Mechanics of cell constriction during division

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The cell division cycle is a central process in biology, the essential mechanism whereby cells grow and duplicate. A decisive step of cell division is the symmetric constriction necessary to cleave the mother cell into two identical daughter cells (see Fig. 1). Independently of the details of the constriction engine, the membrane component responds against deformation by minimizing the elastic energy at every constriction state following a pathway still unknown.

In this work, we address a theoretical study of the mechanics of membrane constriction in a simplified model that describes the cell as a homogeneous membrane vesicle in which a given constriction force is applied to create a circumferential furrow positioned at the cell equator.

The shape of the cell is determined by the minimum of its total energy $E_T = E_b + W$, which is leaded by the bending energy of the membrane E_b, and subjected to the geometric constraints of area A and volume V that require a work $W = \Sigma A + \Delta p V$, where Σ is the membrane tension and Δp is the pressure difference between the outer medium and the cell interior ($\Delta p = p_{out} - p_{in}$). The bending energy of the shell is given in terms of its mean curvature H by the Helfrich form

$$E_b = \frac{\kappa}{2}\int (2H - C_0)^2 \mathrm{d}A, \qquad (1)$$

where κ is the bending rigidity of the membrane and C_0 is the spontaneous curvature that represents the tendency of the membrane to bend in the equilibrium state, usually due to the compositional asymmetry between the inner and the outer sides.

By minimizing the total energy along the constriction pathway, we derive analytical approximate formulas for the main properties of the constricted vesicle (or simplified cell). These results are compared with the exact solution obtained from numerical computations, getting a good agreement for all the computed quantities (energy, area, volume, and forces). The initial cell shape (before constriction) is shown to be determined through the quantity [1]

$$\Lambda = (1 - C_0 R_m)^2 + 2\Sigma R_m^2/\kappa + \Delta p R_m^3/\kappa, \qquad (2)$$

where R_m is the polar radius of the spheroid. $\Lambda = 1$ stands for the sphere, while $0 < \Lambda < 1$ gives prolate (rod-like) and $\Lambda > 1$ oblate (disk-like) spheroids; for $\Lambda < 0$ constriction is not possible (see Fig. 2).

The more favorable conditions for division are determined, obtaining that smaller constriction forces are required for low or negative membrane tension and hypotonic media. Our results evidence that stable symmetric constriction requires positive effective spontaneous curvature, while spontaneous constriction requires a spontaneous curvature higher than the characteristic inverse cell size. We also show that the stability and spontaneity of symmetric constriction increases as constriction progresses.

This work contributes to a better quantitative understanding of the mechanical pathway of cellular division and can serve to get insight on other biological processes involving membrane bending, such as exocytosis and endocytosis. In the emergent area of artificial life our predictions could also assist the design of artificial divisomes in self-actuated microsystems. The method is sufficient general and powerful to accommodate easily further complexities present that participate actively to drive cytokinesis in real cells.

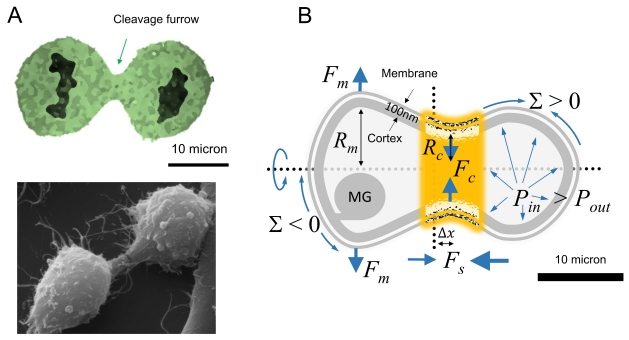

Fig. 1. (a) Real cells undergoing constriction. Upper panel: Formation of the cleavage furrow (from A. Siegel and H. C. Smith, SUNY at Buffalo). Lower panel: Scanning electron micrograph during final stage of constriction (from A. Wilde University of Toronto). (b) Our minimal model cell and its characteristic parameters.

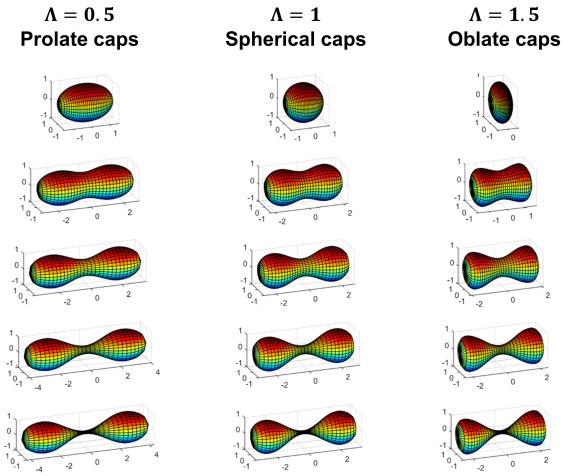

Fig. 2. Minimum energy shapes during division.

[1] E. Beltrán-Heredia, V. G. Almendro-Vedia F. Monroy, and F. J. Cao, Modeling the mechanics of cell division: Influence of spontaneous membrane curvature, surface tension, and osmotic pressure, Front. Physiol. **8**, 312 (2017).

[2] E. Beltrán-Heredia, F. Monroy, and F. J. Cao, Mechanical conditions for stable symmetric cell constriction, (submitted for publication).