Dynamics of Nearly Spherical Vesicles in an External Flow

V. V. Lebedev, K. S. Turitsyn, and S. S. Vergeles

Landau Institute for Theoretical Physics, Moscow, Kosygina 2, 119334, Russia

Tank-treading, tumbling, and trembling are different types of the vesicle behavior in an external flow. We derive a dynamical equation enabling us to establish a state of nearly spherical vesicles. For a 2D external flow, the character of the vesicle dynamics is determined by two dimensionless parameters, depending on the vesicle excess area, fluid viscosities, membrane viscosity and bending modulus, strength of the flow, and ratio of the elongational and rotational components of the flow. The tank-treading to tumbling transition occurs via a saddle-node bifurcation, whereas the tank-treading to trembling transition occurs via a Hopf bifurcation. A slowdown of vesicle dynamics should be observed in a vicinity of a point separating the transition lines. We show that the slowdown can be described by a power law with two different critical exponents 1/4 and 1/2 corresponding to the slowdown of tumbling and trembling cycles.

PACS numbers: 87.16.Dg, 47.15.G−, 47.20.Ky, 83.50.−v

Vesicles are closed membranes that separate two regions occupied by possibly different fluids. Vesicles are attracting significant attention, not only due to their resemblance to biological objects, but also because of their importance in different industries such as pharmaceutics where they are used for drug transportation. A natural problem that arises in these applications is to understand how a single vesicle behaves in an external flow. This nonequilibrium problem has revealed a variety of new physical effects and became a subject of intense experimental and theoretical studies. Laboratory experiments [1] have shown that vesicles immersed in a shear flow exhibit at least two qualitatively different types of behavior, either tank-treading or tumbling motion. In the tank-treading regime a vesicle shape is stationary, whereas in the tumbling regime the vesicle experiences periodic flipping in the shear plane. A novel type of behavior: trembling, discovered experimentally in the work [2], is an intermediate regime between tank-treading and tumbling in which a vesicle trembles around the flow direction. Theoretically, a possibility of such a regime was first discussed by Misbah [3] (vacillating breathing mode) and then by Noguchi and Gompper [4] (swinging mode). We illustrate those regimes in Fig. 1.

Constructing a phase diagram for all these regimes depending on the external parameters is a challenging and an extremely difficult task because the problem in consideration is both strongly nonlinear and nonequilibrium. As long as no analytic solution of this problem exists, theoretical studies were based either on numerical simulations or on some approximations allowing analytical treatment. Numerical investigations of this problem involved several different computational schemes, including boundary element method [5], mesoscopic particle-based approximation [6–10], and an advected field approach [11]. These approaches have shown qualitative agreement with experiment. Analytical studies of the problem can be divided in two major classes. In the first one [4,7,12], phenomenological models of vesicle dynamics based on the classical work of Keller and Skalak [13] were proposed and

proved themselves to be rather efficient in explaining particular experiments. In the second series of works [3,14–16] the studies focused on quasispherical vesicles whose shape can be parametrized by a spherical harmonics expansion. A perturbation scheme around the Lamb solution for spherical body in an external flow allows one to derive the dynamic equations for the shape and the orientation of a vesicle and to investigate them analytically. In this Letter we propose a natural extension of the theory developed for quasispherical vesicles by accounting higher-order expansion terms. We show that these additions produce a qualitative change in the phase diagram and make it significantly more complicated. The resulting diagram, which is the main result of this Letter, contains all three types of vesicle behavior that were observed experimentally. In our work, we analyze how the vesicle dynamics depends on different control parameters, such as viscosity contrast, vesicle excess area, internal membrane viscosity, strength of the flow, and ratio of the elongational and rotational components of the flow.

Speaking about membranes, we have in mind lipid bilayers. Their physical properties have been extensively studied, both experimentally and theoretically (see, e.g., the book [17]). We assume that the vesicle size is much larger than the membrane thickness so it can be treated as a 2D object immersed into a 3D fluid. There are several features of the membranes that are important for our
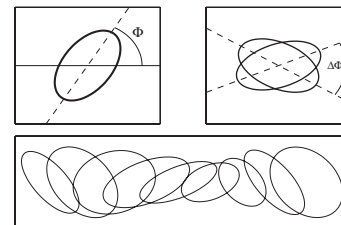

FIG. 1. Vesicle projections to the shear plane in the tank-treading, trembling, and tumbling regimes.

218101-1

analysis. First, we assume that the membrane is in a fluid state (is a 2D liquid), which is typical of lipid bilayers under normal conditions. Second, we assume that the vesicle has an excess area, which enables one to treat the membrane as incompressible. Third, we assume that the membrane is impermeable to the surrounding liquids, and the condition is usually well satisfied in experiment. Finally, we take into account the membrane internal viscosity, which could play an essential role, say, in the vicinity of the lipid-bilayer melting point [18] (see also Refs. [7,10]). The two properties, the membrane incompressibility and impermeability, imply that both the vesicle volume $\mathcal{V}$ and the membrane area $\mathcal{A}$ are conserved. The excess area can be characterized by a dimensionless factor Δ, which is defined as $\mathcal{A} = (4\pi + \Delta)r_0^2$, where r_0 is a vesicle "radius" determined by its volume: $\mathcal{V} = 4\pi r_0^3/3$. The excess area is non-negative, $\Delta \geq 0$, and the minimal value $\Delta = 0$ corresponds to an ideal sphere.

The membrane free energy can be written as the following integral over the membrane position [19]

$$\mathcal{F} = \int dA \left(\sigma + \frac{\kappa}{2} H^2 \right), \qquad (1)$$

where σ is the membrane surface tension, H is its mean curvature, and κ is Helfrich modulus. The last term in Eq. (1) describes energy related to membrane bending distortions. Note that the surface tension, σ, is a quantity adjusting to other membrane parameters (similar to the pressure in an incompressible fluid) to ensure the membrane incompressibility.

The membrane moves together with the surrounding fluid. That is, the velocity field $\boldsymbol{v}$ is continuous on the membrane and $\boldsymbol{v}$ determines the membrane velocity as well as the fluid velocity. We divide the flow near the vesicle into two parts: an external flow that would be present in the fluid in the absence of the vesicle, and an induced flow that is excited as a result of the vesicle reaction to the external flow. We assume that the characteristic scale of the external flow is much larger than the vesicle size. Then the external flow velocity V near the vesicle can be approximated by a linear profile. Generally, the external flow has both strain (elongational) and rotational contributions: $\partial_i V_k = s_{ik} + \epsilon_{ikj}\omega_j$, where $\hat{s}$ is the (symmetric) strain matrix and $\boldsymbol{\omega}$ is the angular velocity vector. The strain can be characterized by its strength s, defined as $s^2 = \text{tr}\hat{s}^2/2$. Note that for a shear flow $s = \omega = \dot{\gamma}/2$, where $\dot{\gamma}$ is the shear rate.

We examine nearly spherical vesicles. That is, the excess area parameter Δ is regarded to be small. Then it is natural to describe the vesicle shape (membrane position) as $r = r_0[1 + u(\theta, \varphi)]$ where r, θ, φ are spherical coordinates in the reference system with origin chosen at the vesicle center. The quantity u is a dimensionless displacement characterizing deviations of the membrane shape from the spherical one. For small Δ the displacement u can be estimated as $u \sim \sqrt{\Delta}$. Therefore $u \ll 1$ and one can formulate a perturbation expansion in this parameter.

We assume that both the interior fluid and the exterior one are Newtonian and that the Reynolds number is vanishingly small, so the fluids can be described in terms of the Stokes equation. Furthermore, we assume that an adiabaticity condition $\max\{s, \kappa/(\eta r_0^3)\} \ll \eta/(\varrho r_0^2)$ is satisfied where η is the viscosity and ϱ is the mass density of the exterior fluid. The same condition is assumed for the interior fluid. Then the flow inside and outside the vesicle can be treated as instantaneously adjusted to the vesicle motions and it is possible to establish a closed dynamical equation for the membrane displacement u. For this purpose, one should find the velocity field $\boldsymbol{v}$ inside and outside the vesicle at a given displacement $u(\theta, \varphi)$ and then equate $\partial_t u$ to the membrane normal velocity. To find the velocity field, one should solve the Stokes equation with boundary conditions dictated by the membrane incompressibility and by the momentum balance that includes membrane forces determined by the energy (1) [14,20,21] and membrane viscosity. To realize the program for a nearly spherical vesicle, one can use a generalization of the Lamb scheme applicable to a spherical body, see Ref. [22]. As a result, one finds the dynamical equation for u as a series in u.

In the main approximation in u one obtains

$$\hat{a}(\partial_t - \omega\partial_\varphi)u = 10 s_{ij} \frac{r_i r_j}{r^2} - \frac{1}{\eta r_0^3} \frac{\delta \mathcal{F}^{(3)}}{\delta u}, \qquad (2)$$

where $\hat{a}$ is some dimensionless operator, reflecting all viscous mechanisms, the Z axis of our reference frame is chosen to be directed opposite to the angular velocity $\boldsymbol{\omega}$, and $\mathcal{F}^{(3)}$ is an expansion up to third order in u of the free energy (1). For an external shear flow $s_{ij} r_i r_j/r^2 = (\dot{\gamma}/2)\sin^2\theta \sin(2\varphi)$, where the X axis is directed along the velocity. The two differences between Eq. (2) and the analogous equations obtained by Misbah [3] and Vlahovska and Gracia [16] are the inclusion of the membrane viscosity and third-order expansion term of the Helfrich energy. An importance of the third-order terms is discussed also by Noguchi and Gompper [4].

We take into account only the main contribution to u determined by second order angular harmonics. That is, the vesicle shape is an ellipsoid. It is justified by the smallness of Δ and by the fact that the nonuniform term in the right-hand side of Eq. (2) is a linear combination of second order angular harmonics. The operator $\hat{a}$ in this case is reduced to a constant,

$$a = \frac{16}{3} \left(1 + \frac{23}{32} \frac{\tilde{\eta}}{\eta} + \frac{\zeta}{2\eta r_0} \right), \qquad (3)$$

where $\tilde{\eta}$ is the viscosity of the interior fluid and ζ is the membrane viscosity. After passing to the variable $u/\sqrt{\Delta}$ the Eq. (2) acquires a self-similar form containing the parameters $\sqrt{\Delta}a\omega/s$, $s\eta r_0^3/(\kappa\Delta)$, and some dimensionless parameters characterizing ratios of the eigenvalues of the matrix $\hat{s}$ and mutual orientation of the vorticity vector $\boldsymbol{\omega}$ and the main axes of the matrix $\hat{s}$.

Below, we consider 2D external flows where the external velocity **V** lies in the X-Y plane and is independent of z. In this case the equation for $u/\sqrt{\Delta}$ includes two dimensionless parameters that can be chosen as

$$S = \frac{14\pi}{3\sqrt{3}} \frac{s\eta r_0^3}{\kappa\Delta}, \qquad \Lambda = \frac{\sqrt{3}}{4\sqrt{10\pi}} \frac{\sqrt{\Delta}a\omega}{s}. \qquad (4)$$

The parameter S characterizes relative strength of the external flow (of its strain), whereas the parameter Λ determines an effectiveness of the rotational part of the external flow. In the case of weak strains, $S \ll 1$, the vesicle conserves its equilibrium shape, and in the case of strong strains, $S \gg 1$, the vesicle shape is determined by the external flow.

For the 2D external flow, one can further reduce the description of the vesicle shape to be characterized by two parameters, Θ and Φ, specifying the displacement u as

$$u = \frac{\sqrt{5\Delta}}{4\sqrt{2\pi}}\left[\frac{\sin\Theta}{\sqrt{3}}(1 - 3\cos^2\theta) + \cos\Theta\sin^2\theta\cos(2\varphi - 2\Phi)\right].$$

The parameter Φ determines the vesicle inclination angle, whereas the parameter Θ determines the vesicle shape (ratios of the ellipsoid main semiaxes). We choose the reference system where the diagonal elements of the stain matrix $\hat{s}$ are zero. Then Eq. (2) is reduced to a couple of equations

$$\tau\partial_t\Phi = \frac{S}{2}\left[\frac{\cos(2\Phi)}{\cos\Theta} - \Lambda\right], \qquad (5)$$

$$\tau\partial_t\Theta = -S\sin\Theta\sin(2\Phi) + \cos(3\Theta), \qquad (6)$$

where

$$\tau = \frac{7\sqrt{\pi}}{12\sqrt{10}} \frac{a\eta r_0^3}{\kappa\sqrt{\Delta}}. \qquad (7)$$

The tank-treading vesicle motion corresponds to stable stationary points of Eqs. (5) and (6). Equating to zero the right-hand sides of the equations, one finds relations determining a stationary point at given parameters S and Λ. To investigate the stability of the point one should linearize Eqs. (5) and (6) near the point to obtain $\tau\partial_t(\delta\Theta, \delta\Phi) = \hat{B}(\delta\Theta, \delta\Phi)$. The point is stable, if both eigenvalues of the matrix $\hat{B}$ have negative real parts. Thus the stability conditions are $\mathrm{tr}B < 0$ and $\det B > 0$. A region in the S-Λ plane where stable points exist is indicated in Fig. 2 as gray.

The stable point is characterized by $\Phi > 0$ if $\Lambda < 2/\sqrt{3}$, and $\Phi < 0$ otherwise. At $\Lambda = 2/\sqrt{3}$, $\Phi = 0$, $\Theta = \pi/6$. The dash-dotted line in Fig. 2 is determined by the condition $(\mathrm{tr}B)^2 = 4\det B$, and it separates regions where oscillatory and damping regimes of approaching the stable point occur. The boundary of the stability domain can be determined either by the condition $\det B = 0$ or $\mathrm{tr}B = 0$. The corresponding lines are drawn in Fig. 2 merging at the point $S = \sqrt{3}$, $\Lambda = 2/\sqrt{3}$. At crossing the lines a saddle-node bifurcation occurs in the first case (corresponding to
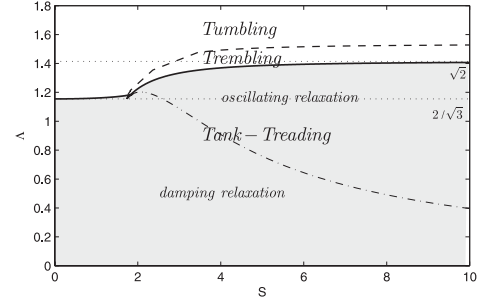

FIG. 2.   Phase diagram of the vesicle states on the S-Λ plane.

$S < \sqrt{3}$), whereas a Hopf bifurcation occurs in the second case (corresponding to $S > \sqrt{3}$). A limit cycle is realized in the system for points above the transition lines. Following the work [2] we distinguish tumbling and trembling regimes. In our terms, trembling corresponds to a limit cycle where Φ varies in a restricted interval (around zero), whereas tumbling means an increase of Φ by 2π during the cycle. The dashed line in Fig. 2 separates the two regimes, and trembling is realized below the line. An arrangement of vesicle states predicted by our theory corresponds to the one observed in experiment [2]. Qualitatively, our picture is also similar to the one observed in recent numerical simulations by Noguchi and Gompper [4].

Linearity of the Stokes equation implies that an expression for $\partial_t u$ has two contributions, proportional to the bending modulus κ and to the velocity gradient $\partial_i V_k$. In Eq. (2) we kept leading terms of both types. There are corrections to the leading gradient term that can be estimated as su. They exceed the κ-proportional term in strong flows, for $S > 1/\sqrt{\Delta}$. However, an account of these corrections does not change our results. This is due to a specific symmetry of the system: the equation for u in the case of $\kappa = 0$ is invariant under the transformation $t \rightarrow -t$ and $\partial_i V_k \rightarrow -\partial_i V_k$. In terms of the variables Φ and Θ the transformation reads $t \rightarrow -t$, $\Phi \rightarrow -\Phi$, $\Theta \rightarrow \Theta$. Next, the system of Eqs. (5) and (6) where the last term in the second equation is omitted (it corresponds to the limit $\kappa \rightarrow 0$ considered in Refs. [3,16]) has an integral of motion $\sin\Theta/[\Lambda - \cos\Theta\cos(2\Phi)]$. It enables one to analyze in detail the system dynamics. For $\Lambda < 1$ the phase portrait of the system is composed of two symmetric nodes, one stable and another unstable. For $\Lambda > 1$ it consists of a system of cycles, each symmetric under the $\Phi \rightarrow -\Phi$ transformation. The $\partial_i V_k$-proportional corrections disturb slightly the system of cycles but do not change the situation qualitatively. Indeed, due to the symmetry $\Phi \rightarrow -\Phi$ each disturbed cycle remains a closed curve. Contrarily, the κ-proportional term breaks the symmetry and leads to destruction of the cycles, except for the only one cycle (or stationary point) that remains stable and becomes an attractor of the system. Thus, only this term is of crucial importance. Following this way, one can reproduce our phase diagram depicted in Fig. 2 with the transition curves slightly shifted by the $\partial_i V_k$-proportional corrections.

Near the tank-treading to tumbling and tank-treading to trembling transitions a critical behavior occurs related to the degrees of freedom describing the corresponding bifurcations. The vesicle dynamics experiences an additional slowdown in the vicinity of the special point $S = \sqrt{3}$, $\Lambda = 2/\sqrt{3}$, where two transition lines terminate. The characteristic period of the trembling cycle is estimated as $\tau_\star (S - \sqrt{3})^{-1/2}$, whereas its amplitude is proportional to the shift from the transition line $\delta\Lambda$ in the Λ direction and does not experience a singular behavior near the point $S = \sqrt{3}$. Similarly, the saddle-node bifurcation is also "smoothed" near the special point. In a vicinity of the special point an effective equation for small variations of the variable Φ can be written as

$$\tau_\star \partial_t \delta\Phi = 3.36\delta\Lambda + 9.36\sqrt{S - S_c}(\delta\Phi)^2, \qquad (8)$$

where $S_c \approx 1.87$. In the tumbling regime, for $\delta\Lambda > 0$, the characteristic tumbling period can be estimated as $\tau_\star (S - S_c)^{-1/4}\delta\Lambda^{-1/2} \gg \tau_*$ for $S - S_c \gg \delta\Lambda^2$. The fine structure of the phase diagram is quite complicated near the special point: there are subdomains in its vicinity where two different stable points do exist and a stable point coexists with a limit cycle (the details are not reflected in Fig. 2).

The role of thermal fluctuations in vesicle dynamics can be investigated in the spirit of Refs. [14,23,24] (see also the book [25]). Equation (8) is similar to the one describing tumbling of single polymer molecules in external shear flow, where the effect of thermal fluctuations was extensively studied [24,26,27]. Based on the analogy, one may expect that the thermal noise strongly affects the tumbling period leading to the estimation $\tau^*(S - S_c)^{-1/3}D^{-1/3}$, in a vicinity of the special point. Here $D = T\kappa^{-1}\Delta^{-1/2}$ (where T is the temperature) is a dimensionless parameter characterizing power of thermal noise. Note that the thermal noise changes scaling of the tumbling period, which implies acceleration of tumbling.

To conclude, we have theoretically investigated vesicle dynamics in an external stationary flow. The general scheme based on solving the Stokes equation with boundary conditions posed on the membrane enabled us to analyze in detail dynamical properties of nearly spherical vesicles. We constructed the phase diagram of the system in terms of two dimensionless parameters (4) that are combinations of physically observed quantities. We demonstrated that in relatively weak flows the tank-treading to tumbling transition occurs, which can be described by a saddle-node bifurcation. In relatively strong flows one observes the tank-treading to trembling transition, which can be described by a Hopf bifurcation. A special critical slowdown of the vesicle dynamics has to be observed near the point separating the transition curves.

[1] K. H. DeHaas *et al.*, Phys. Rev. E **56**, 7132 (1997); N. Shahidzadeh *et al.*, Phys. Rev. Lett. **81**, 4268 (1998); M. Abkarian, C. Lartigue, and A. Viallat, Phys. Rev. Lett. **88**, 068103 (2002); V. Kantsler and V. Steinberg, Phys. Rev. Lett. **95**, 258101 (2005); M. A. Mader *et al.*, Eur. Phys. J. E **19**, 389 (2006).
[2] V. Kantsler and V. Steinberg, Phys. Rev. Lett. **96**, 036001 (2006).
[3] C. Misbah, Phys. Rev. Lett. **96**, 028104 (2006).
[4] H. Noguchi and G. Gompper, Phys. Rev. Lett. **98**, 128103 (2007).
[5] M. Kraus, W. Wintz, U. Seifert, and R. Lipowsky, Phys. Rev. Lett. **77**, 3685 (1996).S. Sukumaran and U. Seifert, Phys. Rev. E **64**, 011916 (2001).
[6] H. Noguchi and M. Takasu, Phys. Rev. E **65**, 051907 (2002).
[7] H. Noguchi and G. Gompper, Phys. Rev. Lett. **93**, 258102 (2004).
[8] H. Noguchi and G. Gompper, J. Phys. Condens. Matter **17**, S3439 (2005).
[9] H. Noguchi and G. Gompper, Proc. Natl. Acad. Sci. U.S.A. **102**, 14159 (2005).
[10] H. Noguchi and G. Gompper, Phys. Rev. E **72**, 011901 (2005).
[11] T. Biben, K. Kassner, and C. Misbah, Phys. Rev. E **72**, 041921 (2005).
[12] F. Rioual, T. Biben, and C. Misbah, Phys. Rev. E **69**, 061914 (2004).
[13] S. R. Keller and R. Skalak, J. Fluid Mech. **120**, 27 (1982).
[14] U. Seifert, Eur. Phys. J. B **8**, 405 (1999).
[15] P. Olla, Physica (Amsterdam) **278A**, 87 (2000).
[16] P. M. Vlahovska and R. S. Gracia, Phys. Rev. E **75**, 016313 (2007).
[17] J. Meuner, D. Langevin, and N. Boccara, *Physics of Amphiphilic Layers*, Springer Proceedings in Phys (Springer-Verlag, Berlin, 1987), Vol. 21.
[18] R. Dimova, B. Pouligny, and C. Dietrich, Biophys. J. **79**, 340 (2000).
[19] W. Helfrich, Z. Naturforsch. **A28**, 693 (1973).
[20] O. Y. Zong-Can and W. Helfrich, Phys. Rev. A **39**, 5280 (1989).
[21] V. V. Lebedev and A. R. Muratov, Sov. Phys. JETP **68**, 1011 (1989).
[22] H. Lamb, *Hydrodynamics* (Cambridge University Press, Cambridge, England, 1932), 6th ed.
[23] E. I. Kats, V. V. Lebedev, and A. R. Muratov, JETP Lett. **63**, 216 (1996).
[24] K. S. Turitsyn, Sov. Phys. JETP **105**, 655 (2007).
[25] E. I. Kats and V. V. Lebedev, *Fluctuational Effects in the Dynamics of Liquid Crystals* (Springer-Verlag, NY, 1993).
[26] M. Chertkov *et al.*, J. Fluid Mech. **531**, 251 (2005).
[27] A. Puliafito and K. Turitsyn, Physica (Amsterdam) **211D**, 9 (2005).