied the swimmer produces a forward stroke and propels the center of mass forward. The removal of the stimulus, on the other hand, leads to a backward stroke, during which the microswimmer moves backwards. Since the forward stroke produces a larger displacement, the microswimmer exhibits a net forward propulsion during each period. Figure 1c also shows that the swimming speed increases with swelling ratio $\varepsilon = V_s/V_c$, where V_s and V_c are the volumes of an unconstrained gel in the swollen and relaxed states, respectively.

Swimmer elasticity plays a critical role in the swimmer kinematics and propulsion. To probe the effect of this parameter the relative thickness of two polymer layers composing the gel swimmer, denoted by, respectively, d_R and d_P for the responsive and passive layers, is investigated. To this end, we systematically vary the thickness of the passive layer d_P . Figure 1d presents the swimmer velocity as a function of the thickness ratio, $R = d_P/d_R$, for three different swelling ratios. The figure reveals a non-monotonic relationship between the swimmer

velocity and the thickness ratio. The microswimmer speed decreases for both small and large R , and is maximized when $R \sim 1.4$. Furthermore, the speed is maximized for a larger swelling ratio $\varepsilon = 6$. For these system parameters, the microswimmer moves with a speed of 0.22 body-lengths per swelling period. Thus, swelling kinetics of the hydrogel defines the swimmer speed.

For hydrogels the swelling/deswelling process is diffusion limited. As a result of this, the length of each period T is defined by the microswimmer thickness, d , i.e. $T = 2\tau \sim 2d^2/D$ [58], where τ is the characteristic swelling time and D is the collective diffusion coefficient for the hydrogel network. Experiments show that for PNIPAM microgels (diameters in the range of $8-60 \mu m$) the diffusion coefficient, D is about $10^{-10} m^2/s$ [58]. Using this value we can estimate the swelling time for a swimmer with thickness about $1 \mu m$ is in the range of $0.02 s$. We therefore expect swimming speeds similar to that of *E.coli* which are 0.2-0.25 body-lengths per flagellar rotation or 25-35 micrometers per second [16].

The origins of the time-irreversible motion of the Janus gel microswimmer can be demonstrated by examining its kinematics in terms of the arc length s and curvature κ of the swimmer's compliant arms. Time evolution of these parameters is shown in Fig. 2a. Upon the stimulus application the swimmer arms first expand rapidly and then bend, as indicated by the more rapid change in s compared to κ (see Fig. 2b). This difference in the time scales associated with arm extension and bending is due to the different viscous drag experienced by the swimmer arms during these motions. Indeed, fluid resistance for a flow along the swimmer arm is lower compared to that normal to its surface. When the stimulus is removed and the swimmer straightens, the arc length again changes faster than the arm curvature (see Fig. 2c). Hence, the length of the swimmer's arms is greater during the forward stroke when the swimmer bends, than during the backward stroke when the swimmer straightens. This difference results in a time irreversible kinematic pattern, enabling the swimmer to achieve unidirectional propulsion in a low-Reynolds-number viscous fluid upon periodic application of an external stimulus.

Thus, we used DPD to design a simple gel microswimmer with an easy to fabricate geometry, which experimentally can be implemented using a variety of stimuli-sensitive polymeric materials with bi-layered structure [25, 59]. One of the challenges in downscaling the swimmer to micrometer scale pertains to the fabrication of a bi-layered structure with sub-micrometer thickness. One way of addressing this challenge is through utilizing rDNA technology to genetically engineer polymers for assembly in layered structures [60]. This method has proven useful in generating a variety of spider-silk assemblies [60]. While the aforementioned microswimmer design only offers unidirectional motion, more advanced microswimmers can be suggested that employ additional environmentally sensitive components to control swimming direction. In the next section, we will describe an example of such a maneuverable microscopic swimmer.

2.2 Maneuverable microswimmer

We employ numerical simulations to design a polymeric microswimmer that can navigate in a microfluidic environment [30]. The swimmer consists of a responsive cubic gel with two attached rigid rectangular propulsive flaps as shown in Fig. 3a. Periodic swelling and de-swelling of the gel swimmer body causes the flaps to beat in a time-irreversible manner that propels the

swimmer forward through a viscous fluid (Fig. 3b). An additional stimuli-sensitive steering flap that bends upon activation is attached at the front of the swimmer (Fig. 3c). This stimuli-sensitive flap, which can be made from bi-layered hydrogel [59] such as described in the previous section, serves as a rudder and is used for swimmer steering

To model the swimmer and its motion in a viscous fluid, the lattice Boltzmann model (LBM) [61] and lattice spring model (LSM) [62] are combined [63] for, respectively, fluid mechanics and solid mechanics. The gel is modeled using a 3-D cubic lattice, while the rigid propulsive flaps and the elastic steering flap are modeled using a 2-D square and triangular lattices, respectively. No-slip boundary condition is imposed on the flap surfaces, whereas the solvent is allowed to penetrate into the gel body coupled through a friction force between the fluid and lattice beads [64]. The effects of the external stimulus on the gel are modeled by dynamically changing the equilibrium length of the springs, representing the gel interior. Specifically, the length of the springs is varied in a sinusoidal fashion with oscillation amplitude a , and the angular velocity ω .

Before examining how the steering flap can be harnessed to direct the gel swimmer, we first discuss the propulsion mechanism utilized by this swimmer. Figure 3b shows snapshots of the microswimmer's motion. Upon application of the external stimulus the gel body of the swimmer swells. This causes the rigid propulsive flaps to move outwards and rotate into the microswimmer's plane of symmetry. When the stimulus is removed the gel shrinks, causing the flaps to now close and rotate out of the plane of symmetry. The beating motion of rigid flaps displaces viscous fluid surrounding the swimmer (instantaneous velocity of which is shown in Figure 3b by the green arrows) and causes the swimmer to move forward. The origin of the time-irreversible motion rests in the phase lag between the swelling/deswelling of the gel and the rotational motion of the propulsive flaps caused by a torque which arises due to the viscous fluid force that opposes the flap's motion.

Figure 4a illustrates the velocity of the swimmer as a function of gel stiffness for several propulsive flap aspect ratios, AR_p . The velocity in the plot is defined as $V = u/V_c$, where u is the average speed of the microswimmer per period and V_c is the characteristic speed with which the gel deforms. The dimensionless gel stiffness is defined as $\xi = T/\tau$, where T is the oscillation period and τ is the relaxation time which is given as $\tau = \mu w_o^2/E\phi$. Here, μ is the viscosity, E is the Young's modulus, w_o is the width of the propulsive flaps, and ϕ is the gel porosity. Figure 4a indicates that the swimming velocity strongly depends on the flap aspect ratio and is maximized when $AR_p = 2$ and $\xi = 3$. As the aspect ratio is increased, stiffer gels are needed for optimal performance.

For all aspect ratios, too high/low stiffness values lead to a poor swimming performance. This observation can be explained by considering forces experienced by the propulsive flaps. The two main force contributions arise from the viscous drag from the fluid and the elastic force imposed on the plates by the deforming gel. The deflection of the propulsive flaps occurs as a result of the balance between these two forces. When $\xi \ll 1$, the elastic force on the plates is weak, which results in minute displacement of the flaps, leading to slow propulsion. For $\xi \gg 1$, the gel strongly resists deformations due to the viscous torques on the propulsive flaps. Thus,

when ξ is large, the flaps no longer rotate in/out of the microswimmer's plane of symmetry but instead remain parallel to one another as the gel body changes the volume. The motion becomes time reversible and as a result, swimmers with large ξ are unable to propel forward at a low-Reynolds-number environment.

Controlling the directionality of the swimmer motion is achieved by utilizing a stimulus-sensitive flexible steering flap at the front of the microswimmer (Fig. 3c). Application of an outside stimulus to the steering flap is modelled by imposing an internal bending moment that deflects the flap. The deformation is characterized in terms of flap curvature $\kappa = w_o M / EI$, where M is the imposed internal bending moment and I is the moment of inertia of the steering flap. The dimensionless bending stiffness of the steering flap is given by $\Lambda = EI / (L^4 \mu \omega)$. When the steering flap is activated the left-right symmetry of the swimmer breaks and a net rotational moment is created which causes the microswimmer to divert from its otherwise straight swimming path. To characterize the swimmer turning, we introduce the turning angle β as the difference between the initial and final swimmer orientations.

Figure 4b shows how the turning angle β varies with flap curvature κ for the steering flap with an aspect ratio $AR_s = 1$. Surprisingly, we find that the sign of the turning angle β changes depending on the magnitude of the flap curvature κ . It means that by varying the strength of the external stimuli that causes the steering flap to bend the swimmer can be directed either to the left or to the right with respect to its initial path. When the steering stimulus is relatively weak leading to small κ , the turning angle β is positive meaning that the swimmer turns in the same direction as the steering flap deflection. However, when the steering moment is increased, more curved steering flap causes the swimmer to turn in the direction opposite to the flap as indicated by the negative values of turning angle for larger κ .

This counter-intuitive response of the swimmer to the deflection angle of the steering flap can be rationalized by the fact that there are two physical mechanisms by which the steering flap alters the swimmer's trajectory. The first mechanism is related to the breaking of the left-right symmetry which causes the swimmer to turn in the direction of the steering flap deflection. This mechanism dominates for relatively small deflection angles. An additional turning mechanism emerges due to the beating motion of a curved steering flap. This beating motion of the flap is induced by the periodical volume changes of the swimmer's gel body that drive swimmer propulsion, and prevails when the steering flap deformation is sufficiently large. The flap beating produces a hydrodynamic force [65] directed along the flap that pushes the swimmer to turn in the negative β direction.

To illustrate the impact of the beating motion of the steering flap on the swimmer's trajectory, we examine the turning of a non-oscillating swimmer. To this end, a velocity is imposed on the swimmer equal to the mean velocity of the oscillatory swimmer. The simulations reveal that a non-oscillatory swimmer always shows a positive turning angle. This is represented by the dotted line in Fig. 4b. Thus, the beating motion of the steering flap indeed produces opposing hydrodynamic forces which cause the swimmer to turn in the direction opposite to the steering flap.

Our computational study demonstrates a new design for a gel-based microswimmer that can self-propel and navigate in microfluidic environment. Our swimmer is actuated by the periodic swelling of its gel body which drives two rigid propulsive flaps that perform non-reciprocal oscillations that combine plunging and pitching. The non-reciprocal motion of the propulsive flaps, in turn, propels the swimmer forward. Swimmer trajectory is controlled by a stimuli-sensitive steering flap that bends when exposed to an appropriate external stimulus. The simulations reveal that by varying the intensity of the external stimulus one can change not only how fast the swimmer turns, but also in what direction it turns. The latter property is especially useful for designing maneuverable microswimmers, since there is a range of polymeric materials that exhibit stimuli-controlled bending [59, 66]. Experimentally, a ferrohydrogel with embedded superparamagnetic nanoparticles [67] could be used to drive the propulsive flaps. Upon application/removal of a high frequency magnetic field [67] the ferrohydrogel swells/deswells reversibly in response to the magnetic heating from the iron nanoparticles. In addition to bi-layered hydrogels [59], the steering flap could be actuated by an ionic hydrogel that bends in response to local changes in the pH [68]. The directionality of the microswimmer could then be controlled via pH gradients.

2.3 Controlling crowding of catalytic swimmers

Catalytic swimmers use a chemical reaction to propel in a fuel-rich fluid [69]. To design catalytic swimmers that can self-navigate to a specific location in space we probe the motion of such swimmers that incorporate a pH sensitive hydrogel [31]. The hydrogel responds to changes in the local level of pH by swelling and, in this manner, can be harnessed to alter swimmer motion depending on the local values of this property. Specifically, diffusiophoretic self-propulsion in a fuel-rich solution is investigated for a spherical hydrogel swimmer decorated with asymmetrical platinum coating applied on one hemisphere.

The variations in size of the swimmer control both the propulsion velocity ($v \sim 1/R$) and rate of swimmer rotation ($\gamma \sim 1/R^3$) as a result of hydrodynamics and Brownian motion [31, 70]. This difference in scaling for propulsion and rotation with swimmer size can be exploited for navigational purposes. Contracted swimmers remain nearly stationary as they have much larger rates of rotation whereas swimmers that are in the expanded state have significantly longer translational motion due to the lower rates of rotation. This behavior resembles the running and tumbling motion of *E. coli*. [71]. We, therefore, use computer simulations to probe how swarms of catalytic gel microswimmers can autonomously navigate to target locations via pH gradients, mimicking chemotaxis of living microorganisms.

The motion of catalytic swimmers, which are assumed to be perfectly spherical, is analyzed using Brownian dynamics simulations. The simulation parameters are set to match experimental size, velocity, and responsive behavior of PMAA microswimmers [70]. The swimmer experimental data and the corresponding fits are shown in Fig. 5. The plot in Fig. 5a shows how the diameter of the swimmer changes as a function of pH. Changes in swimmer size occur over a range $2.86 < \text{pH} < 7.04$, where the swimmer diameter changes linearly with the pH. Outside of this range, the diameter is nearly constant with a lower limit of $1.63 \mu\text{m}$ and upper limit of $2.78 \mu\text{m}$. Figure 5b shows that swimmer velocity rapidly decreases with increasing

swimmer size which can be approximated by a power law function. The approximations shown in Fig. 5 are used in the simulations for determining the propulsion velocity and rate of rotation of the swimmers.

Figure 6a shows how the velocity and rotational time of a swimmer change throughout a domain with varying pH levels (the shaded regions in the plot correspond to higher pH values). In this simulation, the domain is divided into four sections, each of which is 0.5 mm long. In the first (0 – 0.5 mm) and third (1 – 1.5 mm) sections the pH level is changing linearly, whereas in the second (0.5 – 1 mm) and fourth (1.5 – 2 mm) sections the pH is fixed at the maximum (7.04) and minimum (2.86) values, respectively.

The characteristic time of swimmer random rotation can be defined as $t_r = \varepsilon_r / k_b T$, where ε_r is the rotational friction coefficient. When the swimmer motion is examined at a timescale much larger than t_r , the trajectories appear random. For timescales less than t_r , the microswimmer does not have an opportunity to rotate as much and as such its motion appears more directed or ballistic. Figure 6a indicates that as the pH level is increased the rotational time increases while the velocity decreases.

Swimmers are initially uniformly distributed throughout the domain and their positions are tracked with time. Figure 6b shows the time evolution of the probability density function (PDF) of the swimmer's position. The figure reveals that as time progresses the swimmers accumulate in the second section (0.5 – 1.0 mm) which corresponds to the maximum pH value. This demonstrates the self-navigating nature of responsive hydrogel-based catalytic swimmers.

The swimmer accumulation observed in Fig. 6b is due to the size dependence of the velocity and rate of rotation. Computer simulations enable us to probe the respective individual contributions of the swimmer size dependence of velocity and rotation rate. In this study, a swimmer with a diameter of 1.1 μm is used as a reference point. To study the effects of velocity dependence, the rate of rotation is fixed to the reference swimmer value, while the velocity is allowed to change with size. Figure 7 shows that the behavior is similar to the original scenario, with slightly lower particle accumulation in the high pH region. Interestingly, equilibrium is reached much quicker than for the fully responsive swimmers (20 min vs. 60 min for full response). The velocity modulation strongly influences microswimmer accumulation due to the fact that the swimmer velocity decreases in the high pH regions. This causes the swimmers to “linger” and thus accumulate.

Fixing the swimmer velocity to the reference value allows us to examine the effect of the rotation rate response on the swimmer accumulation (see Fig. 7). For this scenario, although particles still accumulate in the high pH region, the accumulation is much weaker than for both the full response and velocity only response swimmers. It is worth noting that the behavior of the rotation rate only response is not in agreement with the previously mentioned running and tumbling behavior. In theory, accumulation in the low pH regions should be expected because the rotation rates there are high (leading to little or no translational movement). This does not occur however, due to the presence of pH gradients. Swimmers which are moving down the pH gradient have an increasing rate of rotation and thus are much more likely to turn around. In comparison swimmers which are going up the pH gradient experience an attenuation in the rate of rotation which decreases their likelihood of turning around. Overall this mechanism helps swimmers accumulate in the high pH region.

The study presents a novel approach for controlling the motion of catalytically driven microswimmers using pH gradients. This approach harnesses the truly autonomous nature of the swimmers, which passively relocate to high pH regions. Similar methods that rely on fuel concentration gradients have been reported [72]. However, the timescale for accumulation in these methods is on the order of days, which greatly limits their applicability. In that regard, the presented method is vastly superior since the timescale for accumulation is on the order of hours.

3. Self-generated motion of microcapsules on surfaces

In addition to modeling the motion of microscopic swimmers, we consider the dynamic behavior of biomimetic capsules. In our attempt to devise mechanisms that could lead to the microcapsules' autonomous movement, we were inspired by experiments on the self-propelled motion of surfactant-filled water droplets, which were localized on an adhesive surface [73]. The surfactants in the droplet adsorbed onto the surface with their hydrophilic heads, exposing their hydrophobic tails, and thereby, creating a gradient in wettability on the surface. Due to this gradient, the droplet underwent spontaneous motion away from the adsorbed surfactants. In effect, this surfactant-filled droplet constitutes the simplest biomimetic material. Namely, all the components necessary for its motion are encased in the system; no external stimuli are needed to drive the movement. Our aim is to apply this fundamental concept to microcapsules, driving them to undergo spontaneous motion on a surface due to the release of encapsulated nanoparticles, which modify the adhesive properties of the underlying surface.

3.1 Designing self-propelled mechano-responsive capsules

In the process known as haptotaxis, biological cells move towards higher concentrations of chemo-attractants along a surface. Biological cells can also exhibit mechanotaxis, undergoing directed motion due to mechanical variations in their environment. For instance, endothelial cells migrate in the direction of an applied fluidic shear stress [74] and fibroblasts have been shown to preferentially migrate from soft to harder surfaces [75]. Inspired by this vital biological behavior, we use our computational model to design a simple mechano-sensitive "cell" that responds to mechanical deformation through a shape change, which allows it to undergo self-sustained, directed movement [46].

We focus on fluid-filled capsules that are immersed in a solution and localized on an adhesive surface. To model the three-dimensional behavior of compliant microcapsules that enclose dissolved nanoparticles,[46-50, 76-80] we utilize an integrated computational approach that allows us to capture the dynamic interaction between the capsule and the surrounding fluid, as well as the motion of the nanoparticles.

The fluid dynamics of the encapsulated and the external solutions are captured via the lattice Boltzmann model (LBM), an efficient solver for the Navier-Stokes equation [61]. The capsule's elastic shell is simulated via the lattice spring model (LSM), which consists of a network of harmonic springs connecting regularly spaced masses [62]; by varying the spring constants for these bonds, we can alter the shell's mechanical compliance [63].

To capture the diffusion of nanoparticles within the encapsulated and host fluids, we use a Brownian dynamics model for the particles [46-50]. The nanoparticle trajectories obey a stochastic differential equation

$$d\mathbf{r}(t) = \mathbf{u}(\mathbf{r}, t)dt + \sqrt{2D_0}d\mathbf{W}(t), \quad (1)$$

where the first term describes the advection due to local fluid velocity $\mathbf{u}(r, t)$ and the second term describes the particle's Brownian motion, with D_0 being the particle's diffusion coefficient and $d\mathbf{W}(t)$ being the differential of a Wiener process with variance $\langle dW_i dW_j \rangle = \delta_{ij}dt$, where $i, j = 1, 2, 3$ label the three spatial coordinates. We neglect backflow effects (i.e., the impact of the particles motion on the flow field); the latter assumption is valid at relatively low concentrations of nanometer sized particles. We also neglect the hydrodynamic interactions between the particles. We use the first order Euler scheme to solve Eq. (1) [81].

The diffusing nanoparticles can bind to the surface and, thereby, modify the capsule-surface interaction. This interaction between a site on the external shell of the capsule and a site on the surface is modeled via a non-specific Morse potential:

$$\phi(r) = \varepsilon_s \left(1 - \exp \left[- \frac{(r - r_0)}{\kappa} \right] \right)^2, \quad (2)$$

where ε_s and κ characterize the respective strength and range of the interaction potential. The variable r represents the distance between lattice nodes on the capsule's outer surface and the substrate, which is also composed of lattice nodes, and r_0 is the distance where this force equals zero.

In the case of the mechano-responsive capsules, the bound nanoparticles decrease the strength of capsule-surface interaction and thus, ε_s (in Eq. (2)) is written as: $\varepsilon_s = \varepsilon(1 - \theta)$, where ε is the adhesive strength of the bare surface, θ is fractional coverage of the surface by the nanoparticles. Each discrete site on the surface can absorb a maximum number of nanoparticles $n_{\max}$ (e.g. $n_{\max} = 100$). (Once a site is full, the walls become non-interactive and the particles undergo a specular reflection at the surface, and re-enter the fluid.) Through dynamic variations in θ , the absorbing species create an adhesion gradient along the surface. If the gradient is sufficiently asymmetric, the capsules are driven by enthalpic forces to spontaneously move from a less adhesive to a more adhesive area.

Figure 8 shows the graphical output from the simulations for stationary, compliant capsules on an adhesive surface. In accordance with recent experimental studies, [43] we assumed that the permeability of the capsule's shell, P , is affected by mechanical deformation of the capsule. The dependence of P at a point $\mathbf{r}$ on the surface of the shell is given by the following smoothed step function:

$$P(\mathbf{r}) = \frac{1}{2} P_{\max} \left(1 + \tanh \left(\frac{K(\mathbf{r}) - K_{\text{thresh}}}{\Delta K} \right) \right). \quad (3)$$

Here, $P_{\max}$ is the maximum permeability of the capsule's shell, and $K(\mathbf{r})$ is the Gaussian curvature of the shell (as defined below). The sharpness of the transition from zero permeability to the maximum permeability is equal to $\Delta K = 0.1 \times K_{\text{thresh}}$, where K_{thresh} is the threshold curvature parameter. Via the simulations [46], we focused on values of K_{thresh} from $1.1K_0$ to $1.4K_0$, where $K_0 = 1/R^2$ is the Gaussian curvature of an un-deformed, spherical shell. The diffusion of the particles through the permeable shell is still described by Eq. (1), with the relevant diffusion coefficient being $D_s(\mathbf{r}) = P(\mathbf{r})h$, where h is the distance between the two surfaces that make up the shell.

In the absence of an external force, the shape of the capsules is determined by their adhesive interaction with the substrate. As seen in Fig. 8a, the bottom of the capsule is flattened by its relatively strong attraction to the surface and consequently, the entire object assumes an almost hemispherical shape. The color bar in the figure indicates the curvature of the capsule; the dark shades correspond to regions of low curvature, while yellow marks regions of high curvature. A dark blue area is visible at the bottom of the capsule.

For both capsules in Figs. 8a and 8b, the positions of the capsules are held fixed for the time t_{def} , so that the capsules remain stationary during this interval. The encased nanoparticles diffuse through the permeable shells of the immobilized microcapsules and into surrounding solution. As indicated by Eq. (3), the permeability $P(\mathbf{r})$ depends on the local curvature of the shell. Due to flatness of the bottom of the shell in Fig. 8a, the permeability in this region is relatively low. On the other hand, the curvature, and hence, the permeability, of the sides of the capsule are relatively high. This asymmetry in permeability gives rise to a high concentration of particles at the edge of the capsule and fewer particles near the center (see Fig. 8a.) Viewed from the top, the deposited nanoparticles form a symmetric ring around the capsule.

Due to the symmetric ring of nanoparticles deposited during $t \leq t_{\text{def}}$ for the capsule in Fig. 8a, the adhesion profile about the capsule's center is also symmetric. Consequently, there is no driving force for a single capsule to move either to the left or the right, and the capsule remains stationary even at time $t > t_{\text{def}}$.

In the case of the capsule in Fig. 8b, however, we apply a steady force to the left side of the shell (see arrow) for a time period t_{def} . Due to this force, the curvature on the left side of the capsule is higher than that on the right, as is clearly visible from the figure. This structural asymmetry leads to an asymmetry in the permeability. The permeability of the most deformed part of the shell (shown in yellow in Fig. 8b) is $P \approx 1.5P_0$, where P_0 is the permeability of an undeformed, spherical shell. The minimum permeability of the shell, $P \approx 0.5P_0$, is reached at the least curved regions of the shell (top and bottom parts of the capsule, shown in violet). This asymmetry in the permeability in turn yields a non-symmetric distribution of nanoparticles around the capsule. As can be seen in the plot of θ vs. x for this case, the concentration of nanoparticles is higher on the left side of the capsule than on the right. Recall that the deposited nanoparticles make the surfaces less adhesive, and thus, the surface is more adhesive on the right side of the capsule. This adhesion gradient, which was formed at $t \leq t_{\text{def}}$, initiates the directed motion of the capsule from the less adhesive region toward the stickier area. We remove the

mechanical deformation at $t_{def} = 2 \times 10^5$, and at $t > t_{def}$, the capsule continues to release nanoparticles and sustains the self-propelled motion (as explained below). Furthermore, the capsule maintains the direction of its initial path.

Figures 9a-c depict the motion of this microcapsule and the evolution of the adhesion profile on the surface at $t > t_{def}$. The gradients in the nanoparticle distribution on the surface formed by the time t_{def} result in a net adhesion force directed along the x axis that initiates the microcapsule's motion. At later times (Figs. 9b,c), the microcapsule continues to move in the direction of the initial "push". The latter behavior can be explained as follows. Consider that the nanoparticles released from the moving capsule in Fig. 9b form a symmetric cloud around the capsule. Nonetheless, particles newly deposited on the left will increase the already high surface coverage on the left and thus, contribute to the existing gradient. Driven by this gradient, the capsule again moves to the stickier region on the right. With each move to the right, newly released nanoparticles not only adsorb on the region ahead of the capsule, but also deposit behind the capsule, and thus, continue to build up the asymmetry that was initiated by the mechanical deformation. In effect, subsequent particle depositions on the left act to amplify the initial asymmetry at time $t = t_{def}$. In this manner, the particles sustain and propagate the gradient on the substrate, and thereby, provide a continuous driving force for the directed movement of the capsule. (The behavior occurs until the capsule is ultimately depleted of nanoparticles.) Figure 9d shows that θ , and hence, the adhesion profile around the microcapsule remains asymmetric at later times.

It is noteworthy that these responsive microcapsules mimic features of the behavior of keratocyte cells [46]; namely, both alter their shapes in response to a local perturbation and subsequently undergo sustained motion. Moreover, both objects respond to chemical gradients as they undergo this movement. Finally, for both the keratocyte cell and microcapsule, the direction of motion is dictated by the initial shape deformation.

The findings from these studies can facilitate the development of a new generation of devices (e.g., sensors, actuators, microfluidic mixers) that are powered by motile, artificial cells. Our mechano-responsive capsules can also play a vital role within artificial microvascular networks that are embedded in materials and intended to deliver healing agents to the system [82]. In particular, when the material is sufficiently stressed, the capsules would initiate their motion within the network and could deliver nanoparticles to nanoscopic cracks in the surfaces, thereby mending the material [76, 77]. On a more fundamental level, our results provide design rules for using synthetic components to create "cell-like" objects, which can mimic elemental behavior exhibited by biological cells.

3.2 Utilizing feedback loops to propel multiple capsules

In the above scenario, we introduced mechanical deformation on a part of the capsule to break the symmetry in the system, and thereby, prompt the capsule's autonomous motion. Here, we establish an alternative way to drive both autonomous motion and self-organization in the system by utilizing two different types of capsules: target and signaling. Our inspiration comes from biological cell signaling that involves the release of signaling molecules from the

“signaling” cells that are recognized by “target” cells. Specifically, in our studies [47, 48, 50], the signaling capsules release agonists and the target capsules release antagonists. The released species are again modeled as nanoparticles, which serve to modify: 1) the permeabilities of the capsules’ shells and 2) the capsule-surface interaction energies.

In our model, the permeabilities of the capsules’ shells (and, hence, the particle release rates) depend on the local concentration of the nanoparticles in the external solution. The agonists provide positive feedback by enhancing the permeability of the target capsules, P^t . On the other hand, the antagonists introduce negative feedback since they decrease the permeability of the signaling capsule, P^s . To model this dependence of the capsules’ permeability to variations in the concentration of agonist, C^t , and antagonist particles, C^s , we set:

$$P^s = \frac{1}{2} P_{\max}^s \left(1 - \tanh \left(\frac{C^s - C_{\text{thresh}}}{\Delta C} \right) \right), \quad P^t = \frac{1}{2} P_{\max}^t \left(1 + \tanh \left(\frac{C^t - C_{\text{thresh}}}{\Delta C} \right) \right). \quad (4)$$

Here, $P_{\max}^s$ and $P_{\max}^t$ are the maximum permeabilities of the signaling and target capsules’ shells, respectively. The sharpness of the transition from a “dormant” state with low permeability of the capsules’ shells to an “active” state with near-maximum permeability is taken equal to $\Delta C = 0.1 \times C_{\text{thresh}}$. We also set the threshold concentration for this transition, C_{thresh} , equal for the signaling and target capsules. (The value of C_{thresh} plays an important role on the dynamic behavior and structure of the assembled clusters [47].)

The adsorbed agonists increase the strength of the capsule-surface interaction and adsorbed antagonists decrease this quantity. Thus, ε_s is written as $\varepsilon_s = \varepsilon(1 - \theta + \theta')$, where ε is the adhesive strength of the bare surface, θ is fractional coverage of the surface by the antagonists and θ' is the corresponding value for the agonists [47].

An example of the combined effects of the self-regulating behavior (due to the feedback loops) and self-generated gradients is shown in Fig. 10, which displays a signaling and a target capsule that initially sit on a bare surface. At the onset, the signaling capsule emits agonists; the bound agonists leave a symmetric “sticky” blue ring around this capsule. Initially, the adhesion profile around the signaling capsule is symmetric and at this stage, the capsule does not move. As more agonists are deposited on the surface, this ring grows and soon creates an adhesion gradient near the target. Due to this gradient, the target moves closer to the signaling capsule (i.e., in the direction of greater adhesion).

Once the target is sufficiently close to the signaling capsule, it becomes activated (by the agonists in solution) and releases antagonists, which make the surface less “sticky”. Consequently, the adhesion profile in the region between the target and the signaling capsules is no longer symmetric and now both capsules move away from the less adhesive region (the yellow region in Fig. 10) towards the stickier area. The movement of the signaling capsule shifts the location of the maximum in the adhesion gradient and again the pair moves towards the more attractive region around the signaling unit; at this point, the entire process repeats, so that both capsules continue to move as a pair along the plane.

This fundamental behavior gives rise to the collective, self-propelled motion of the structure shown in Fig. 11. Here, one signaling capsule is initially located in the outer layer of a 16-capsule array (Fig. 11a) and $P_{\max}^t / P_{\max}^s = 1/4$. As Fig. 11b shows, the system self-organizes into a long “snake”, with the signaling “head” leading a tail of targets. Notably, the capsules self-organize and move in the absence of an applied stimulus.

The self-regulation of the capsule permeabilities introduced through the coupling of the positive and negative feedback, and imposed by Eq. (4), are vital to the formation of the self-propelled snakes. If this interaction is turned off, and thus, there is a constant release of agonist and antagonist nanoparticles, the capsules are seen to scatter [47], much like colliding billiard balls. Hydrodynamic interactions are also found to be vital to the formation of long snakes [47].

Finally, we mention the remarkable behavior that emerges when two colonies of the 16 array capsules are brought together. Namely, as one colony starts to form a traveling snake, it modifies the local environment of the neighboring group. In other words, the separate clusters can “sense” each other through the self-generated patterns of surface adhesion. Depending on the initial conditions [47], this responsive behavior can prompt two colonies to merge into one larger unit that continues to move as a coherent group (Fig. 12a), or lead to dynamics resembling that of social insects (ants and termites), where a group will follow the trail left by the other members (Fig. 12b). The examples in Fig. 12 indicate that our colonies of synthetic capsules are capable of spontaneously coordinating their actions through the trace of particles left on the surface.

In order to demonstrate the robustness and generality of the observation that self-generated and self-modulating signals can drive the organized, collective motion of synthetic capsules, we recently implemented another biomimetic feedback loop in a system of capsules localized on a surface in solution [49]. In particular, we adapted the negative feedback loop exemplified by the repressilator network [83], which was specifically engineered to exhibit oscillatory dynamics so it could act as an artificial clock that imposed temporal organization within a living cell.

In our study involving the repressilator network [49], we consider three different capsules, ‘A’, ‘B’ and ‘C’, which produce the respective chemicals ‘a’, ‘b’ and ‘c’. The negative feedback loop is implemented by specifying that chemical ‘a’ suppresses the activity of microcapsule ‘B’, ‘b’ suppresses ‘C’ and ‘c’ suppresses ‘A’. In other words, each chemical species represses the production of the next in a cycle. We first fix the positions of the capsules on the surface so that they form the vertices of an equilateral triangle. Fixed in spaced, we find that the immobilized capsules exhibit either steady or oscillatory chemical production. We then take into account the adsorption of the released ‘a’, ‘b’ and ‘c’ onto the underlying surface and consider the capsules’ motion on this surface in response to gradients in surface energy that are generated by the adsorbed chemicals. We find that with the oscillatory production of ‘a’, ‘b’ and ‘c’, the capsules can self-assemble into a close-packed triad that undergoes net translation as a cohesive group [49].

Feedback loops play a ubiquitous role in regulating biological activity. Such interacting loops, are not, however, commonly considered as a design element in the construction of synthetic material systems. Our findings highlight the utility of these self-regulating networks in controlling the dynamic behavior of collections of polymeric microcapsules, which could play a vital role in microfluidic devices, as we discuss below.

3.3 Using patterned surfaces to guide the motion of the self-regulating capsules

As an extension of the above studies, we design a system of active polymeric microcapsules that pick up, convey and drop off a cargo between locations on a patterned surface [50]. To create this system, we harness the signaling and target capsules that are coupled by positive and negative feedback loops. We specifically focus on one signaling and two target

capsules, which are observed to form a stable triad [50]. Namely, these three capsules move as a cohesive group along the surface due to the self-generated adhesion gradients.

In order to guide the motion of this triad, we introduce a “sticky” stripe on the surface, which is shown in green in Fig. 13. Both the signaling and target capsules are more attracted to this stripe than the rest of the substrate. Moreover, we specify that the signaling capsules are more attracted to the stripe than the targets. This behavior can be achieved experimentally if the signaling and target capsules are functionalized with different types of ligands.

Figure 13a shows the configuration of our system at early times, when the triad moves autonomously along the stripe, which directs the motion of this “mini-mover” on the surface. A four-target cargo is situated ahead of the mini-mover. As the triad navigates along the stripe, agonists emanating from the leading signaling capsule become bound to the surface. The adsorbed agonists create an adhesion gradient that makes the region near the cluster more attractive. Pulled by favorable enthalpic forces, the four capsules spontaneously move along the gradient, towards the more adhesive region. Drawn to the triad, the cluster comes in range of the stripe and due to the relatively strong attractive interaction between the capsules and this green stripe, the four-target cargo becomes localized on this band. In effect, the triad has deposited a nanoparticle trail that leads the cargo onto the stripe.

As can be seen in Fig. 13, the stripe contains a blue patch; the target capsules experience a weaker adhesive interaction with this blue patch than with the green stripe. (The signaling capsules experience the same attractive interaction for both the green and blue regions.) The presence of this blue patch is important for the drop-off of the cargo. In particular, the green-blue interface forms a sharp adhesion gradient, and thus, presents a potential barrier for the capsules’ motion. Due to their interaction with the barrier, the four-target cargo is arrested at the green-blue interface. On the other hand, the difference between the adhesion strengths of the blue and green regions is not sufficient to stop the triad moving at the head of the train. As a consequence, the triad passes the blue region and continues its movement along the stripe (Fig. 13b).

Once the triad has deposited its cargo, it can move on to potentially pick up a new payload at another location. Thus, this system could provide an effective means of autonomously transporting a broad range of encapsulated substances within microfluidic devices. Notably, the cooperative behavior exhibited by the capsules is driven simply by the self-generated gradients in the presence of the chemically patterned stripe, which is the only externally imposed “stimulus” in this system.

4. Summary and outlook

Systems of motile and self-propelling microscopic particles often exhibit behaviors that resemble those of living microorganisms, including cooperative modes of motion, self-organization, and adaptability to the changing environment. Whereas significant progress has been achieved over the past decades in understanding the behavior of suspensions of passive colloids, our knowledge of dissipative systems composed of active particles is still rather limited. Such active systems function away from thermodynamic equilibrium and often exhibit rather counter-intuitive responses. In these cases, computer simulations offer a valuable and effective tool for probing the behavior of active microscopic objects in different environments.

In this article, we describe several examples where computer simulations are employed to investigate the self-propelled motion and self-organization in the microscale realm of synthetic swimmers and microcapsules that release different signaling compounds. A range of mesoscale

computational methods based on dissipative particle dynamics, Brownian dynamics, lattice Boltzmann method and lattice spring model is used in these simulations.

In particular, we examine how a bilayered hydrogel can be utilized to create a self-propelling microswimmer that is actuated by a repeating external stimulus. Bilayered hydrogels that are composed of two bonded layers of hydrogels with dissimilar properties offer a unique polymeric material that is mechanically robust and can undergo large scale stimuli-controlled cyclic deformations [84]. Furthermore, recent advances in polymer synthesis and assembly have allowed researchers to create bilayered hydrogels at the nanoscale [59], which make these materials especially attractive for applications in micro- and nanorobotics as large amplitude actuators and high sensitivity sensors. Further research in bilayered and multi-layered responsive materials will open new possibilities for designing multifunctional microscopic devices and machines.

By properly selecting the elasticity of the two hydrogel layers in a bilayered configuration, we design a self-propelling microswimmer that can effectively move through a low-Reynolds-number viscous fluid. In this case, the propulsion is created by the difference in time scales related to the stretching and bending modes of swimmer deformation. The bilayered gel swimmer can be readily implemented experimentally using currently available fabrication techniques [59].

We show that materials with large, out-of-plane stimuli-controlled deformation can be effectively harnessed to direct swimmers in microfluidic environments. In these simulations, we model a gel swimmer with a stimuli-sensitive steering flap attached at the front end of the swimmer. When an external stimulus is imposed, the steering flap is deflected, causing the swimmer to change its path. The navigation control arises as a result of two competing physical mechanisms inducing oppositely directed turning moments. These mechanisms are related to, respectively, swimmer symmetry breaking and hydrodynamic thrust due to the beating motion of the steering flap. The competition between the two turning mechanisms leads to the unique behavior of the swimmer, whose direction can be set by simply varying the strength of the stimulus controlling the steering flap bending.

Stimuli-sensitive hydrogels can also be useful for controlling the motion and self-organization of catalytic microswimmers. To demonstrate this, we investigate the spatial distribution of catalytic swimmers that are integrated with spherical hydrogel particles whose swelling depends on the local pH. We show that local concentration of microswimmers can be directly controlled by the pH level. The aggregation of the microswimmers at the locations with high pH is associated with the different dependence of propulsion velocity and swimmer rotation on the microgel size. This behavior of gel-based catalytic microswimmers closely resembles the chemotaxis of bacteria.

We show that microscopic synthetic capsules emitting different signaling compounds can be designed to capture salient features of biological cells. We simulate the behavior of microcapsules that are localized on an adhesive surface and encapsulate “signaling” particles that can diffuse from a capsule’s inner core and into the outer solution. We specifically design a capsule or synthetic “cell” that responds to mechanical stimulation by undergoing spontaneous motion. Furthermore, the capsule maintains its directed motion by responding to self-generated adhesion gradients on the surface. The fundamental system considered here, a nanoparticle-releasing micro-carrier, can readily be fabricated [44, 45, 47, 48, 50] and the mechanically induced release of the nanoparticles can also be experimentally achieved [43]. Thus, the building blocks for creating this system are already in place. Our findings reveal that this purely synthetic

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4 system is capable of basic cellular behavior: 1) changing its environment, 2) sensing this change,
5 and 3) responding to the change by initiation of self-sustained motion.
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7 We also consider systems involving multiple capsules that are coupled through bio-
8 inspired feedback loops, which regulate the release of the encapsulated particles. In the system
9 involving the coupling of positive and negative feedback loops, the individual capsules can self-
10 organize into long, self-propelled trains. With distinct colonies of capsules, the system can
11 display tracking behavior analogous to that performed by ants and termites. In particular,
12 capsules from one group can follow the chemical trail left by capsules from another mobile
13 group. We exploit this behavior to design a stable trio of capsules that can pick up and drop off
14 cargo, guided by a chemically patterned stripe on the surface.
15

16 Finally, we examine the effect of imposing a cycle of negative feedback loops onto the
17 system that is inspired by the biomimetic repressilator dynamics. As in the system described
18 above, the self-regulation enabled by the feedback loops leads to the self-organization and
19 directed motion of the three communicating capsules.
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21 The results provide guidelines for creating artificial cells that mimic the communication
22 and chemotaxing behavior of biological cells. Our findings also provide guidelines for
23 addressing one of the challenges in the design of microfluidic devices [50]: providing a means of
24 autonomously transporting cargo (encapsulated payloads or other capsules) within the fluid-filled
25 microchannels.
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Figure 1. Bi-layered hydrogel microswimmer. (a) X-shaped geometry of microswimmer. Here L is the height/width of the swimmer and b is the thickness of the microswimmer's legs. (b) Swimmer deformation for one swimming period. The solid black circles show the initial center of mass of the microswimmer for each snapshot (at $t = 0$). The Janus swimmer is comprised of two polymeric layers: an active and passive layer, shown in green and gray respectively. When the stimulus is applied ($t = 0$) the microswimmer first expands and then bends. Upon removal of the stimulus ($t = 0.5T$) the swimmer contracts and straightens back into the original configuration. The swimmer propels in the positive x direction. (c) Center of mass of swimmer vs. time for different swelling ratios, ε . The highlighted regions in the plot indicate the portion of time the stimulus is applied. Upon stimulus application the swimmer experiences a large forward displacement as it expands and then bends. Removal of the external stimulus causes the swimmer to contract and then straighten which leads to a small backward displacement (in the negative x direction). (d) Velocity vs. thickness ratio for different swelling ratios. The dashed line designates the thickness ratio which leads to the fastest swimming speeds ($R_v = 1.4$). Reproduced from Ref. [29].

Figure 2. (a) Arc length (s) and curvature (κ) vs time for swimmer with $R = 1.4$ and $\varepsilon = 6$. Highlighted regions show portion of time the external stimulus is applied. Periodic applications of stimulus lead to periodic microswimmer deformations. Plots (b) and (c) show time scale difference between arc length and curvature right after stimulus application and removal, respectively. Changes in arc length always occur more rapidly than changes in curvatures. This leads to observed time-irreversible motion. Reproduced from Ref. [29].

Figure 3. (a) Steerable microswimmer actuated by periodically swelling gel body. (b) Simulation snapshots of microswimmer deformation for one period. (c) Snapshot of swimmer with steering flap curvature $\kappa = 1$ and $AR_s = 1$. Colors represent material strain ε . The green cones represent fluid velocity vectors in the x - y plane, which is taken through the geometric center of the microswimmer. Reproduced from Ref. [30].

Figure 4. (a) Period-averaged swimmer velocity (V) vs body stiffness (ξ) for different propulsive flap aspect ratios. Maximum velocity occurs for $AR_p = 2$ and $\xi = 3$. (b) Turning angle (β) vs. flap curvature (κ) for different bending stiffness values (Λ) and $AR_s = 1$. The dotted line represents data for non-oscillatory swimmer. Reproduced from Ref. [30].

Figure 5. Catalytic microswimmer parameters. (a) Size response of spherical microgel swimmer as a function of pH. (b) Propulsive velocity as a function of swimmer size. In both plots solid lines represent numerical fits to experimental data. Reproduced from Ref. [31].

Figure 6. (a) Illustration how propulsive velocity and rotational time (t_r) change as a function of distance in simulation domain. Shading specifies pH concentration (lighter regions represent low pH levels). (b) Plot showing how probability distribution function of swimmer's position changes with time (t) and space (x). Swimmers appear to accumulate in high pH regions. For PDF data in (b) modulations of both velocity and rotation rate are taken into account (full response). Reproduced from Ref. [31].

Figure 7. Plot showing PDF of swimmer's position as a function of distance for full, velocity only, and rotation only responses. Shading used to signify the pH profile throughout the simulation domain. Reproduced from Ref. [31].

Figure 8. Upper row: (a) equilibrium and (b) deformed shape of the microcapsule on an adhesive surface when pressed on one side by an external force (thick arrow). The local curvature of the capsule's shell is indicated by the color scale. The curvature-dependent membrane permeability is shown schematically by small arrows and circular nanoparticles released from the capsule. The asymmetrically deformed capsule in (b) releases more nanoparticles near the substrate on the left than on the right, leading to asymmetric surface coverage. Bottom row: The fractional coverage of nanoparticles along a line in the x -direction under the microcapsule calculated at $t = 2 \times 10^5$ time steps (in LBM units) for the capsules shown in the upper row. The center of the capsule is located above the position $x = 0$. Reproduced from Ref. [46].

Figure 9. (a–c) Top-down views of a capsule undergoing self-sustained motion. Times (in LBM units) are indicated in the frames. The color bar indicates the density of the nanoparticles deposited on the substrate. (d) Cross section of the fractional coverage of the surface by the nanoparticles along the line of motion ($y = 0$) for the time frame shown in (c). Reproduced from Ref. [46].

Figure 10. Map of adhesion strength on the surface around a moving pair of capsules. The x -axis is drawn in the direction from the target capsule to the signaling capsule. The signaling capsule releases “sticky” agonists, which activate the target capsule, generating an adhesion gradient in the x -direction that propels the pair. Reproduced from Ref. [47].

Figure 11. A group of capsules initially arranged in a 4 x 4 array (a) self-organizes into a mobile snake (b). The signaling capsule is drawn in red and the targets in green. Reproduced from Ref. [47].

Figure 12. Interactions between two mobile groups of capsules. (a) The initial arrangement of capsules. (b) The two mobile groups merge and form a new cluster. (c) The group on the right is held dormant until $t = 500$ time steps while the left group moves. Once active, the right group starts to move and follows the trail of nanoparticles deposited by the left group. Reproduced from Ref. [47].

Figure 13. Pick-up and drop-off of four cargo capsules. (a) The signaling capsule (red) releases “sticky” nanoparticles that drive the motion of the mini-mover triad and draw four cargo capsules toward the adhesive green stripe. The cargo capsules then follow the trail left by the moving triad, but are arrested at the blue patch, where they are dropped off (b). Reproduced from Ref. [50].