SETTLING INDUCED FORMATION OF MEMBRANE TUBE ON A VESICLE

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Summary Biological membranes often exhibit tubular structures, whose apparition is closely related to the mechanical properties of the membrane. Considering the model situation of a settling vesicle, we study numerically and theoretically the apparition of membrane tethers induced by hydrodynamic forcing. The existence of a stationary tether is reported and it is shown that both bending and tension forces are important in the understanding of tether formation.

INTRODUCTION

Living cells, whose typical size ranges between a few microns to a tens of microns, often present a variety of structures at the nanometer scale. Among them, membrane nanotubes (or tethers) are found in many situations, be it by the action of motor proteins such as kinesins [11], or by the growth of microtubules inside the cell [6]. These tethers may be involved in biological processes like neutrophils rolling on the endothelium [14], or intercellular communication [13]. Their study has also been proven to be a valuable tool to probe mechanical properties of cells, like attachment of the membrane to the cytoskeleton [7] or measurements of membrane viscosities [15]. The possibility to pull a thin tether out of a biological membrane, which is composed of a phospholipid bilayer, is closely related to the mechanical properties of this bilayer. Along with in vitro studies on living cells [3], some effort has also been devoted to the study of tether formation on vesicles, which are small drops (typical radius $\sim 10\ \mu\mathrm{m}$) enclosed by a phospholipidic bilayer membrane. These systems are thus ideal candidates to study specifically the mechanical properties of the lipid bilayer, in particular in tether formation. The formation of a tether onto a vesicle submitted to a point-like force has received a lot of attention in various setups, like micropipette extrusion [5], or micro-electrodes [9]. Theoretical studies [12, 4] predict a first order transition for the formation of a tube, that is, the existence of a critical force necessary to pull a tube out of the membrane. Yet, these models assume that the membrane tension is fixed and constant, and hydrodynamical effects are limited to the dynamics of formation or retractation [3]. In this perspective, the setup formed by a deflated vesicle settling into an infinite viscous fluid constitutes an original configuration to study both the importance of membrane tension as well as the influence of the hydrodynamics on the formation of a tether. Recent experiments [8] have shown the formation of tubes onto settling vesicles. In this paper, we would like to report on the first numerical simulations of tether formation taking into account both the membrane and the flow fields in the fluids surrounding it, and show that the membrane mechanical properties lead to the formation of stationary tethered shapes.

METHOD

The membrane forms a closed surface which separates two viscous fluids. This is a fluid-structure interaction problem, with the inner and outer fluids being well described by the Stokes regime. The common mechanical modelling of a lipid bilayer is to consider it as a two dimensional incompressible surface fluid, with a resistance to bending described by Helfrich energy : $F = \kappa/2 \int_S (2H)^2 \mathrm{d}S$ with H being the mean curvature of the surface S and κ being the bending modulus. A specifity of this system is that it is both highly deformable (the intensity of bending modulus is a few times the thermal agitation energy $\kappa \sim 15 k_B T$) and highly constrained (both the enclosed volume as well as the surface are conserved, as a consequence of the volume and surface incompressibility constraints). In the settling case, the behavior of the system is controlled by two dimensionless parameters. First, Δ, which is called the excess area, is defined by $A = (4\pi + \Delta)R_0^2$, where A is the surface of the vesicle and $R_0 = (3V/4\pi)^{1/3}$ is the radius of the sphere having the same volume V. This parameter is a geometrical parameter which characterize the fact that a perfectly spherical vesicle is not deformable whatever the external forcing is, due to the simultaneous conservation of volume and surface. Second, the Bond number $\mathrm{Bo} = (\Delta\rho g R_0^4)/\kappa$ measures the importance of the external forcing induced by the density contrast ($\Delta\rho = \rho^i - \rho^o$) between the inner (density ρ^i) and the outer (density ρ^o) fluids compared to the intensity of bending.
A systematic exploration of the behavior of the system in the (Δ, Bo) phase space has been performed numerically by a direct simulation of the coupled system (inner and outer fluid flows as well as membrane mechanics). A modified boundary integral method to solve the inner and outer fluid flows taking into account surface incompressibility constraint as well as a method of computation of membrane forces based on discrete differential geometry have been developed[2] and are used here to study the case of a settling vesicle.

RESULTS

In the small deformation regime, a analytical study of the system is possible [1], permitting also a validation of the numerical method. We focus here on the case of large deformations, when tether formation is expected. A typical

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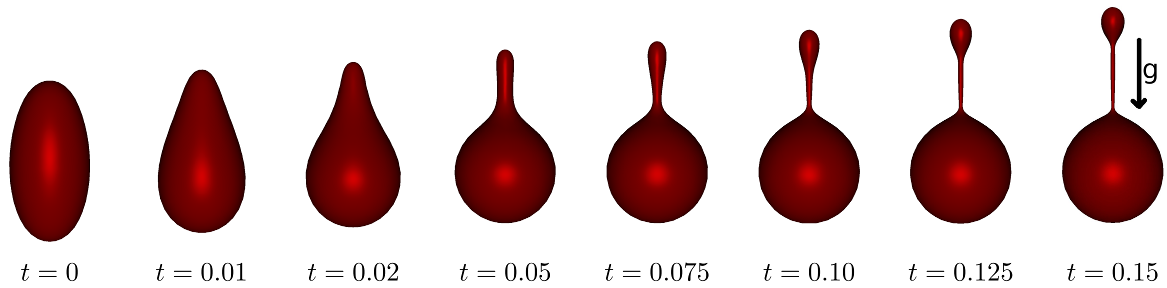

Figure 1. Evolution of a settling vesicle ($\Delta = 0.97, \mathrm{Bo} = 490$) starting from an ellipsoidal shape.

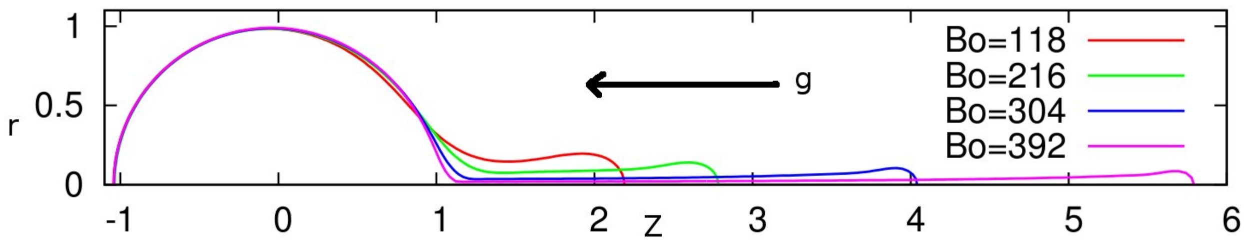

Figure 2. Stationary shapes at $\Delta = 0.93$. Gravity is oriented horizontally, and only the profile $r(z)$ is represented.

evolution of a settling vesicle starting with an ellipsoidal shape in presented in figure 1. The shape evolves rapidly, with the formation of a protusion at the rear of the vesicle. There is thus a pinch of this protusion, which leads to the formation of an almost cylindrical tether connecting two quasi-spheres : a "mother" vesicle at the front, where almost all the volume is stored, and a "daughter" vesicle at the rear, which contains most of the excess area. The tether then grows while the daughter vesicle radius decreases, until a stationary state is reached. In this stationary state, the ratio between the radius of the tether to the radius of the mother vesicle can reach 2%, which would correspond to a 200 nm tether out of a $10\ \mu\mathrm{m}$ vesicle. The stationary shape attained depends on both control parameters. An example of the evolution of stationary shapes as a function of the Bond number for a fixed excess area is shown in figure 2. Tether properties (lentgh, radius) depend continuously on the forcing strength.

CONCLUSION

We have studied numerically and theoretically tether formation on a settling vesicle. Contrary to drops [10], vesicle membrane properties permits the stationarity of the shape, while the two control parameters of the system allow a continuous evolution of the tether length and radius.

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