Dynamics of Vesicle Unbinding under Axisymmetric Flow

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The competition between adhesion and external flow to unbind settled vesicles from substrates is investigated. An experimental setup is developed to apply a hydrodynamic pulling force in the range of a few piconewtons to a vesicle with retained axisymmetry. In the limit of a small excess of membrane area, vesicles are found to transit during unbinding from a process of fluid film thickening at constant contact area to a finite-time process of contact radius drop to zero with an exponent 1/2. Both characteristic times vary linearly with the inverse flow rate. On the contrary, deflated vesicles under a moderate pulling force exhibit a decrease of contact area at a constant film thickness before a film thickening.

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The understanding of the dynamics of vesicles [1] under nonequilibrium conditions is receiving increased interest through several approaches: biomimetism applied to active membranes [2], adhesion under pulling force from unbinding [3] to tethers [4,5], and understanding the rheology of biofluids. Indeed, in this last case, recent noteworthy work has furnished new insights—such as a trembling motion (or swinging) for example [6–8]—into the question concerning the effect of shear flow on vesicle shape dynamics in experiments [9–11] as well as in theoretical and numerical investigations [12–15], and broadened significantly the well-known result of Keller and Skalak [16].

If understanding the dynamics of a single vesicle in an unbound fluid is a preliminary essential step, only a few studies have dealt with the interactions between either two (or more) vesicles under flow or fluid constraining walls and vesicle. One notable exception is the theoretical [17] and experimental [18] determination of the 3D lift force which corresponds to the critical force necessary for vesicle detachment under shear flow. Other results are still sparse. This previous physical phenomenon is also reminiscent of vesicle unbinding under a pointlike pulling force, an active research field due to consequences for adhesion between cells, a cell-biological substrate, and more largely, for adhesion between soft substrates (shells here) [3,4,19,20]. In this case also, the critical pulling force (minus its weight) has been determined to be proportional to the equatorial radius \( R_v \) (Fig. 1) and to the adhesion energy per unit area \( W \) [3] as expected [21]. A power law for the decreasing contact radius \( R_c \) (Fig. 1) during unbinding is also predicted with an exponent 1/4. However, the dynamics of unbinding has not yet been addressed experimentally.

In this Letter, we report the first experimental study of unbinding dynamics of a vesicle under an external flow, subject to a wall normal pulling force. To our knowledge, flow has only been used to move a bead stuck to a vesicle [22] and lift-off [18]. Our study is motivated on the one hand by the interaction between wall effects and vesicle dynamics and on the other hand by vesicle unbinding under a pulling force. The necessary critical force is not investigated as this problem has already been studied. In the bulk, a vesicle is characterized by its size \( R = (3V/4\pi)^{1/3} \) and its excess area \( \Delta = S/R^2 - 4\pi, S \) and \( V \) are its surface and volume. Various shapes have been identified during unbinding from truncated spheres (\( \Delta < 0.1 \)), egg shape (\( \Delta \sim 0.21 \)) to lipidic tube emergence (deflated vesicles and pointlike force, \( \Delta \sim 0.75 \)). Some shapes are peculiarly reminiscent of recent simulations of vesicle detachment under a pointlike pulling force [19]. Here, we study the unbinding dynamics of an inflated vesicle (\( R_c \ll R_v \)) and show that it occurs in a two-stage process.

An original experimental setup has been developed to apply hydrodynamic forces, preserving axisymmetry in the

![FIG. 1. Schematic setup and example. A settled vesicle is characterized by its radius \( R_v \), its height \( h \) and the contact radius \( R_c \). A fluid film of thickness \( e \ll R_c \) between vesicle and substrate results from repulsive disjoining pressure. A large capillary of radius \( R_p \) is located above the vesicle to preserve axisymmetry. A suction flow pulls up the vesicle. Visualization is achieved by either the side view or the bottom view (RICM). (a), (b), (c): an inflated vesicle (\( R_c \ll R_v \)) unbinds.](image-url)
The lipid solution consisted of 240 mM. Temperature is maintained at 200 mM concentration of sucrose whereas the exter-
methanol (PhosphatidylCholine, Sigma) dissolved in chloroform-
capillary isolated the microscope is upright. Thanks to the well design of the
to the substrate down to 10 nm accuracy. For the side view,
vesicle at height
change if observed with phase contrast. With slightly
deflated vesicles, the vesicle height
change if observed with phase contrast. With slightly
deflated, and deflated with more or less visible
thermal fluctuations. The largest ones are chosen to have
the best spatial accuracy: 40 ≤ h ≤ 60 μm for phase con-
trast and 40 ≤ h ≤ 95 μm for RICM visualizations.

Inflated vesicles.—An inflated vesicle characterized by a
small contact radius—R_c ≪ R_v—looks like a truncated
sphere. Beyond a critical flow rate U_c, the shape does not
change if observed with phase contrast. With slightly
deflated vesicles, the vesicle height h increases (pearlike
shape) but, it still binds as already observed with a point-
like force [20]. Above U_c, vesicles unbind. It corresponds
to a critical pulling force F_{pull,c} which balances buoyancy
and adhesion. U_c is unambiguously determined for each
vesicle by repeating acquisitions at different flow rates: close
to U_c, the total unbinding time diverges (Fig. 2).

A second report is that during the entire process, before
the final detachment, the vesicle height (size) changes less
than 1 μm (in the experimental error range), even when R_c
decreases. In addition, the contribution of the flow near the
wall to the force is small and the excess area conserved, the
pulling force remains constant as in the experiments with a
pointlike force.

The third report is that the contact radius R_c has the same
general variation with time whatever the pulling force (or
flow rate U): a plateau (no variation of R_c with time)
followed by a finite-time decrease of R_c to zero. During
the plateau, the maximum deviation from the resting value
is 1 μm: R_c = R_{c,0} ± 1 μm with no continuous decrease
at this experimental accuracy. After a time τ_1, the contact
radius decreases sharply to zero during a finite time τ_2: see
Fig. 2. τ_1 and τ_2 vary with pulling force, vesicle size and
contact radius. The curves of Fig. 2 determined by phase
contrast do not collapse if time is scaled by τ_1 + τ_2, the
total time of unbinding. As τ_1 + τ_2 is not the relevant time,
a more subtle analysis is necessary, involving two different
physical mechanisms during the two stages τ_1 and τ_2.

During τ_1, only RICM provides a new insight as the
thickness ε of the water film is less than 200 nm ≪ R_{c,v}
due to the balance between attractive forces (Van der Waals
(VdW), buoyancy) and repulsive ones (electrostatic, Helfrich).
The water film thickens at the constant contact area (Fig. 3).
Quantitatively, RICM measurements show a remarkable exponential growth of the relative film thick-
ness (ε − ε_0) whatever the pulling force and the initial size
of inflated vesicles. The same dynamics appears with
slightly deflated vesicles at moderate pulling forces (data
not shown) but after a delay. Such a variation can be
understood by establishing the balance between viscous
dissipation inside the fluid film and the applied pulling force:

\[ \eta \pi R_c^2 \varepsilon (\varepsilon/\varepsilon_0)^2 \approx (F_{\text{pull}} - F_{\text{pull,c}}) \dot{\varepsilon}; \]
\[ e(t) = e_0 e^{(F_{\text{pull}} - F_{\text{pull,c}})/\eta \pi R_c^2 t}. \]

FIG. 2 (color online). Contact diameter 2R_c and height h
dynamics of one inflated vesicle for decreasing flow rates: U =
37 (○), 38 (●), 39 (□), 43 (*) μm s^{-1}. Above a critical value U_c
(here, U_c ≈ 37 μm s^{-1}), the vesicle unbinds and its dynamics
slows down close to U_c. Two different stages are identified.
During a time τ_1, there is no microscopic shape change. During
a finite time τ_2, the contact radius decreases to zero while h does
not change.
After integration, the exponential growth of the thickness (Fig. 4 Left) is effectively recovered. This result can also be found by the Reynolds equation in the relaxation regime: $F_{\text{pull}} < F_{\text{pull,c}}$.

Finally, the criteria for defining the two stages is deduced from the following fit: $R_c/R_{c,0} = \Theta(t - t_1) + \Theta(t - t_2)\left[1 - (t - t_1)/(t_2 - t_1)\right]^n$ where $\Theta$ is the Heaviside function and $n$ the characteristic exponent of the finite-time second step of unbinding. Phase contrast measurements (see Fig. 4 Right) show that $1/\tau_1$ is a linear function of the excess of flow rate $U - U_c$, a variation predicted by Eq. (1): $1/\tau_1 = (F_{\text{pull}} - F_{\text{pull,c}})/(\pi R_c^2 \eta)$.

Using force deduced from numerical simulations, $\tau_1 = \pi R_c^2 U/\Delta U R_c^2$ where $\Delta U = U - U_c$. Indeed, no measurable effect of viscosity on $\tau_1$ was detected using 20% of glycerol in water inside and outside, in the limit of a small excess area. For larger $\Delta$, tip instability and tube emergence are promoted over egg shape. For the cases $U = 38-43$ $\mu$m/s (Fig. 2) for example, $\tau_1$ is approximately a few seconds. For $(R_c, R_v, H) = (8, 20, 100)$ $\mu$m, $\Delta U = U - U_c = 1$ $\mu$m/s, $\tau_1 = 5$ s in agreement with experiments.

During $\tau_2$, the physical mechanism is different. Adhesion is overcome. Membrane tension pulls on the contour line of the binding zone to reduce the contact area and lifts off the vesicle. Dynamics results from a balance between viscous dissipation in the region of the corner $\eta \pi R_c^2 e (R_c/e)^2$ and the power supplied to the system $-2\pi (\gamma - \gamma_c) R_c \dot{R}_c$ where $\gamma$ and $\gamma_c$ are the mechanical tension and its critical value, proportional to the pulling force. Then, the contact radius variation is obtained:

$$R_c(t)/R_{c,0} = (1 - (t - \tau_1)/\tau_2)^{1/2},$$

where $1/\tau_2 \approx \gamma - \gamma_c$. Here, for the sake of simplicity, the thickness has been assumed constant as for the deflated vesicles (see further). Consequently, $1/\tau_2$ is a linear function of the excess flow rate, a variation experimentally checked Fig. 5 Right) whatever the inflated vesicle. The finite-time second stage is a power law of exponent $n = 0.47 \pm 0.09$, close to the theoretical value $1/2$. This average has been performed on 28 inflated vesicles and for each one on at least 3 flow rates. The exponent value is statistically dominated by the short times.

These results differ from models proposed in the literature [3,25]. In our experimental case, the first stage of the unbinding involves viscous dissipation in the lubrication layer, with no equivalent stage in the models. The adhesion energy is assumed to be constant in the models, whereas the experimental interaction with the substrate varies during the film thickening. During the second stage, the proposed finite-time process involves an exponent $1/4$ [3] differing from our $1/2$ value. The usual assumption of an evanescent contact angle does not correspond to the experimental situation; however, Fig. 5 shows no marked evolution of the exponent when vesicles with different $R_c/R_v$, and thus different contact angle, are used. The thickness $e$ of the fluid layer between vesicle and substrate lies in the micrometer range, interestingly close to a value determined by lift-off experiments [18]. As a consequence, this probably weakens the using of the dissipative law of triple line motion. Lastly, the fluid-structure interaction on the large scale of the vesicle does not correspond to the pointlike force of the models. As well, the linear variations of $1/\tau_1$ and $1/\tau_2$ are not explainable by considering two solids submitted to a VdW potential, a pulling force $F_{\text{pull}}$.

![FIG. 3](image1.png) Contact area of an inflated vesicle during the first stage of duration $\tau_1 = 14.5$ s. The disc at the center corresponds to the contact area observed by RICM: (a) $t = 0$ s, (b) $t = 2$ s, (c) $t = 6$ s, (d) $t = 10$ s, (e) $t = 12$ s and (f) $t = 14$ s. Each jump corresponds to 100 nm [23]. Here, $2R_v = 110 \mu$m, $H = 150 \mu$m and $U = 105 \mu$m s$^{-1}$.

![FIG. 4](image2.png) (color online). Stage 1. Left: Dimensionless thickness dynamics of the film $e - e_0$ between the membrane and the substrate. The time scale is nondimensionalized by $\tau_1 = 14$ s (●, green [light gray]), 11 s (●, red [medium gray]), 9 s (■, blue) with $2R_v/h = 9.95$ $\mu$m respectively ($H = 150 \mu$m). Right: Linear variation of $1/\tau_1$ with the flow rate determined on three vesicles ($H = 100 \mu$m): $2R_v/h = 12.56$ $\mu$m, $U = 72$ $\mu$m s$^{-1}$ (●), $2R_v/h = 15/51$, $U = 38$ (○), $2R_v/h = 11/83$, $U = 170$ ( ) and the blue (dark gray) vesicle ($2R_v/h = 14/40$; $U_c \approx 37$) at different flow rates $U = 37$ (○), $45.6$ (●), $48.6$ (•) $\mu$m s$^{-1}$. The mean value of the exponent is 0.47 ± 0.09 (black line). Right: Linear variation of $1/\tau_2$ with the flow rate, $\tau$ and $U_c$ depend on the vesicle characteristics. See Fig. 4 Right for symbols.

![FIG. 5](image3.png) (color online). Stage 2. Left: Power law of the finite-time process of unbinding. After the time $\tau_1$, contact radius falls to zero in a finite time $\tau_2$: the red (light gray) vesicle (●, $2R_v/h = 12/63$ $\mu$m, $U = 72$ $\mu$m s$^{-1}$) (●), $2R_v/h = 15/51$, $U = 38$ (○), $2R_v/h = 11/83$, $U = 170$ ( ) and the blue (dark gray) vesicle ($2R_v/h = 14/40$; $U_c \approx 37$) at different flow rates $U = 37$ (○), $45.6$ (●), $48.6$ (•) $\mu$m s$^{-1}$. The mean value of the exponent is 0.47 ± 0.09 (black line). Right: Linear variation of $1/\tau_2$ with the flow rate, $\tau$ and $U_c$ depend on the vesicle characteristics.
and a constant viscous friction between the solids (1/τ₁,₂ ∝ (U − U₀))₁/₂ is expected in this case). Finally, as in the case of lift-off [17,18], the film lubrication plays a central role.

**Deflated vesicle at moderate flow rate.**—A wide range of dynamics results from the increase of excess area: vesicles elongate, so as to look like truncated eggs. R_e decreases linearly with time. Beyond, a shape singularity appears and a lipid tube results as with pointlike forces [4,5]. By decreasing H to 25–45 μm and the flow rate, hydrodynamic stress is smoothed over a large part of the vesicle. Thus, tip instability is inhibited. During the first stage, as the vesicle elongates strongly along the symmetry axis, the contact radius decreases to zero. The relative fluid film thickness ε − ε₀ remains constant during almost all the detachment (Fig. 6) contrary to inflated vesicles. During the second stage, ε − ε₀ increases quickly compared to the first stage. As 2R_e/h has increased (in Fig. 2, 2R_e/h = 0.37 and in Fig. 7, 2R_e/h' = 1.13), the characteristic time τ₁ from Eq. (2) rises: τ₁/τ₁ ≤ 0.1 for the same excess force F − F_c. Moreover, membrane fluctuations reduce the adhesion energy (ε₀ increases): this promotes the beginning of stage 2 compared to the slowing of stage 1. However, with our experimental setup, the pulling force is time dependent making it difficult to go beyond this qualitative picture here ([25] for a track).

To conclude, we have developed an hydrodynamical tool to apply an axisymmetric force (a few pN) to study unbinding dynamics of soft matter. As the thickness is under the optical resolution, RICM was used to complete phase contrast visualization. For inflated vesicles, film thickening at constant contact radius precedes the second stage of decreasing contact radius. In the limit of a small excess area, the approach based on the balance of viscous dissipation corresponds quite satisfactorily to experiments. On the contrary, for deflated vesicles, the contact radius falls to zero at constant thickness before the final rise.

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**References**