Engulfment of Nanoparticles by Membranes: A Comprehensive Theory

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Abstract

Nanoparticles are used to deliver drugs, imaging agents, and toxins to biological cells. The delivery requires the engulfment of the nanoparticles by cell membranes, a process that is governed by the interplay of particle adhesion and membrane bending and can be mimicked in model systems consisting of lipid or polymer vesicles. Previous theoretical studies of these systems have focussed on the engulfment of nanoparticles by planar membranes and symmetric bilayers. Here, we consider the general case of nanoparticles interacting with asymmetric bilayer membranes that form complex shapes with non-uniform curvature. Even small bilayer asymmetries lead to two critical particle sizes that determine four distinct engulfment regimes: particles are either (i) free, (ii) partially engulfed, (iii) completely engulfed, or (iv) display bistability between free and completely engulfed states.[1] These regimes depend on two material parameters, the contact mean curvature and the spontaneous curvature, as well as on the local curvature of the membrane segments in contact with the nanoparticles. As a consequence, different segments of the same membrane can belong to different engulfment regimes and a single vesicle in contact with many nanoparticles can display ten distinct engulfment patterns as well as morphological transitions between these patterns,[2] see Figure. In order to address the more complex process of receptor-mediated endocytosis, we extend our results to account for adhesion-induced segregation of the membrane components and increased spontaneous curvatures arising from protein coats.[1] We derive explicit expressions for the engulfment rate and total uptake of nanoparticles by cells, which are both predicted to depend nonmonotonically on the particle size. These expressions provide a quantitative fit to experimental data[3] for the size-dependence of clathrin-dependent endocytosis of gold nanoparticles by HeLa cells.

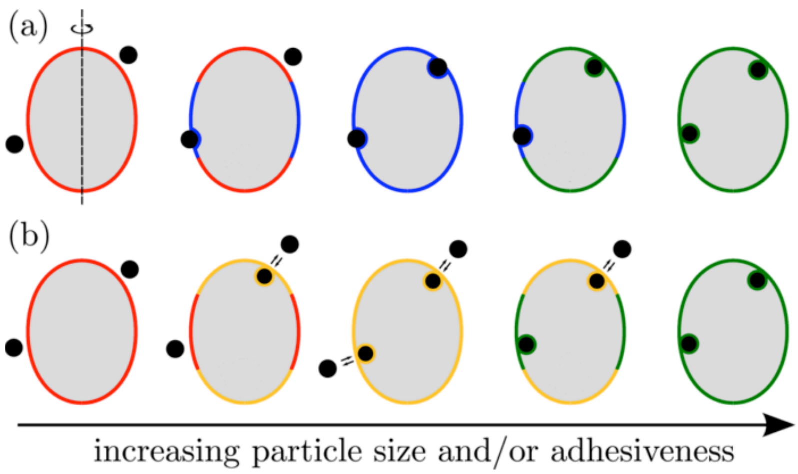

Figure: Different engulfment patterns of nanoparticles (black) on a prolate vesicle. The spontaneous curvature of the vesicle membrane is positive in (a) and negative in (b). The patterns involve four types of membrane segments: free segments with no engulfment (red) and bistable segments with activated engulfment and release (yellowish orange) as well as segments decorated by partially engulfed (blue) and completely engulfed (green) particles. A change in particle size or adhesiveness leads to continuous morphological transitions between these patterns.

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[1] J. Agudo-Canalejo and R. Lipowsky. ACS Nano 9, 3704 (2015)
[2] J. Agudo-Canalejo and R. Lipowsky. Nano Letters 15, 7168 (2015)
[3] B. D. Chithrani and W. C. W. Chan. Nano Letters 7, 1542 (2007)