Computational design of microscopic swimmers and capsules: From directed motion to collective behavior

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ABSTRACT

Systems of motile microscopic particles can 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.

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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 microorganisms [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, hydrogels exhibit large and reversible mechanical deformations [28]. As such, hydrogel-based swimmers are particularly interesting for in vivo biomedical applications.

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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 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 facilitate 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. Fig. 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. Fig. 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. Fig. 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 bodylengths per swelling period. Thus, swelling kinetics of the hydrogel defines the swimmer speed.