Supplementary Information for "Emergent membrane morphologies in relaxed and tense membranes in presence of reversible adhesive pinning interactions"

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S1. Dynamical Triangulated Monte Carlo (DTMC)

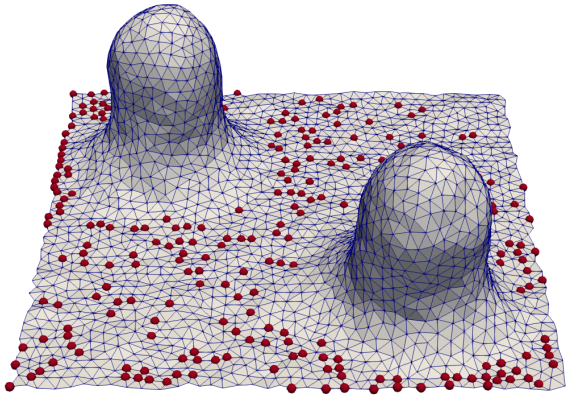

Figure S1. A patch of a membrane represented by a randomly triangulated surface in presence of pinning sites when $A_{ex} = 44\%$ and $N_p = 10\%$.

We model a patch of an undulating membrane using a mesoscale membrane model that treats the membrane as a continuum elastic surface and accounts for the morphological changes in cell membranes [1]. The continuum surface of the membrane is discretized into a set of interconnected triangles with each triangle on the surface representing a patch of a bilayer whose size is much smaller than the persistence length of the bilayer. A surface with N_{tri} triangles is constructed with N_v vertices and N_l links that connect the vertices. The elastic energy of the surface is defined by the well known Canham-Helfrich Hamiltonian [2, 3]. The discretized form of this Hamiltonian is given by

$$\mathbf{H}_{\text{elastic}} = \frac{\kappa}{2}\sum_{v=1}^{N_v}(2H_v - C_0)^2 A_v, \tag{S1}$$

where κ is the bending rigidity of membrane, A_v is the area, H_v the mean curvature and C_0 the spontaneous curvature at vertex v. C_0 accounts for the presence of an asymmetry in the membrane which may arise either due to lipid asymmetry between monolayers or the presence of a curvature inducing protein. To compute the mean curvature H_v, we follow the method introduced by Ramakrishnan et al. [4]. In addition to the elastic energy, we account for the self-avoidance of the vertices through a link potential given as

$$U_{SA}(l) = \begin{cases} 0, & \text{if } a_0 \leq l < \sqrt{3}a_0 \\ \infty & \text{otherwise.} \end{cases} . \tag{S2}$$

where l is the length of the link connecting two vertices and a_0 is vertex diameter. This is in general not sufficient to impose strict self-avoidance, hence a constraint on the largest angle between the normals of the two faces sharing a link is imposed. The cutoff angle is set to be $60°$. A patch of the simulated membrane in the randomly triangulated representation in the presence of pinning is shown in Figure S1.

MC procedure: The MC procedure to equilibrate membrane patch involves a set of vertex moves and link flips which are accepted through the Metropolis algorithm [5]. Each MC step contains N_v vertex moves and N_l link flips. In a vertex move, the position of a vertex is updated to a new location within a cubic box through a random displacement. The size of the box is selected such that 50% of moves are accepted. The vertex move allows the membrane shape to relax to an equilibrium conformation. In a link flip move a randomly selected link, between two triangles is disconnected, and new a link is established with the unconnected vertices of the same two triangles. This move makes the triangulation dynamic and preserves the fluid nature of the bilayer membranes by ensuring the in-plane displacement of vertices.

S2. Constant projected area and constant frame tension ensemble

We consider a patch of the plasma membrane of a cell in a quiescent state wherein the membrane surface area and projected area, set by the density of cytoskeletal anchorages, remains nearly constant. Structural reorganization events occur throughout the plasma membrane. We assume the events in a patch of plasma membrane used in our simulations (with length scales ~ 600 nm) are independent of those events occurring elsewhere. This is a good approximation as was previously shown in our earlier in silico study on extracting tethers from a membrane patch of similar dimensions. Finally, it should be noted that the membrane projected area and surface area can be changed independently of each

other. The inflow of lipids holding the cortical contacts intact can lead to an increase in surface area given a constant projected area. Similarly, contractile or extensile motion of the cortical contacts can lead to change in the projected area holding the frame tension constant.

A membrane patch in our simulations is bounded and subjected to periodic boundary conditions by a square frame of size L that defines the projected area of the surface as $A_p = L^2$. An equilibrated membrane patch has a curvilinear area A_{mem} that is greater than A_p. To obtain a membrane patch subject to various tension values in the physiological range, we construct systems with different excess areas (A_{ex}). We initialize the membrane as a planar square grid with grid size l_0 and $50l_0 = L$. Each square is subdivided into two triangles with diagonal length $\sqrt{2}l_0$ to form a triangulated surface. This grid is then equilibrated using the MC procedure described in section S1. To satisfy the self avoidance condition the initial length of the sides and diagonals should be within the limit a_0 and $\sqrt{3}a_0$, which implies the choice of l_0 should satisfy $a_0 < l_0 < \sqrt{3/2}a_0$. In a constant projected area ensemble, the various A_{ex} values are obtained by holding A_p constant. Hence A_{ex} is fixed by the choice of l_0 which gives A_{ex} in the limit $2 - 55\%$.

As an alternative to the above constant projected area method, we can incorporate the membrane tension explicitly through a constant frame tension ensemble. Here, we apply a frame tension τ to the membrane and allow the projected area A_p to fluctuate [6]. In the constant frame tension ensemble, the Hamiltonian for the MC simulations is modified as:

$$\mathbf{H}_{\text{elastic}} = \frac{\kappa}{2}\sum_{v=1}^{N_v}(2H_v - C_0)^2 A_v + \tau A_p + K_A(A_{\text{mem}} - A_0)^2. \tag{S3}$$

The last two terms represent frame and stretch contributions to the membrane energy, which set the area of the membrane. The choice of $K_A = 4.1\ \mu N/m$ sets the membrane area to a preferred area A_0 with the maximum allowed fluctuations of $.01\%$. In the constant frame tension ensemble the MC procedure includes an additional boundary move that allows for a change in projected area A_p by rescaling a_0. The boundary MC move is performed at every 20 MC steps.

S3. Free energy calculations

For the free-energy analysis on the membrane patch with adhesive interactions, we adopt a standard free energy estimation technique for MC simulations called the thermodynamic integration method [7]. In this method, we define a new potential energy function for the

system H_{TI} that depends on a coupling parameter λ. When $\lambda = 0$, H_{TI} corresponds to the potential energy of the system without pins, denoted as state I, and when $\lambda = 1$, H_{TI} correspond to the potential energy of the system with N_p pins, denoted by state II. The system is evolved with a Hamiltonian $H_{TI} = (1 - \lambda)H_I + \lambda H_{II}$ where $H_I = H_{\text{elastic}}$ and $H_{II} = H_{\text{elastic}} + H_{\text{bell}}$ using the same set of MC moves defined earlier. The path between state I and II is obtained by varying $\lambda = 0$ to $\lambda = 1$ for a membrane with N_p pins. The free energy difference between these two states is given by $\Delta F = F_{II} - F_I = \int_0^1 \langle \frac{\partial H(\lambda)}{\partial \lambda} \rangle d\lambda$, where $\langle\rangle$ represents the ensemble average obtained from the simulations. The values of thermodynamic integration parameter λ are chosen, such that $0 \leq \lambda \leq 1$ with an interval of 0.1. The integration over λ is computed using Simpson's rule.

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