Hydrodynamic lift on bound vesicles

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Abstract

Bound vesicles subject to lateral forces such as arising from shear flow are investigated theoretically by combining a lubrication analysis of the bound part with a scaling approach to the global motion. A minor inclination of the bound part leads to significant lift due to the additive effects of lateral and tank-treading motions. With increasing shear rate, the vesicle unbinds from the substrate at a critical value. Estimates are in agreement with recent experimental data.

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Introduction. The equilibrium aspects of the interactions between membranes or vesicles and substrates have been explored intensely over the last decade [1]. Quantitative experimental data for both the mean shape and the fluctuations of the bound part of a vesicle have been obtained by using phase contrast microscopy and reflection interference contrast microscopy (RICM) [2]. A qualitative new step concerns the study of bound membranes under controlled non-equilibrium conditions such as the behavior of bound vesicles under shear flow. Apart from its fundamental significance, this system can serve as a model for the biologically ubiquitous situation of adhesion of membranes under flow. A prominent example occurs for leucocyte or platelet adhesion in capillary flow. Clearly, for biological systems, the non-trivial kinetics of specific adhesion molecule pairs under a ramped force contributes essentially to the dynamic unbinding of these cells (see, e.g., [3–5] and references therein). Still, a thorough understanding of the model case of a bound vesicle with its interplay between unspecific interactions and flow will be a prerequisite for gaining a comprehensive picture of these important dynamic interactions.

A significant experimental step in this direction has been achieved recently by combining RICM with a flow chamber [6]. With this set-up one can study the configurations of bound vesicles under shear flow. It was observed that these vesicles unbind from the substrate at a critical shear rate. However, the effective lift force was found to be about two orders of magnitude larger than what was predicted in previous theoretical work [4].

The purpose of this letter is to analyze theoretically the dynamically induced interaction between a substrate and a bound vesicle under a lateral force such as arising from shear flow. This problem is challenging since it involves two vastly different length scales. Typically, the
vesicle size is of the order of 10 \( \mu m \) whereas the distance between substrate and vesicle is of order 10 nm. A brute force approach trying to solve numerically the equations of motion of such a configuration as it has been done for free vesicles in shear flow \[7\] is bound to require a very fine discretization and, consequently, to face high computational costs. A first step in this direction has been achieved recently for the computationally less expensive two-dimensional case \[8,9\].

For the experimentally relevant three-dimensional case, a two step approach will be followed here. First, the bound part of the vesicle will be treated quantitatively within the lubrication approximation which holds if the lateral extension of the bound part is significantly larger than the distance from the substrate. As a result we will find that whenever this bound part is tilted a significant hydrodynamic lift arises even for small tilt due to the additive effects of translation and relative membrane motion, i.e. tank-treading. In a second step, we couple this lubrication analysis into a scaling approach of the overall vesicle motion. As a result, we predict a critical lateral force beyond which vesicles will detach from the bound state and, thus, undergo a dynamically induced unbinding transition. This transition must be distinguished from an equilibrium unbinding transition due either to fluctuations \[10,11\] or a competition between adhesion energy and curvature energy \[12\].

**Geometry.** In equilibrium, a vesicle bound to a substrate by a potential \( V(h) \) acquires a spherical cap-like shape if the depth \( W \) of the potential is sufficiently deep, see Fig. 1. The shape can then be characterized by two parameters, the radius \( R \) of the spherical cap and the radius \( R_a \leq R/2 \) of the adhesion disc. The distance \( h_0 \) of the adhesion disc from the substrate is determined by the location of the minimum of the adhesion potential. In equilibrium, the adhesion disc is parallel to the substrate but we will here allow a small inclination or tilt angle \( \alpha \).

We now apply a force \( F_x \) parallel to the substrate. The physical origin of this force can either be a linear shear field with shear rate \( \dot{\gamma} \) or a gradient in adhesion energy \( \nabla W \). The force then scales as \( F_x \sim \dot{\gamma} \eta R^2 \), or \( F_x \sim \nabla W R_a^2 \), respectively. As a result the vesicle moves with a velocity \( v \) into the same direction. Since the membrane is fluid, we have to allow for tank-treading motion which we assume for the spherical part to be a uniform rotation in the \( x, z \) plane at an angular speed \( \bar{v}_m/R \). This membrane flow on the spherical part enters (or leaves) the rim of the adhesion disc with a \( y \) dependent velocity

\[
v_m(y) = \bar{v}_m(1 - y^2/R^2)^{1/2},
\]

where \(|y| \leq R_a\). The velocities \( v \) and \( \bar{v}_m \) will later be determined from force balances but for the moment they are assumed to be given. We show first that such a motion generates a significant hydrodynamic lift on the vesicle.

**Lubrication theory.** For future reference, the lubrication approximation will be set up not just for a tilted adhesion disc but for a general membrane configuration parametrized by \( h(r) \) in a Monge representation above a substrate at \( z = 0 \) with \( r = (x, y) \). The lateral extension \( R_a \) of the membrane is much larger than the average height \( h_0 \) above the substrate. The velocity field is written as \( \mathbf{v}(r, z) = \mathbf{u}(r, z) + w(r, z)\mathbf{e}_z \) where \( \mathbf{u}(r, z) \) is the component parallel to the substrate. At the membrane, we specify the velocity as \( \mathbf{v}(r, h(r)) = \mathbf{u}^h(r) + w^h(r)\mathbf{e}_z \). At the substrate, no-slip boundary conditions imply \( \mathbf{v}(r, 0) = 0 \).

The Stokes equations for the incompressible fluid between substrate and membrane read
\[ \eta(\partial_z^2 + \nabla^2)u = \nabla p, \]  

(2)

and

\[ \eta(\partial_z^2 + \nabla^2)w = \partial_z p. \]  

(3)

Here \( \nabla \) is the gradient operator in the plane, i.e. \( \nabla = (\partial_x, \partial_y) \) in Cartesian coordinates. From the continuity equation \( \partial_z w + \nabla u = 0 \), it follows that \( w/|u| \sim O(h_0/R_a) \) for small \( h_0/R_a \). This scaling is the essential observation in lubrication theory. It implies via (2) and (3) that the pressure is a function of \( r \) but independent of \( z \) to leading order in \( h_0/R_a \).

Likewise the \( \partial_z^2 \) term can be ignored compared to the \( \partial_z^2 \) term in (2). The latter equation can hence be integrated as

\[ u(r, z) = \nabla p(r) \frac{z(z-h)}{2\eta} + u^h(r)z/h, \]  

(4)

which satisfies the boundary conditions at \( z = 0 \) and \( z = h \). Applying the \( \nabla \) operator to this equation, inserting the resulting expression into the equation of continuity and integrating the latter over \( z \) from 0 to \( h \) yields a Reynolds-type equation

\[ \nabla^2 p + 3\nabla p \nabla h/h = 12\eta w^h/h^3 + 6\eta \nabla (u^h/h)/h. \]  

(5)

This equation for the pressure holds for any membrane configuration in the lubrication approximation. We now specialize to the circular adhesion disc of radius \( R_a \) tilted at a small angle \( \alpha \), i.e. \( h(r) = h_0 + \alpha x \), see Fig. 1. No slip boundary conditions between membrane and fluid imply for the translational and tank-treading motion introduced above the boundary values \( u^h(r) = -\alpha v_m(y) \) and \( u^h(r) = (v - v_m(y))e_x \) for small \( \alpha \). With \( \nabla h = \alpha e_x \), equation (5) becomes

\[ \nabla^2 p(r) \approx -6\alpha \eta (v_m(y) + v)/h_0^3 \]  

(6)

to lowest order in \( \alpha \). First, assume that there was no tank-treading motion, \( \bar{v}_m = 0 \), and, hence, no \( r \) dependence of the inhomogeneity in this Poisson equation. The solution then is

\[ p(r) = 3\alpha \eta v(R_a^2 - r^2)/2h_0^3 + p(R_a)(r/R_a) \cos \phi \]  

(7)

where \( p(R_a) \cos \phi \) is the ambient pressure along the rim of the adhesion disc parametrized by the azimuthal angle \( \phi \). Integrating the excess pressure over the entire adhesion disc yields the total lift force on the membrane disc as

\[ F_l \equiv \int dA \ p(r) = 3\pi \alpha \eta v R_a^4/4h_0^3. \]  

(8)

For \( \bar{v}_m \neq 0 \), the solution of the Poisson equation (4) is slightly more involved because of the \( y \) dependence of the rhs. We are interested only in the total lift, which involves averaging over the whole adhesion disc. Given the form (4), it is then clear that (8) still holds with \( v \) replaced by \( \bar{v}_m \) up to a dimensionless function \( f(R_a/R) \) of order unity which will not be needed for the scaling analysis to follow. The important point is that both translational motion and tank-treading motion contribute similarly to the hydrodynamic lift (8). This lift increases strongly with decreasing distance \( h_0 \) of the membrane from the substrate. Note
that the reversibility of the Stokes equations implies that there is no hydrodynamic lift for a non-tilted configuration with $\alpha = 0$.

**Scaling analysis of global motion.** We now have to link this lubrication analysis of the adhesion disc to the overall vesicle dynamics. We apply the force $F_x$ parallel to the substrate and assume first the rotational degree of freedom being locked at $\alpha = 0$. Then, there are two conditions which fix the two velocity parameters $v$ and $\bar{v}_m$ uniquely. We write these conditions in scaling form which means that we ignore all numerical prefactors of the respective terms with the understanding that these prefactors do not exhibit singular behavior for small $h_0/R_a$.

(i) **Force balance in the $x$ direction:**

$$F_x \sim \eta \Delta v R_a^2 / h_0 + \eta v R,$$

where $\Delta v \equiv v - \bar{v}_m$ is the velocity of the bound part of the vesicle relative to the substrate. The first term on the rhs is the lateral force exerted by the lubrication layer, the second term is the hydrodynamic drag of the exterior fluid outside of the lubrication layer.

(ii) **Dissipation balance:**

$$F_x v \sim \eta (\Delta v)^2 R_a^2 / h_0 + \eta v^2 R + \eta \bar{v}_m^2 R.$$  

The lhs represents the power applied by the external force on the system. The first term on the rhs is the dissipation in the lubrication layer. The second one is dissipation in the exterior fluid outside of the lubrication layer. The third term is the dissipation within the vesicle due to tank-treading. We now divide the first equation by $\eta R$, the second one by $\eta v R$ and introduce with $v_S \equiv F_x / 6\pi \eta R$ the Stokes velocity of a spherical vesicle in infinite space.

The two equations (9,10) then read

$$v_S \sim \beta \Delta v + v $$

and

$$v_S \sim \beta (\Delta v)^2 / v + v + \bar{v}_m^2 / v$$

where $\beta \equiv R_a^2 / h_0 R$ is a dimensionless variable measuring the relevance of the substrate. For the scaling analysis, we have to distinguish three cases.

(i) For $\beta \ll 1$, the vesicle is too far away from the substrate to be affected significantly in its motion. We will not consider this case further.

(ii) For $\beta \sim 1$, we have $\Delta v \sim v \sim \bar{v}_m \sim v_S$. In this case, both translational and tank-treading velocity are of the order of the Stokes velocity.

(iii) For $\beta \gg 1$, equations (11,12) imply $\Delta v \sim 1/\beta$ and, consequently, $\bar{v}_m \approx v \sim v_S$. In this limit, tank-treading and translational velocity become equal and both are of the order of the Stokes velocity [9]. Tank-treading thus restores (up to factors of order unity) the free mobility which would be impossible for a rigid object with finite $R_a$ so close to a substrate.

In summary, we can write in each of the two interesting cases

$$\bar{v}_m \sim v \sim v_S \sim F_x / \eta R \quad \text{and} \quad \Delta v / v \sim h_0 R / R_a^2.$$  

(13)
**Hydrodynamic lift.** Using these results, which will hold within perturbation theory also for small nonzero tilt angle $\alpha$, the lift can be written as

$$F_l \sim \alpha \eta v R_4^4 / h_0^3 \sim \alpha F_x (R_a / R)(R_a / h_0)^3.$$  

(14)

This expression still depends on the unknown tilt angle $\alpha$ which must be determined next.

In general, the transversal motion considered so far for the rotationally locked shape at $\alpha = 0$ generates a torque $M$ acting in the $x, z$ plane. The origin of this torque are the lateral force and hydrodynamic interactions. Their sum will scale as $M \sim \eta v R^2 \sim F_x R$. Counteracting to such a torque is a torque arising from the confining adhesion potential which favors $\alpha = 0$. The energy $E(\alpha)$ of a tilted adhesion disc compared to a non-tilted one is given by $E(\alpha) \approx (\pi / 4) \alpha^2 V'' R_4^4$ where $V'' = V''(h_0)$ is the curvature of the adhesion potential at the minimum $h_0$. Balancing the torque $\partial_\alpha E$ derived herefrom with the hydrodynamic one leads to $\eta v R^2 \sim \alpha V'' R_4^4$ or

$$\alpha \sim \eta v R^2 / V'' R_4^4 \sim F_x R / V'' R_4^4.$$  

(15)

We have written these relations as if $\alpha$ was positive. Thus, we have implicitly assumed that the hydrodynamic torque acts to increase $\alpha$. While this cannot be proven without a full hydrodynamic calculation, evidence for this assumption in the case of shear flow arises from the fact that for free vesicles the strain component of the shear orients slightly elongated shapes towards a positive tilt angle [7]. Note that if the sign of $\alpha$ was reversed, the scaling relations derived so far would still hold with lift being replaced by an additional force pushing the vesicle towards the substrate.

With this expression for the tilt angle $\alpha > 0$, we can now calculate the lift force from (8) as

$$F_l \sim \eta^2 v^2 R^2 / h_0^3 V'' \sim F_x^2 / h_0^3 V''.$$  

(16)

For further evaluation, we need the specific form of the adhesion potential $V(h)$. A fairly universal relation can be derived if we assume that this potential can be characterized by two scales only, the location $h_0$ of its minimum and its depth $W \equiv |V(h_0)|$, see Fig. 1. Then, one has $V'' \sim W / h_0^2$, which implies $F_l \sim F_x^2 / W h_0$.

For a comparison with experimental quantities, it is convenient to express the adhesion energy $W$ in terms of an effective tension $\Sigma$ using a Young Dupre equation [12]. Except in the tense spherical limit $R_a \rightarrow 0$, both quantities are of the same order, i.e. $\Sigma \sim W$. For vesicles in shear flow, we can thus write for the lift

$$F_l \sim F_x^2 / W h_0 \sim (\eta^2 v^2 R^2 / \Sigma)(R / h_0).$$  

(17)

This result is a factor of order $R / h_0 \approx 10^2 - 10^3$ larger than a previous theoretical estimate [4]. On the basis of the latter, it was argued in Ref. [4] that the experimentally observed lift was 2 to 3 orders of magnitude larger than theoretically expected. In the light of the present theory, this apparent discrepancy is most likely due to the factor $R / h_0$ missed in Ref. [4].

**Dynamical unbinding.** The lift, if small enough, will displace the vesicle slightly from the static equilibrium at $h_0$. The new dynamical equilibrium position can now be found by
balancing the lift with the restoring force, \( F_z \approx -\pi R_a^2 (h - h_0) V'' \), arising from an expansion of the potential around its minimum. The relative shift thus becomes

\[
(h - h_0)/h_0 \sim F_x^2/h_0^4 V'' R_a^2 \sim F_x^2/W^2 R_a^2. \tag{18}
\]

Typically, if \((h - h_0)/h_0 \sim 1\), the lift will be too strong to be compensated by the attractive potential. Then, the vesicle will unbind from the substrate under the action of a lateral force. Using this criterion, we can determine the critical lateral force \( F_x^c \) as \( F_x^c \sim h_0^3 V'' R_a \sim W R_a \). If the lateral force arises from a shear field, the critical shear rate is

\[
\dot{\gamma}^c \sim W R_a/\eta R^2. \tag{19}
\]

Depending on the specific conditions, measurements for the adhesion energy \( W \) have obtained a vast range of values from \( 10^{-1} \) to \( 10^{-6} \) erg/cm\(^2\) \cite{13,14,2}. Consequently, the critical shear rate will also depend strongly on the conditions. Rather than using \( \dot{\gamma}^c \) to estimate this force, we chose a typical shear rate of \( \dot{\gamma} = 1/\text{s} \) and determine the critical adhesion energy \( W^c \) at which the dynamical unbinding should occur. For a vesicle with \( R = 10 \mu \text{m}, R_a/R = 0.1 \) and a fluid viscosity of \( \eta = 10^{-2} \text{erg s/cm}^2 \), we find a critical adhesion energy of \( W^c \sim 10^{-4} \text{erg/cm}^2 \) which is well within the above range. For \( W > W^c \), vesicles with the above geometry will unbind from the substrate.

The tilt angle \( \alpha^c \) at the critical value is

\[
\alpha^c \sim F_x^c R/V'' R_a^4 \sim F_x^c R h_0^3/W R_a^4 \sim h_0^2 R/R_a^3. \tag{20}
\]

Within this simple assumption about the adhesion potential, the scaling of the critical tilt is thus predicted to be determined exclusively by geometrical quantities. Note that since \( h_0 \ll R_a \ll R \), the critical tilt angle can be very small, e. g., \( \alpha_c \approx 10^{-3} \) for \( h_0 = 10 \) nm and \( R, R_a \) as above.

**Beyond unbinding.** What happens with the vesicle for larger lateral forces \( F_x > F_x^c \)? If the adhesion potential decays to 0 for large \( h \), one can expect that the vesicle will continuously drift away from the substrate presumably in a combination of tank-treading and tumbling motion. This regime has been studied perturbatively for large \( h_0/R \) in Ref. \cite{15}.

If, however, as often in experiments, the vesicle is filled with a slightly denser fluid than the surroundings, gravity will keep it close to the substrate since the lift necessarily gets weaker with increasing distance. Such a state where after detachment the vesicle still keeps its spherical cap like configuration and translates at about 100 nm above the substrate has been reported experimentally \cite{6}. We close with a somewhat speculative theoretical analysis of this state. The jump in separation from the substrate of about 100 nm could indicate that a short range adhesion potential is no longer responsible to the energetics after detachment. Neither can the potential then exert a restoring torque. Therefore, the total hydrodynamic torque must vanish. At which angle \( \alpha \) this happens (if at all) can only be determined by a full hydrodynamic theory. The present scaling approach, however, allows to relate this tilt angle \( \alpha \) to the separation \( h \) by balancing the lift force \( \dot{\gamma}^c \) with the gravitational force \( F_g = g \Delta \rho V \), where \( g \approx 1000 \text{ cm/s}^2 \) and \( \Delta \rho \) is the density difference. Such a balance leads to \( \dot{\gamma}^c \sim (h_0/R_a)^3 (F_g/\dot{\gamma}^c)(R/R_a) \). Using typical experimental values \( F_g \approx 10^{-7} \text{ erg/cm}, F_x \approx 10^{-8} \text{ erg/cm}, h_0/R_a \approx 0.1, \) and \( R/R_a \approx 10 \), one finds with \( \alpha \approx 0.1 \) that a quite
small tilt angle could generate enough lift to sustain such a stationary state. It must be emphasized that this estimate is speculative in two respects. First, we have not shown that the full hydrodynamics allows such a torqueless state but have rather postulated it. Secondly, numerical prefactors could easily conspire and change such an estimate about one order of magnitude.

**Summarizing perspective.** We have analysed the hydrodynamics of a bound vesicle under a lateral force allowing for tank-treading motion. A positive tilt of the bound part will generate lift. By combining a lubrication analysis with scaling arguments, a dynamically induced unbinding transition is predicted when the lateral force exceeds a critical value. Even though our analysis used for simplicity the spherical cap configuration, the scaling relations will also hold for weakly bound states with rounded contact regions. More quantitative theoretical calculations will be needed to fill in numerical prefactors necessarily missing in such a scaling analysis. Such full scale calculations will also reveal the role of transients and assess whether the theoretically somewhat speculative stationary translating state after unbinding exists. On the experimental side, special efforts should now be undertaken to measure the here theoretically predicted but so far not yet experimentally reported tilt angle which, even if minute, is ultimately the source of the lift.

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[16] Note that this estimate is larger than the critical value derived above for unbinding from a short-range potential.
FIG. 1. A bound vesicle under a lateral force $F_x$ (left) in a potential well $V(h)$ with minimum at $h_0$ and depth $W$ (right). The radius of the adhesion disc is $R_a$, its tilt angle is $\alpha$. The vesicle translates at velocity $v$ and tank-treads at velocity $v_m$. This motion generates a lift $F_L$. 