Theory of cell membrane-cortex adhesion dynamics

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Adhesion between cell membrane and cytoskeletal cortex is involved in several cellular functions, including apoptosis, cell spreading, cytokinesis, virus uptake or even cell motility. Membrane-cortex adhesion is carried out by molecular linkers attached both to membrane lipids or proteins and cytoskeletal proteins[1,2]. These molecular linkers are stretched or compressed by membrane and cytoskeleton movements and continuously attach and detach, so that the network they form is highly dynamic. When a large membrane patch detaches from the cortex, a bleb can form. Blebs are cell membrane protrusions arising from membrane-cortex detachment, so that they constitute one of the most prominent consequences of complex membrane-cortex interactions (FIG. 1). The formation of blebs constitues a mechanism of cell crawling on substrates with reduced adhesion, and it could be relevant for tissue invasion by cancerous cells[3,4]. The so-called bleb-based motility, then, crucially depends on how membrane-cortex detachment is controlled by the cell.

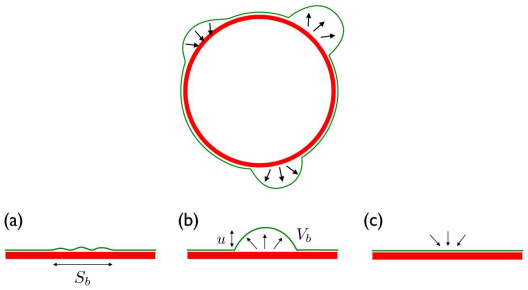

FIG. 1. (Top) Schematic illustration of a blebbing cell, with two expanding and one retracting bleb (black arrows). The cortex is shown in red and the membrane in green. (Bottom) Bleb nucleation. The detachment of a membrane patch (a) can lead to the formation of a bleb (b) or to a resealing of membrane-cortex adhesion (c). Adapted from Brugués[5].

We have extended a kinetic model for membrane-cortex adhesion (FIG. 2) to include both thermal and chemical fluctuations and spatial modulations along the membrane, which allows us to study the kinetics bleb nucleation. Numerical simulations provide information about the typical lengths and times involved in spontaneous membrane-cortex detachment and their dependence on external conditions and the internal state of the cell. We also study analytically how membrane fluctuations and spatial correlations mediated by hydrodynamics do influence membrane-cortex adhesion and, thus, how the cell can act on it. Moreover, the spatially extended model sets the range of validity of the simpler zero-dimensional model via the identification of a correlation length λ^* of membrane fluctuations (FIG. 3).

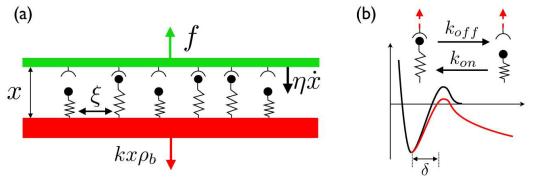

FIG. 2. Schematic illustration of the kinetic model for membrane-cortex adhesion. From Brugués[5]. (a) Rigid and flat cortex (red) and membrane (green) are dynamically linked through model springs (black). (b) Energy landscape of a linker, both in the absence (black) and in the presence of force (red).

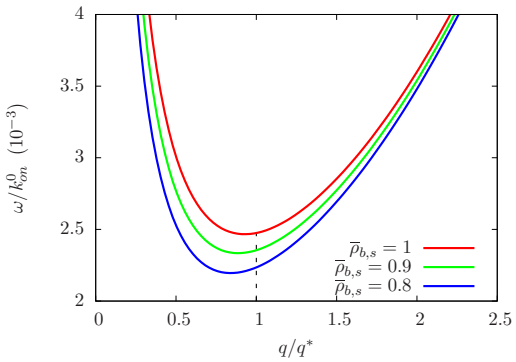

FIG. 3. Relaxation rate of a membrane fluctuation of wave-vector q for some values of the density of bound connectors. $\lambda^* = 2\pi/q^*$ is identified as a correlation length of membrane fluctuations.

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