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Self-assembled vesicle–colloid hybrid swimmers: Non-reciprocal strokes with reciprocal actuation

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We consider a self-assembled hybrid system, composed of a bilayer vesicle to which a number of colloids are adhered. Based on known results of membrane curvature elasticity, we predict that, for sufficiently deflated prolate vesicles, the colloids can self-assemble into a ring at a finite distance away from the vesicle equator, thus breaking the up–down symmetry in the system. Because the relative variation of the position of the colloidal ring along the vesicle endows the system with an effective elasticity, periodic cycles of inflation and deflation can lead to non-reciprocal shape changes of the vesicle–colloid hybrid, allowing it to swim in a low Reynolds number environment under reciprocal actuation. We design several actuation protocols that allow control over the swimming direction.

Keywords: vesicles, colloids, microswimmers, curvature

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1. Introduction

Vesicles are biomimetic, microscale containers, which can self-assemble from natural lipids,[1] as well as from synthetic polymers.[2] As such, they hold great promise as biocompatible carriers in drug delivery,[3,4] and as "cell mimics" in the context of bottom-up synthetic biology.[5,6] Moreover, simple vesicle-like containers are thought to be relevant in the context of the origins of life, as candidates for early protocells.[7,8]

Both in the drug delivery and in the cell mimicry contexts, it is of great interest to design vesicles that are able to actively swim, rather than passively diffuse. In the former case, active swimming would allow for enhanced and more targeted drug delivery. In the latter case, active swimming by vesicles would provide a minimal system with which phenomena such as e.g. collective motion in swimming microorganisms[9,10] could be probed.

However, in the absence of chemical reactions which may drive motion through phoretic mechanisms without any moving parts,[11–13] swimming at the microscopic scale requires nontrivial body deformations.[14] In particular, due to the absence of inertia and the consequent linearization of the field equations, microswimmers need to periodically deform their bodies in a way that is non-reciprocal: The shape deformations cannot remain unchanged under a time reversal. For a single swimmer, this means that the shape variation needs to describe a cycle in a two-dimensional or higher-dimensional shape space.[14–19]

In the context of vesicles, this implies that simple inflation and deflation cycles via external osmotic actuation cannot make a vesicle swim, even if the vesicle's up–down symmetry is broken, as is the case for stomatocyte-shaped vesicles.[20] Evans *et al.*[21] showed that swimming by vesicles can be achieved only if the external actuation on the system is non-reciprocal, using two actuation parameters. In their proposed method, their actuation protocol describes a cycle in vesicle volume–membrane composition space, achieving a non-reciprocal shape deformation of the vesicle that leads to a net propulsion.

Non-reciprocal swimming strokes can also be achieved via reciprocal actuation, if the elasticity of the body is taken into the account.[17] For a slender filament clamped at one end, a reciprocal actuation of the other end can result in a propulsive thrust, when the filament is flexible.[22] In another example, a swimmer composed of two spheres joined together by an arm can in principle swim upon actuation of only one degree of freedom (the length of the arm), when the spheres exchange their unequal volume at the end of each stroke,[23] or when one of the spheres is elastic.[24,25]

Here, we design a self-assembled vesicle–colloid hybrid that can swim in response to reciprocal actuation of the vesicle volume, see Fig. 1. In previous work, it was found that adhesive colloids that bind to a vesicle are subject to curvature-induced forces that direct them towards regions of minimal mean curvature,[26] in a process governed by the competition between membrane bending and particle–membrane adhesion forces.[27,28] In particular, for a prolate vesicle such as the one considered here, it is expected that half-adhesive Janus colloids will spontaneously form a ring of equally-spaced colloids along a minimal curvature line. The presence of the colloids

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endows the system with an effective elasticity, in regards to the position of the colloidal ring along the vesicle. We devise reciprocal inflation–deflation protocols that exploit this effective elasticity to generate a propulsive thrust that allows for vesicle swimming. Then, using a minimal model, we determine the swimming direction and speed of the vesicle for each of these protocols.

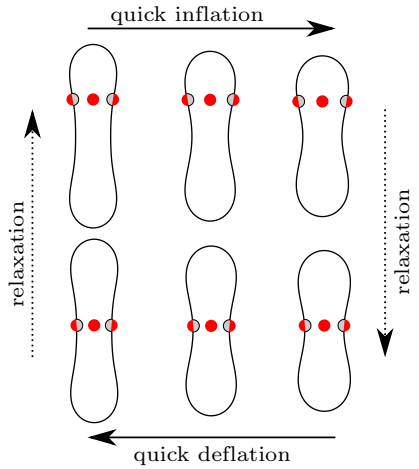


Fig. 1. Schematic of one of the reciprocal actuation protocols (in this example, the quick inflation–quick deflation protocol) developed in this work for a vesicle–colloid hybrid microswimmer. The Janus colloids (four in this example), with one adhesive side (grey) and one non-adhesive side (red) preferentially locate in a ring along the line of lowest mean curvature of the (axisymmetric) prolate vesicle, which is further away from the equator for more deflated vesicles. Quick inflation and deflation are followed by spontaneous relaxation of the colloid ring location towards its equilibrium position, resulting in a cyclic non-reciprocal swimming stroke.

2. Theoretical method

2.1. Vesicle shapes upon inflation and deflation

We consider a vesicle of spherical topology, with a bilayer membrane composed of a fixed number of lipids and thus a fixed surface area A. The membrane is described within the spontaneous curvature model,[20,29] and we focus on the case of a symmetric bilayer and identical solutions in the inner and outer compartments, so that the spontaneous curvature of the membrane is zero.

Under these conditions, the equilibrium (lowest bending energy) shape of the vesicle is governed by a single parameter, namely, its volume-to-area ratio[20]

$$v \equiv \frac{V}{\frac{4\pi}{3}\left(\frac{A}{4\pi}\right)^{3/2}}, \tag{1}$$

which compares the volume V enclosed by the vesicle to the volume of a sphere with identical surface area. The volume-to-area ratio v can thus vary from $v = 1$, corresponding to a fully inflated spherical vesicle, to $v = 0$, corresponding to a fully deflated vesicle. For $v < 1$, the vesicle necessarily takes non-spherical shapes. Minimization of the membrane bending energy shows[20] that these equilibrium shapes are axisymmetric, and correspond to prolate shapes when $0.65 \lesssim v < 1$, oblate-discocyte shapes for $0.59 \lesssim v \lesssim 0.65$, and stomatocyte shapes for $0 < v \lesssim 0.59$, with discontinuous transitions between these shapes at $v \approx 0.65$ and $v \approx 0.59$.

The enclosed volume V, and therefore the volume-to-area ratio v, can be experimentally controlled by adjusting the concentration in the outer compartment of an osmotically-active solute, i.e., a solute to which the membrane is impermeable, such as salts and sugars.[29] If a vesicle has volume-to-area ratio v at a certain outer concentration c_v of osmotically-active solute, increasing or decreasing this concentration to a new value $c_{v'} \neq c_v$ will lead to deflation or inflation of the vesicle, respectively, towards a value $v' = (c_v/c_{v'})v$. Inflation and deflation of the vesicle can therefore be externally actuated by controlling the concentration of osmotically-active solutes in the system.

2.2. Curvature-induced forces on adhesive Janus colloids

In Ref. [26], we investigated the adhesion of Janus colloids, with one strongly adhesive and one non-adhesive hemisphere, to non-spherical vesicles. We found that such colloids, when adhering to the outside of the vesicle, will be subject to curvature-induced forces that direct them towards regions of minimal mean curvature of the vesicle, in order to minimize the bending energy of the system. More precisely, the binding energy of the colloid was found to depend on the local mean curvature M of the membrane (when unperturbed by the colloid) as

$$\Delta E = 4\pi\kappa R M + O(\kappa R^2/R_{\rm ve}^2), \tag{2}$$

where we note that the energy ΔE is given with respect to the reference configuration of a colloid in contact with a flat membrane with $M = 0$. Here, κ is the bending rigidity of the membrane, with typical values in the range $\kappa = 10$–$100\ k_{\rm B}T$, R is the radius of the colloid, and $R_{\rm ve} \equiv \sqrt{A/(4\pi)}$ is the typical size of the vesicle.

Typically, prolate vesicles have minimal mean curvature at their equatorial line. Thus, when adhering to such a prolate vesicle, a colloid will preferentially locate at the equatorial line. Moreover, the membrane-mediated interactions between two half-adhesive Janus colloids adhered on the outside of a vesicle have been shown to be repulsive.[30] Putting both contributions together, one would generally expect that when $N \geq 2$ Janus colloids are put into contact with a prolate vesicle, they will self-assemble into a ring of equally-spaced particles around the vesicle equator (for the particular case of $N = 2$, this implies that the two particles will be located on opposite sides of the vesicle equator).

In fact, this is also what both experiments[31] and computer simulations[32] have found for partially-adhered uniform (non-Janus) colloids. However, as described in detail

in Ref. [26], such uniform colloids are found in the partially engulfed state, which is sensitive to curvature-induced forces, only when the membrane–colloid adhesive strength is within a very narrow, finely-tuned range. Janus colloids, on the other hand, will always be in the curvature-sensitive partially engulfed state, as long as one side is non-adhesive and the other strongly adhesive, independently of the precise value of the adhesive strength. Therefore, we will focus here on Janus colloids as a more robust choice for the construction of vesicle–colloid hybrid swimmers.

2.3. Hydrodynamic interactions

We now look into the hydrodynamic interactions of the deforming vesicle and the adhered colloidal particles. These identical colloidal particles are uniformly distributed in a ring around the vesicle, and their motion is solely driven by the curvature-induced forces exerted by the membrane. As noted earlier, due to their microscopic sizes, the motion of the vesicle and the colloidal particles in the fluid is dominated by viscous dissipation. Thus, we may use the Stokes drag law to determine the instantaneous velocity of the vesicle as[33,34]

$$\boldsymbol{V}_{\rm ve} = N\boldsymbol{K}_{\rm ve}^{-1}\boldsymbol{F}_{\rm ve} + \mathcal{F}_{\rm ve}\left[\boldsymbol{v}_\infty(\boldsymbol{x}_{\rm ve})\right], \tag{3}$$

where $\boldsymbol{K}_{\rm ve}$ is the hydrodynamic resistance tensor of the deforming vesicle, $\boldsymbol{F}_{\rm ve}$ is the body force applied by each colloidal particle on the vesicle, $\mathcal{F}_{\rm ve}$ is the Faxèn operator, and $\boldsymbol{v}_\infty$ is the background flow-field induced by the colloidal particles at the surface of the vesicle ($\boldsymbol{x}_{\rm ve}$). We can similarly write the drag law for the colloidal particles as

$$\boldsymbol{V}_i = \boldsymbol{K}_i^{-1}\boldsymbol{F}_i + \mathcal{F}_i\left[\boldsymbol{v}_\infty(\boldsymbol{x}_i)\right], \tag{4}$$

where, this time, these parameters express the motion of the i-th colloidal particle with $i \in \{1,\ldots,N\}$ (e.g., $\boldsymbol{F}_i$ is the force applied on each particle). In the absence of an external force, the whole assembly must remain force free, thus we have

$$N\boldsymbol{F}_{\rm ve} + N\boldsymbol{F}_i = \boldsymbol{0}. \tag{5}$$

To close the system of equations, we now assume that the colloidal particles are driven by the deflation/inflation of the vesicle, and so one can claim

$$\boldsymbol{V}_i - \boldsymbol{V}_{\rm ve} = \boldsymbol{V}_0, \tag{6}$$

where $\boldsymbol{V}_0$ is prescribed by the body deformation of the vesicle. To evaluate the net propulsion of the system, we define the net velocity as the average velocity of all the moving entities. The cycle-averaged swimming velocity of the system is then derived as

$$\bar{\boldsymbol{V}}_{\rm net} = \frac{1}{T}\int_0^T \frac{\boldsymbol{V}_{\rm ve} + N\boldsymbol{V}_i}{N+1}\,{\rm d}t, \tag{7}$$

where T is the period over which the vesicle completes a full cycle of inflation/deflation.

3. Results and discussion

3.1. Symmetry breaking in the location of a ring of colloids on a prolate vesicle

In Subsection 2.2., we described how $N \geq 2$ half-adhesive Janus colloids in contact with a prolate vesicle will typically self-assemble into a ring of equally-spaced colloids around the vesicle equator. However, it is crucial to note that, for prolate vesicles with $v \lesssim 0.72$, spontaneous symmetry breaking occurs, and the minimum mean curvature line at the equator splits into two minimum curvature lines located a finite distance above and below the equator, see Fig. 2. Thus, we expect that for reduced volumes $v \lesssim 0.72$, the adhesive colloids will tend to localize in a ring a certain distance away from the vesicle equator. The distance of this ring from the vesicle equator can be decreased or increased by changing the volume v to be closer or further away from the upper limit $v \approx 0.72$, respectively. This allows for the up–down symmetry of the vesicle–colloid hybrid to be broken.

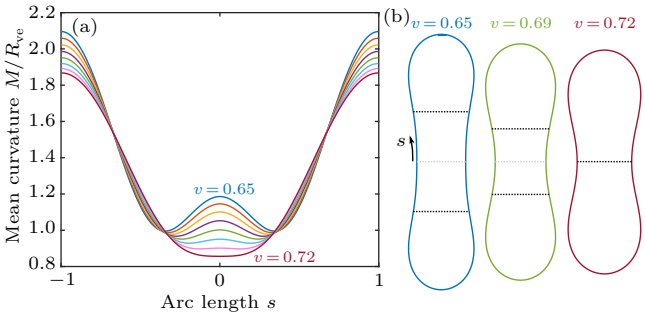


Fig. 2. (a) Mean curvature, in units of $1/R_{\rm ve}$, along the surface of axisymmetric prolate vesicles for eight values of v ranging from 0.65 to 0.72 in increments of 0.01. The arc length s goes from $s = -1$ corresponding to the south pole to $s = 1$ corresponding to the north pole, with $s = 0$ corresponding to the equator. For $v \lesssim 0.72$, there are two lines of lowest mean curvature, a finite distance away from the equator. (b) The location of the lowest mean curvature line (black dotted lines) on the vesicle, for three different values of v.

Indeed, for the lowest volume-to-area ratio $v = 0.65$ considered here, see the blue line in Fig. 2(a) and blue vesicle in Fig. 2(b), we find that the mean curvature at the minimum away from the equator is $M \approx 0.995/R_{\rm ve}$, whereas the mean curvature at the local maximum along the equator is $M \approx 1.186/R_{\rm ve}$. From Eq. (2), this implies that the energy barrier constraining a colloid to remain along the lowest mean curvature line and preventing it from jumping over the equator is of the order of $2.4\kappa R/R_{\rm ve}$. For a colloid with radius $R = 0.1R_{\rm ve}$, by using an estimate of the bending rigidity $\kappa = 10$–$100\ k_{\rm B}T$, we find that the energy barrier is of the order of 2.4–24 $k_{\rm B}T$. The colloids are expected to remain along the lowest curvature line for significant periods of time if the energy barrier is sufficiently larger than the thermal activation energy, which implies that the colloid ring will be more stable in systems with higher bending rigidities such as polymer vesicles[2] (as well as systems with larger $R/R_{\rm ve}$).

We note that we have chosen $v = 0.65$ as the lower limit of the volume-to-area ratio because, at this value, a discontinuous transition from prolate shapes to oblate-discocyte shapes is expected to occur.[20] Nevertheless, because this transition is discontinuous, the prolate shapes will remain metastable for a wider range of values $v < 0.65$, and thus we expect that one could in practice deflate the vesicles even further. In fact, metastable prolates with volume-to-area ratios $v < 0.65$ have been observed both in experiment[35] and in computer simulations.[36]

3.2. Non-reciprocal swimming strokes with reciprocal actuation

The breaking of up–down symmetry in the location of the adhesive colloid ring for $v \lesssim 0.72$ suggests that cycles of inflation and deflation between $v = 0.65$ and $v = 0.71$ could be used to induce directed swimming of the vesicle–colloid hybrid; see Fig. 3(a). In low Reynolds number regime, however, it is not sufficient to break the up–down symmetry: to evade Purcell's "scallop theorem",[14] we must also ensure that the swimming strokes are non-reciprocal. In particular, this implies that slow, quasistatic deflation and inflation cannot lead to swimming: in this case, the trajectory of the ring of colloids during deflation would be identical to the trajectory during inflation, just reversed; see Fig. 3(b). Such a stroke cannot possibly lead to swimming at low Reynolds number, due to the kinematic reversibility of the field equations.[17]

However, this limitation is overcome if we allow for quick inflation or deflation. In this limit, the ring of colloids cannot adapt its location fast enough to the change in shape of the vesicle, and thus remains at a fixed location (as dictated by conservation of the membrane area above and below the ring during the shape change). Using this technique, we can design three different actuation protocols, leading to three different non-reciprocal swimming strokes:

(1) **Slow inflation, quick deflation**: the ring of colloids approaches the equator quasistatically during slow inflation, remains there during quick deflation, and finally moves back towards its initial position along the deflated shape during a relaxation period; see Fig. 3(c).

(2) **Quick inflation, slow deflation**: the ring of colloids remains far from the equator during quick inflation, moves towards the equator along the inflated shape during a relaxation period, and finally moves back quasistatically towards its initial position during slow deflation; see Fig. 3(d).

(3) **Quick inflation, quick deflation**: the ring of colloids remains far from the equator during quick inflation, moves towards the equator along the inflated shape during a relaxation period, remains near the equator during quick deflation, and finally moves back towards its initial position along the deflated shape during a relaxation period; see Fig. 3(e).

The possibility of designing non-reciprocal strokes in response to reciprocal actuation of a single degree of freedom (the volume v of the vesicle) arises due to the effective elasticity of the vesicle–colloid system, in a similar way as proposed for other low Reynolds number swimmers with a single degree of freedom, such as two-sphere swimmers with deformable spheres,[24,25] or flexible filaments.[22] In our case, the location of the colloid ring can "lag behind" the shape changes of the vesicle, leading to non-reciprocal swimming strokes in response to reciprocal actuation.

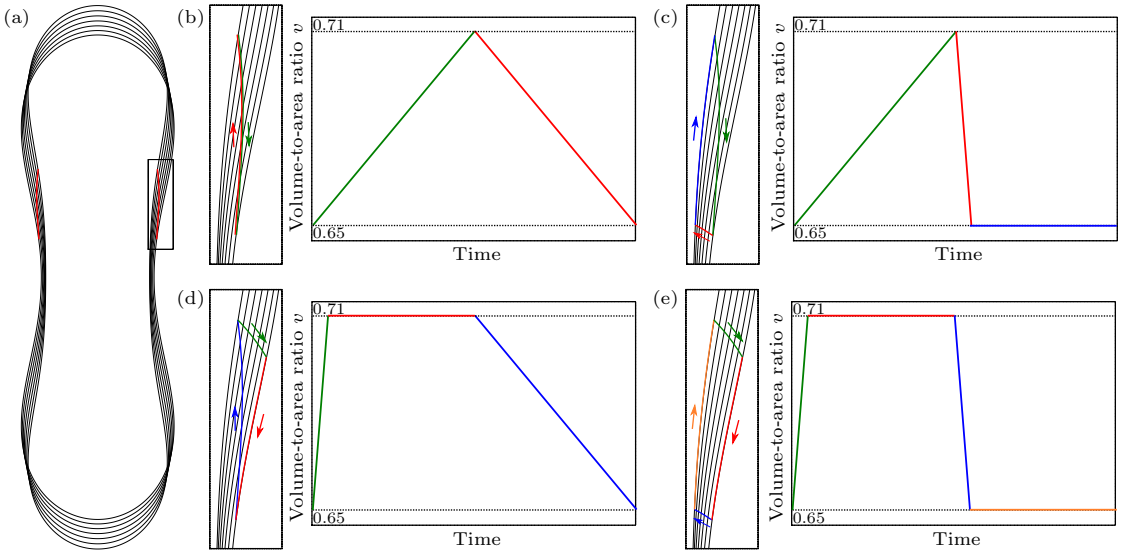


Fig. 3. (a) Sequence of axisymmetric shapes of a vesicle (black) during an inflation and deflation cycle between $v = 0.65$ and $v = 0.71$, including the equilibrium location of the colloid ring (red). The rectangle refers to the region depicted in (b)–(e). (b)–(e) Different actuation protocols for the periodic change of volume as a function of time, leading to different swimming strokes. (b) Slow inflation–slow deflation induces a reciprocal stroke which does not allow for swimming; (c) slow inflation–quick deflation, (d) quick inflation–slow deflation, and (e) quick inflation–quick deflation all induce non-reciprocal strokes.

Note that the actuation protocols considered here make use of the limit cases of "very fast" inflation/deflation, in which the colloid ring does not have any time to respond to the shape changes, and "very slow" or quasistatic inflation/deflation, in which case the ring is at its equilibrium position at all times. The typical timescale for response of a colloid to shape changes can be estimated as follows: given overdamped dynamics $\dot{s} = -\mu \mathrm{d}\Delta E/\mathrm{d}s$, where s is the arc length determining the location of the colloid ring along the vesicle surface, μ is the colloid's mobility, and ΔE is the binding energy given by Eq. (2); and using a harmonic expansion $M(s) \approx \frac{\alpha}{2}(s - s_*(t))^2$ around the location of the mean curvature minimum (see Fig. 2(a)) which we take to be located at $s = s_*$; we arrive at $\dot{s} = -\mu 4\pi\kappa R\alpha(s - s_*(t))$. This shows that the typical time scale that it takes for the location of the ring s to respond to changes in the location of the mean curvature minimum $s_*(t)$ is given by $\tau \equiv (\mu 4\pi\kappa R\alpha)^{-1}$. For $v = 0.65$, we find $\alpha \approx 1.7/R_{\mathrm{ve}}^3$. The mobility μ can be estimated as the hydrodynamic mobility $\mu = (6\pi\eta R)^{-1}$, resulting in $\tau \approx \eta R_{\mathrm{ve}}^3/\kappa$. Using the viscosity of water $\eta \approx 10^{-3}$ N·s/m^2, $\kappa \approx 10^{-19}$ J, and $R_{\mathrm{ve}} = 20$ μm, we find $\tau \approx 80$ s. Note, however, that accounting for the viscosity of the membrane associated with motion of the bound membrane segment, as well as the increased viscosity of the medium in physiological conditions, will further increase τ. Moreover, τ also increases strongly with increasing vesicle size. Therefore, fast inflation or deflation will correspond to volume changes in timescales of tens of seconds (or shorter), as can be obtained e.g. by osmotic shock,[37] whereas slow inflation or deflation will correspond to volume changes over hundreds of seconds.

Of course, at intermediate inflation and deflation speeds, there will be an interplay between the dynamics of colloid motion along the vesicle due to the curvature-induced forces, and the dynamics of vesicle shape changes due to the osmotic inflation and deflation. The limit-case protocols presented here serve as a proof of concept, and we expect that any moderately fast inflation and deflation protocol (so that the 'slow' quasistatic limit, shown in Fig. 3(b), can be avoided) will generically lead to non-reciprocal strokes.

The energy required for the cyclic motion of the vesicle–colloid system ultimately comes from the external changes in the concentration of osmotically active solute that cause inflation and deflation of the vesicle. If the vesicle initially has a volume V at a concentration c_v of solute in the external compartment, and the external concentration is rapidly changed to a value $c_{v'}$, the vesicle will experience an osmotic pressure difference $\Delta P = P_{\mathrm{in}} - P_{\mathrm{ext}} = (c_v - c_{v'})k_{\mathrm{B}}T$. The work exerted by the osmotic pressure when the volume changes from the initial volume V to the final volume $V' = Vc_v/c_{v'}$ is then given by $W = \int_V^{V'} \Delta P \mathrm{d}V$, leading to $W = k_{\mathrm{B}}Tc_vV\left[\frac{v}{v'} - 1 - \log\frac{v}{v'}\right] \approx \frac{1}{2}k_{\mathrm{B}}Tc_vV\,(\Delta v/v)^2$, where the last approximation is valid for small changes in the reduced volume $\Delta v = v' - v$. Using the osmolarity of blood $c_v = 300$ mM as a typical value of biological relevance, $V = (10\ \mu\mathrm{m})^3$ as a typical vesicle volume, as well as $v = 0.65$ and $v' = 0.72$ for the changes in volume, the work exerted by the osmotic pressure in every inflation or deflation event is found to be of the order of $10^9\ k_{\mathrm{B}}T$.

3.3. Swimming velocity of the vesicle–colloid hybrid

Following the governing equations in Subsection 2.3., we can determine the leading-order swimming speed of the whole assembly. We assume that each colloidal particle is a sphere of radius R, so that we have $\boldsymbol{K}_i = 6\pi\eta R\boldsymbol{I}$ and $\mathcal{F}_i = 1 + \frac{R^2}{6}\nabla^2$, with η being the viscosity of the fluid. Due to the axisymmetric nature of the system, we define $\boldsymbol{e}$ as a unit vector representing the axis of symmetry (pointed from the center of the vesicle towards the center of the colloidal ring), and express the shape of the vesicle in the spherical coordinate system set in the center of the vesicle as

$$r_{\mathrm{ve}} = R_{\mathrm{ve}}\left[1 + \sum_{k=0}^{\infty}\alpha_k P_k(\cos\theta)\right], \tag{8}$$

where R_{ve} characterizes the size of the vesicle, and P_k is the Legendre polynomial of order k, with θ being the polar angle from the axis of symmetry ($\boldsymbol{e}$). Given that for a weakly-deformed vesicle as considered here we have $\alpha_k \ll 1$, we find $\boldsymbol{K}_{\mathrm{ve}} = 6\pi\eta R_{\mathrm{ve}}\left[\boldsymbol{I} + \left(\alpha_0 - \frac{1}{5}\alpha_2\right)\boldsymbol{ee}\right]$, and $\mathcal{F}_{\mathrm{ve}} = 1 + \alpha_0 + \alpha_2\nabla_{\boldsymbol{e}}\nabla_{\boldsymbol{e}}\left(r_{\mathrm{ve}}^2 P_2\right) + O(\alpha_k^2)$, where $\nabla_{\boldsymbol{e}} \equiv \boldsymbol{\nabla}\cdot\boldsymbol{e}$.[33] We now define the actuations by $\mathbf{V}_0 = U(t)\boldsymbol{e}$, where $U(t)$ specifies the time-varying motion of the colloidal particles with respect to the vesicle. Using the far-field approximation to describe the flow fields,[33,38] and that in our case $R/R_{\mathrm{ve}} \ll \alpha_k \ll 1$, we find the leading-order cycle-averaged swimming velocity as

$$\bar{\boldsymbol{V}}_{\mathrm{net}} = -\frac{R}{5R_{\mathrm{ve}}}N\left[\frac{1}{T}\int_0^T \alpha_2 U(t)\mathrm{d}t\right]\boldsymbol{e}. \tag{9}$$

We may now evaluate the swimming velocity for the three actuation protocols introduced in Subsection 3.2. When both deflation/inflation occur slowly, the motion of the colloidal particles can be assumed as quasi-static: the particles relax as the vesicle shape deforms. The relative velocity is thereby always zero ($U(t) = 0$), and so the vesicle cannot propel itself forward. In the slow inflation–quick deflation protocol (actuation I), although the first half of the cycle does not contribute to the motion $U(t < T/2) = 0$, in the second half we have $U(t > T/2) > 0$. Similarly, quick inflation–slow deflation (actuation II) results in $U(t < T/2) < 0$, $U(t > T/2) = 0$; and for quick inflation–quick deflation (actuation III) we find $U(t < T/2) < 0$, $U(t > T/2) > 0$. Now, considering that the shape of the vesicle can be well approximated via the second mode of Legendre polynomials, we describe the shape

deformations of the vesicle by the two bounding values corresponding to the most inflated and most deflated shapes as $\alpha_{\rm inf} < \alpha_2 < \alpha_{\rm def}$. In the case of quick inflation/deflation we may assume the shape change to be abrupt, which leads to

$$\bar{V}^{\rm I}_{\rm net} = -\frac{R}{10R_{\rm ve}} N \alpha_{\rm def} \bar{U}_{\rm def} \boldsymbol{e}, \tag{10}$$

$$\bar{V}^{\rm II}_{\rm net} = \frac{R}{10R_{\rm ve}} N \alpha_{\rm inf} \bar{U}_{\rm inf} \boldsymbol{e}, \tag{11}$$

$$\bar{V}^{\rm III}_{\rm net} = -\frac{R}{10R_{\rm ve}} N \left(\alpha_{\rm def} \bar{U}_{\rm def} - \alpha_{\rm inf} \bar{U}_{\rm inf}\right) \boldsymbol{e}, \tag{12}$$

where $\bar{U}_{\rm def} \equiv \frac{2}{T}\int_{T/2}^{T} |U(t)| {\rm d}t$ and $\bar{U}_{\rm inf} \equiv \frac{2}{T}\int_{0}^{T/2} |U(t)| {\rm d}t$ are the average magnitudes of the colloid velocity during relaxation along the deflated and inflated shapes, respectively. These averages may be explicitly calculated from a model of relaxation dynamics along the energy landscape given by Eq. (2). Note that, because $\alpha_{\rm def}$, $\alpha_{\rm inf}$, $\bar{U}_{\rm def}$, and $\bar{U}_{\rm inf}$ are all positive quantities, our results suggest that relaxation along the deflated shape (as in actuation I) pulls the vesicle backwards ($-\boldsymbol{e}$; away from the colloidal ring), while relaxation along the inflated shape (as in actuation II) pushes it forwards ($\boldsymbol{e}$; towards the colloidal ring). Thus, remarkably, depending on the actuation strategy, the vesicle can change its swimming direction. For actuation III, we expect that relaxation along the deflated shape dominates over relaxation along the inflated shape, since $\alpha_{\rm def} > \alpha_{\rm inf}$ and $\bar{U}_{\rm def} \approx \bar{U}_{\rm inf}$, leading to backwards swimming, albeit with smaller speed than for actuation I. Moreover, we note that in all cases the swimming speed is proportional to $R/R_{\rm ve}$ and N, implying that the swimming speed increases with colloid size and number.

4. Conclusion

In summary, we have proposed here a design for a vesicle–colloid hybrid that can swim at low Reynolds number, despite its reciprocal actuation. The vesicle–colloid hybrid will self-assemble under the right conditions: (i) the vesicle must be sufficiently deflated, so that its volume-to-area ratio is $v \lesssim 0.72$; and (ii) the Janus colloids must have a side that strongly adheres to the membrane, and a side that does not. The actuation involves periodic changes in the volume of the vesicle, which can be induced via external control of the osmotic conditions in the system, e.g., the concentration of an osmotically active solute in the solution.

In this system, swimming in response to reciprocal actuation of the vesicle becomes possible thanks to two key innovations. First, we have found that for volume-to-area ratios of the vesicle below $v \lesssim 0.72$, the line of lowest mean curvature of the vesicle (to which adhering colloids are spontaneously directed) moves away from the vesicle equator, thus allowing for the up–down symmetry of the vesicle shape to be spontaneously broken in the presence of the colloids. Second, the effective elasticity in the location of the colloid ring with respect to the vesicle results in non-reciprocal shape changes of the vesicle–colloid hybrid in response to reciprocal inflation–deflation cycles. We have proposed, as a proof of concept, three different actuation protocols that lead to swimming, but we expect non-reciprocal shape changes to be generic whenever inflation and deflation occur fast enough to avoid the quasistatic limit. We determined the swimming speed using a minimal model, and showed that the swimming directions in these protocols are remarkably different.

While the presence of the colloids allows for an easy route to non-reciprocal shape changes in response to reciprocal actuation, it is possible to think of other ways to achieve this goal even in a pure vesicle system, which could be explored in future work. One intriguing possibility would be to exploit the presence of hysteresis along the discontinuous discocyte-to-stomatocyte transition occurring at $v \approx 0.59$ in the spontaneous curvature model,[20] in response to quasistatic (slow) changes in volume. Typically, one would expect the vesicle to remain in a metastable stomatocyte state as it is inflated beyond $v > 0.59$, and on the other hand to remain in a metastable discocyte state as it is deflated below $v < 0.59$. This process will thus automatically lead to a cyclic non-reciprocal shape change of the vesicle.

Lastly, we note that, while throughout the paper we have considered that inflation and deflation of the vesicle are externally actuated, strictly making the system externally driven rather than self-propelled, it is perfectly conceivable that the changes in volume could be programmed to be self-generated, e.g., by a catalytic reaction that produces or consumes osmotically-active solutes within the vesicle interior. Such a chemically-active vesicle would then constitute a fully autonomous microswimmer.

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