Long-range attraction of particles adhered to lipid vesicles

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Many biological systems fold thin sheets of lipid membrane into complex three-dimensional structures. This microscopic origami is often mediated by the adsorption and self-assembly of proteins on a membrane. As a model system to study adsorption-mediated interactions, we study the collective behavior of micrometric particles adhered to a lipid vesicle. We estimate the colloidal interactions using a maximum likelihood analysis of particle trajectories. When the particles are highly wrapped by a tense membrane, we observe strong long-range attractions with a typical binding energy of $150k_BT$ and significant forces extending a few microns.

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I. INTRODUCTION

The geometry of lipid membranes is essential to living cells. Their topology defines the boundaries of the cell, nucleus, and organelles [1]. Their shape and size also play an essential role in cellular physiology, from the contraction of muscle [2] to the creation of vivid structural color [3]. Therefore, regulation of membrane geometry is of fundamental importance to cell biology.

In many cases, the folding of lipid membranes into complex three-dimensional structures is achieved by the adsorption and self-assembly of proteins on the surface of a lipid membrane [4]. While many of the essential molecules have been identified, relatively little is known about the basic physics of protein-assisted membrane folding. Experiments have demonstrated a coupling between membrane curvature, tension, and binding affinity [5,6]. Furthermore, membrane folding is intricately related to the organization of adsorbed proteins into supermolecular structures [4]. These observations have inspired a number of theoretical studies considering the adsorption and interaction of proteins on membranes [7,8]. However, experimental measurements of the interactions of membrane-bound proteins are unavailable.

The mechanics of bare lipid membranes is a compromise of tension and bending energy [9,10]. When particles adsorb, the physics is enriched by the particles' adhesion energy and geometry. More precisely, for a piece of membrane of shape $\mathcal{S}$ bound to a particle, the energy of the system is described by the Helfrich Hamiltonian

$$\mathcal{H}(\mathcal{S}) = -wa_c + \int \left(\tau + \frac{1}{2}\kappa C^2\right) dA, \qquad (1)$$

where τ is the membrane tension, κ the bending rigidity, C the local total curvature, and w and a_c the adhesive surface energy and area of contact between the membrane and the particle. An important material length scale emerges, $\lambda = \sqrt{\kappa/\tau}$. Bending dominates on shorter scales, and tension dominates on longer ones. Bending rigidities of lipid bilayers are typically around $20k_BT$, so for moderately tensed vesicles ($\tau \sim 10^{-5}$–10^{-4} N/m), $\lambda \sim$ 50–100 nm [11].

While membrane-mediated interactions of bound proteins are challenging to access experimentally, a few studies have made observations of membrane-induced attractions between micrometric colloidal particles [12–15]. These observations are not consistent with analytical theories of interactions of spherical particles which assume small deformations and predict repulsive interactions [16]. On the other hand, numerical studies in the large deformation regime have found attractions between spheres [7,17–19].

Here, we investigate the interactions of membrane-bound particles using micron-sized colloidal particles attached to a giant unilamellar vesicle (GUV). When particles are highly wrapped by a tense membrane, they spontaneously aggregate. We describe a maximum likelihood analysis to estimate the pair potential from the approach to binding of individual particle pairs. The potential is strongly attractive ($> 100k_BT$ deep), and long ranged ($> 4\ \mu$m).

II. EXPERIMENTAL RESULTS

Giant unilamellar vesicles of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) (98%), enhanced with lipids functionalized by rhodamine (1%) and PEG-biotin (1%), are fabricated by electroformation [20]. They are resuspended in a hypotonic buffer, and settle onto a nonadherent coverslip. The vesicles have a wide range of tensions: some exhibit large shape fluctuations, while others are smooth and nearly spherical [Fig. 1(a)]. Using optical tweezers (1064 nm), we bring streptavidin-functionalized polystyrene spheres (radius $R = 1\ \mu$m) in contact with GUVs of diameters from 15 to 20 μm. There is strong adhesion of the particles to the bilayer due to the interaction of biotin with streptavidin. The extent of adhesion varies somewhat from bead to bead, but the membrane typically wraps the bead past its equator, as shown in Fig. 1(a).

Even though individual particles are stable in the bulk, beads bound to tense GUVs formed clusters, as shown by the micrograph in Fig. 1(c). Thermal fluctuations were not able to dismantle these clusters, but they did cause significant

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