Red Blood Cells and Other Nonspherical Capsules in Shear Flow: Oscillatory Dynamics and the Tank-Treading-to-Tumbling Transition

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We consider the motion of red blood cells and other nonspherical microcapsules dilutely suspended in a simple shear flow. Our analysis indicates that depending on the viscosity, membrane elasticity, geometry, and shear rate, the particle exhibits either tumbling, tank-treading of the membrane about the viscous interior with periodic oscillations of the orientation angle, or intermittent behavior in which the two modes occur alternately. For red blood cells, we compute the complete phase diagram and identify a novel tank-treading-to-tumbling transition as the shear rate decreases. Observations of such motions coupled with our theoretical framework may provide a sensitive means of assessing capsule properties.

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Early observations of dilutely suspended human red blood cells in steady simple shear flow showed that while cells suspended in a low viscosity media tumble continuously, cells suspended in a fluid with sufficiently high viscosity exhibit tank-treading [1]. Here, we use the term tank-treading to describe a cell that maintains almost constant shape and orientation in the laboratory frame, but whose membrane circulates around the interior much like the motion of a tank tread. Motivated by the observations of tank-treading red blood cells, Keller and Skalak [2] analyzed the motion of a viscous ellipsoid and concluded that the behavior depends on the ratio of the viscosities of the inner and outer fluids and was independent of the shear rate. Moreover, for a given geometry, there was a critical viscosity ratio separating two distinct behaviors: less viscous ellipsoids tank treaded at a steady orientation to the shear, while more viscous ellipsoids tumbled. Although simple, this theory coherently explains many observations for both capsules and vesicles.

Because of the control of size, shape, and material parameters, vesicles have proved to be a useful system for the study of soft objects in viscous flow [3–5]. Studies of synthetic vesicles have revealed unsteady types of behavior and tested the limits of [2]. Thermal fluctuations changing the vesicle shape can lead to measurable fluctuations in the vesicle orientation [6]. Moreover, a dynamical regime has been observed in which the vesicle trembles around the flow direction, while exhibiting large oscillatory shape changes [7]. Theoretical analyses for deformable particles predicts both oscillatory and steady regimes [8,9].

It has recently been observed that the dynamics of synthetic microcapsules in simple shear flow depend not only on the viscosity ratio, but also on the shear rate: when the capsule surface tank treads about the interior, the orientation oscillates; as the shear rate is lowered, the capsule transitions from tank treading to tumbling [10]. Similarly, red blood cells oscillate about a fixed angle while tank treading and tumbling can be induced by lowering the shear rate [11]. Although both unsteady vesicle [7–9] and capsule dynamics arise from the coupling between elasticity and orientation, the details of the elastic mechanism produce distinct dynamics. In this Letter, we provide a theoretical framework for analyzing the motion of a capsule in simple shear flow. We attribute the observed behavior to a periodic variation in the elastic membrane energy during tank treading, which is a consequence of the capsule's nonspherical undeformed shape and resistance to shear deformation. When the shear rate is decreased sufficiently, the stress exerted by the flow is no longer sufficient to drive the tank-treading motion through the maximum of the elastic energy, and the capsule becomes solidlike and tumbles.

Here, we model the cell or capsule as a viscous ellipsoid of axes lengths a_i, viscosity μ', contained in an elastic membrane and immersed in a fluid of viscosity μ and density ρ. The external flow unperturbed by the ellipsoid is a simple shear flow of rate $\dot{\gamma}$ in the laboratory reference frame [see Fig. 1(a)]. We assume that material elements in the membrane move along elliptical paths in the reference frame of the ellipsoid as in [2]. Then, the position of each membrane element is defined by a phase angle $\phi(t)$, and the tank-treading frequency is $\partial_t\phi(t)$. When $\phi = 2\pi$, a point on the surface has returned to its starting point. We are concerned with low Reynolds number flows ($\mathrm{Re} = \frac{\rho a_i^2 \dot{\gamma}}{\mu} \ll 1$) so that inertial effects can be neglected. Our formulation extends prior analysis of a viscous ellipsoid to include the effect of an elastic membrane, and we refer the reader to [2] for derivations of the rate of change of the orientation, θ, the rate of work done by the external fluid on the ellipsoid, W_p, and the internal dissipation, D:

$$\partial_t\theta = -\frac{\dot{\gamma}}{2} - \frac{2a_1a_2}{a_1^2 + a_2^2}\partial_t\phi + \frac{\dot{\gamma}}{2}\frac{a_1^2 - a_2^2}{a_1^2 + a_2^2}\cos 2\theta, \tag{1}$$

$$W_p = V\mu[f_2\partial_t\phi^2 + f_3\dot{\gamma}\partial_t\phi\cos 2\theta], \tag{2}$$

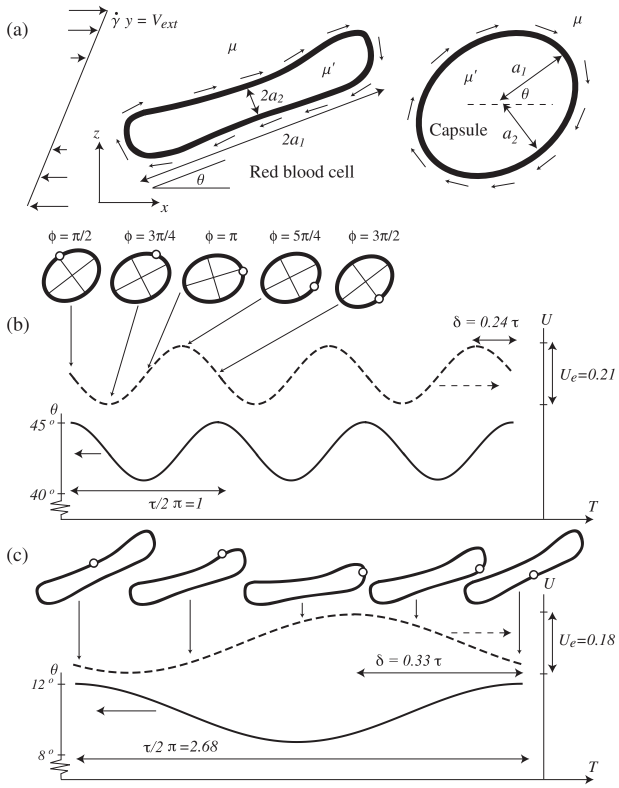

FIG. 1. (a) Schematic diagram of a tank-treading red blood cell (left) and capsule (right) filled with a fluid of viscosity μ' while immersed in a fluid of viscosity μ sheared at a rate $\dot{\gamma}$; $\lambda = \mu'/\mu$. θ defines the orientation to the shear flow, and ϕ defines the membrane orientation. The red blood cell and capsule are modeled as ellipsoids of axes a_i. U_e is the dimensionless ratio of the elastic resistance to tank treading to the surface stress applied by the external fluid. δ is the phase lag between the oscillations in θ and the elastic energy. (b) Capsule parameters: $a_1/a_2 = a_1/a_3 = 1.1$; $\lambda = 0$; $\gamma = 5$; $U_e = 0.21$. We note that the phase shift of $T/4$ between the shape and orientation has been experimentally observed [10]. (c) Red blood cell parameters: $a_1/a_2 = 4$, $a_1/a_3 = 1$; $\lambda = 1.5$; $\gamma = 5$; $U_e = 0.18$.

$$D = V\mu' f_1 \partial_t \phi^2, \tag{3}$$

where V is the volume of the ellipsoid, and f_i are functions of the ellipsoid geometry defined in the endnote [12].

In a series of recent experiments on red blood cells in a transient shear flow, Fischer [13] showed that after relaxation from deformation, the rim of a red blood cell is always formed by the same part of the membrane. This shape memory could not be eliminated by continuous deformation for periods up to 4 hours, showing that the effect is not due to visco-elastic relaxation. These results imply the existence of an elastic energy that has a minimum when the membrane is in static equilibrium. Since an element displaced from the rim can return to either side of the rim depending upon its proximity [13], the elastic energy must pass through two minima during a tank-treading revolution. Similarly, for the case of a polyamide capsule, the unperturbed shape is a slightly nonspherical ellipsoid, and we assume that the elastic energy during tank treading has the same π-rotational symmetry as the undeformed shape. Consequently, we take the elastic energy to have the form

$$E = E_0 \sin^2(\phi). \tag{4}$$

Fischer's experiments [13] can also be used to estimate the size of the elastic energy change, E_0. When the shear flow is stopped, the rate of work done by the external fluid W_p vanishes. The slender geometry of the red cell allows us to neglect dissipation in the external fluid in this analysis so that the rate of change in the elastic energy (4) balances the internal dissipation (3) so that $E_0 \sin(2\phi)\partial_t\phi \approx V\mu' f_1 (\partial_t \phi)^2$. The volume of a red blood cell is $V \approx 7 \times 10^{-17}$ m^3 and $f_1 \approx 15/4$. The internal viscosity μ' is due to a combination of the cytoplasm viscosity and the membrane viscosity. The dissipation due to the membrane viscosity has been shown experimentally to be between 2 and 4 times the dissipation in the cytoplasm [14,15], and we choose the value $\mu' = 4\mu_{\text{interior}} = 4 \times 10^{-2}$ Pa · s corresponding to a membrane dissipation equal to 3 times the dissipation in the cytoplasm. Fischer's data show the maximum tank-treading frequency to be approximately $\partial_t \phi \approx 0.25$ s^{-1} so that

$$E_0 = V\mu' f_1 |\partial_t \phi|_{\max} \approx 10^{-17}\ \text{J}. \tag{5}$$

We can now estimate the amount of strain corresponding to the stored energy E_0. For a membrane of shear modulus $E_s \approx 6 \times 10^{-6}$ N/m [16] covering a surface $S \approx 1 \times 10^{-10}$ m^2 and undergoing a shear strain u, the elastic energy is approximately $E_0 \approx \frac{E_s u^2 S}{2}$. Equation (5) then yields the characteristic shear strain $u \approx 0.2$, a reasonable value. The properties of the red blood cell membrane are determined by both the phospholipid bilayer and the adjacent protein network. The high resistance to change in membrane surface area insures that shear (area preserving) deformations dominate. The observed resistance to shear and the shape memory are most likely due to the underlying protein network [13]. Thus, shape memory arises from the essential difference between capsules and lipid bilayer vesicles: resistance to shear deformation.

Equating the rate of work by the external fluid (2) with the internal dissipation (3) and the rate of elastic energy storage (4) yields

$$V\mu(f_2 \partial_t \phi^2 + f_3 \dot{\gamma} \partial_t \phi \cos 2\theta) = V\mu' f_1 \partial_t \phi^2 + E_0 \sin(2\phi)\partial_t \phi, \tag{6}$$

which can be solved for the tank-treading frequency $\partial_t \phi = \frac{\dot{\gamma} f_3}{f_2 - \lambda f_1}(U_e \sin 2\phi - \cos 2\theta)$ where $\lambda = \mu'/\mu$ is the viscosity ratio and $U_e = \frac{E_0}{V\mu\dot{\gamma} f_3}$ is the ratio of the change in the elastic energy to the work done by the external fluid during a rotation, i.e., how stiff the cell or capsule is relative to the forcing from the external shear flow. Scaling time, $t = T/\dot{\gamma}$, yields the dimensionless system of equations for θ and ϕ,

$$\begin{aligned}\partial_T\phi &= \frac{f_3}{f_2-\lambda f_1}(U_e\sin 2\phi-\cos 2\theta),\\ \partial_T\theta &= -\frac{1}{2}-\frac{2a_1a_2}{a_1^2+a_2^2}\partial_T\phi+\frac{1}{2}\frac{a_1^2-a_2^2}{a_1^2+a_2^2}\cos 2\theta.\end{aligned}\tag{7}$$

The system's behavior is now completely determined by U_e, λ, and the geometric ratios a_1/a_2, a_1/a_3. Although observations of micro capsules have shown that the capsule geometry oscillates periodically during tank treading [10,17], these oscillations amount to only a few percent of the axes lengths. Solving (7) with the additional equations $a_i = a_{i0} + \delta_i \sin^2\phi$ shows that length oscillations of the order of a few percent are a minor contributor to the dynamics. In contrast to experiments on vesicles demonstrating that shape changes were the main contributor to changes in orientation [7], here, the influence of the stored elastic energy on the tank-treading velocity dominates.

A simple way to understand the relationship between the tank treading and oscillation periods is to expand (7) using U_e as a small parameter: $\phi = \phi_0 + U_e\phi_1$, $\theta = \theta_0 + U_e\theta_1$. Hence, $\theta = \theta_0 + U_e c\sin(2wT - \delta)$, where δ and c are constants, and the two minima of the elastic energy in each tank-treading cycle cause the system to oscillate twice about a fixed angle in the time it takes a surface element to tank tread back to its initial position. Furthermore, we see that the amplitude of the oscillation scales as $U_e \sim 1/\dot{\gamma}$. Slightly nonspherical polyamide microcapsules [10] and numerical simulations of slightly nonspherical liquid capsules enclosed by elastic membranes [18] in shear flow have shown oscillations at frequencies twice the tank-treading frequencies.

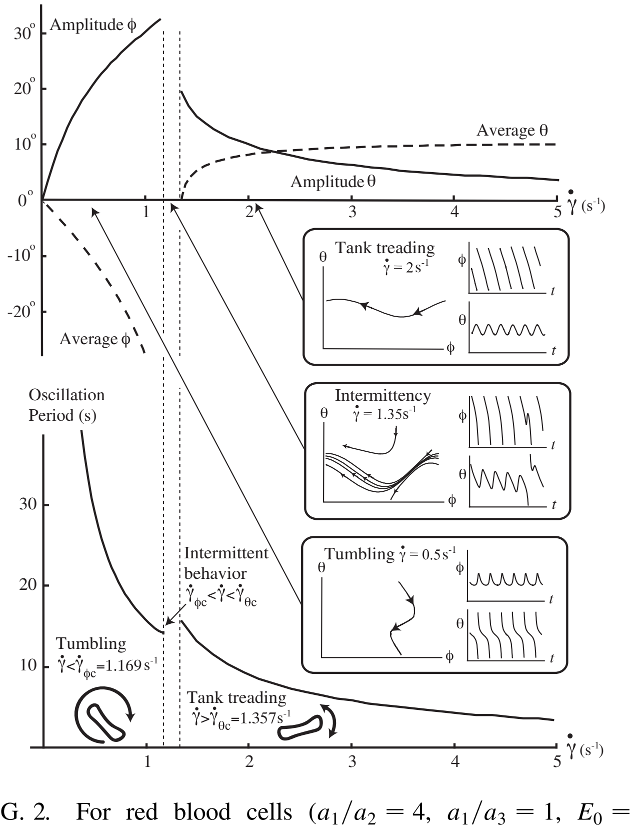

FIG. 2. For red blood cells ($a_1/a_2 = 4$, $a_1/a_3 = 1$, $E_0 = 10^{-17}$ J, and $\lambda = 1.5$) a novel transition from tank treading to tumbling is predicted as the shear rate is decreased. For $\dot{\gamma} > \dot{\gamma}_{\theta c}$, the membrane tank treads, and the cell orientation θ oscillates. For $\dot{\gamma} < \dot{\gamma}_{\phi c}$, the cell tumbles, and the orientation ϕ of the membrane relative to its unperturbed position oscillates. For $\dot{\gamma}_{\phi c} < \dot{\gamma} < \dot{\gamma}_{\theta c}$, the cell exhibits intermittent behavior, with a series of tank-treading revolutions followed by a tumble or a series of tumbles followed by a revolution. Insets show the dynamical regimes for $\dot{\gamma} = 2$, 1.35, 0.5.

The transition to tumbling behavior as the shear rate is deceased occurs when the fluid shear stress acting on the particle is no longer sufficient to force the membrane to tank tread up the elastic energy gradient. The surface velocity decreases as the capsule "solidifies" and begins to tumble. In contrast to the tank-trading-to-tumbling transition for a purely viscous drop described by Keller and Skalak [2], in which there is no dependence on the shear rate, the transition described here depends on the shear rate since $U_e \sim 1/\dot{\gamma}$. The transition point is a function of the system parameters: $U_{ec}(\lambda, \frac{a_1}{a_2}, \frac{a_1}{a_3})$. When the viscosity ratio is small, $\lambda \ll 1$, the transition occurs at $U_e \approx 1$, which corresponds to the critical shear rate $\dot{\gamma}_c \approx \frac{E_0}{V\mu f_3}$. Figure 2 illustrates the tank-treading-to-tumbling transition for a red blood cell.

Beyond the critical shear rate, the system exhibits type I intermittent behavior [19,20], i.e., a series of oscillations periodically interrupted by a tumble [21]. This transition is most easily understood by studying the return map onto the line $\phi = 0$ in the $\theta - \phi$ plane modulo π. For the initial condition $\theta = \theta_0$, $\phi = 0$, the trajectory crosses the $\phi = 0$ line again at $F(\theta_0)$, thus defining the return map. Periodic trajectories appear as fixed points in the return map, $F(\theta_0) = \theta_0$, and the tank-treading-to-tumbling transition occurs via a saddle-node bifurcation in which an unstable limit cycle and a stable limit cycle coalesce and disappear. Near the bifurcation $U_e - U_{ec} \ll 1$, [20] showed that the number of oscillations before an intermittent tumble scales as $n \sim 1/\sqrt{(U_e - U_{ec})}$, as seen in Fig. 3. As U_e is in-

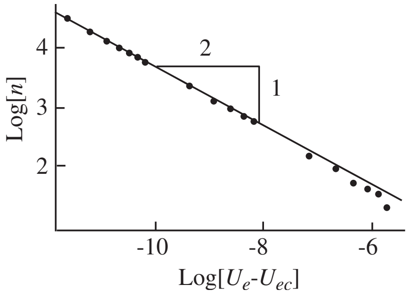

FIG. 3. Type I intermittency: n is the number of tank-treading oscillations per tumble; $U_e - U_{ec}$ is the difference between U_e and its value at the boundary between the tank-treading and the intermittent regions. The plot is shown for $\lambda = 1.5$ and a red blood cell geometry ($a_1/a_2 = 4$, $a_1/a_3 = 1$). The $-1/2$ slope on a log-log plot is indicative of Type I intermittency (see text).

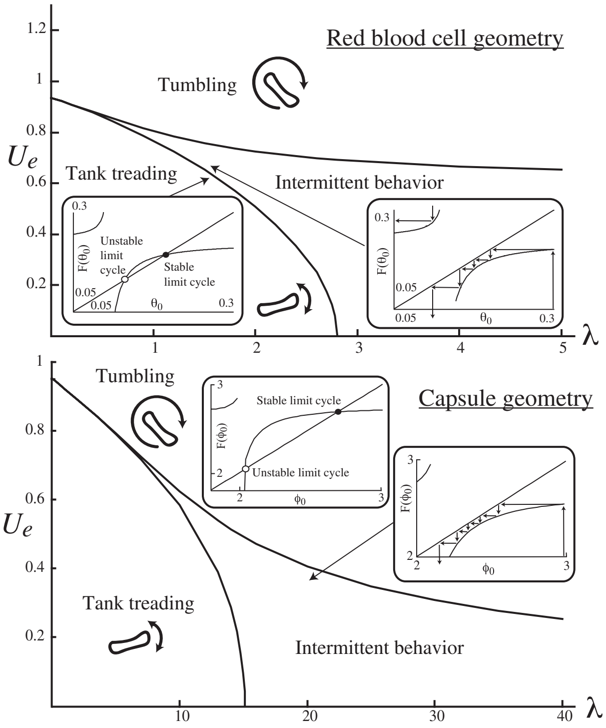

FIG. 4. Phase diagrams for the red blood cell ($a_1/a_2 = 4$, $a_1/a_3 = 1$) and capsule ($a_1/a_2 = a_1/a_3 = 1.1$) geometries. For a given geometry, the system behavior is determined by U_e, the dimensionless ratio of the elastic resistance to tank treading divided by surface stress from the external flow, and λ, the ratio of internal to external viscosity. For the red blood cell geometry, the insets ($\lambda = 1.5$, $U_e = 0.6557, 0.65$) show how the return map [$F(\theta_0)$ gives the value of θ when the trajectory modulo π beginning at $\theta = \theta_0$, $\phi = 0$ again crosses $\phi = 0$] changes as the system crosses the boundary between tank treading and intermittent regions. The stable and unstable fixed points of the return map coalesce in a saddle-node bifurcation and intermittent behavior ensues. Similarly, for the capsule geometry, a return map is shown for ϕ for $\lambda = 20$, $U_e = 0.6, 0.37$. Both transitions occur for the two geometries investigated.

creased further, the system enters a regime where the intermittent behavior consists of a series of tumbles periodically interrupted by a tank-treading revolution. Finally, for $U_e > U_{ec*}$, the system fails to exhibit full tank-treading rotations and simply tumbles. In this case, the relevant return map is onto the line $\theta = 0$ in the $\theta - \phi$ plane so that for the initial condition $\phi = \phi_0$, $\theta = 0$, the trajectory crosses the $\theta = 0$ line again at $F(\phi_0)$. This transition is also a type I intermittent transition caused by the coalescence of two limit cycles. The phase diagram illustrating the different regimes is shown for both the capsule and red blood cell geometries in Fig. 4. The insets in Fig. 4 show the return map in different regions and two examples of intermittent trajectories.

By modifying (4) to include visco-elastic membrane properties, our framework can also account for the shear flow induced oscillations observed for oil drops coated with a visco-elastic protein layer [17,22]. The details of the behavior discussed in this Letter, particularly in and around the intermittent regime, are sensitive to parameter values. Therefore, mechanical characteristics of cells and capsules could potentially be deduced from observations of such behavior.

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