# Role of interplay between surface and bending energy in membrane protrusion formation

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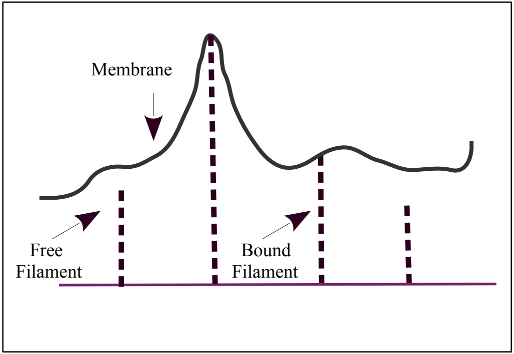
# Introduction

- Inside a cell, actin filaments grow and push against the plasma membrane to create membrane protrusions
- An important role in cell motility
- Rate of protrusion formation goes down as membrane tension is increased [Gauthier et al. PNAS 2011]
- Membrane tension can also enhance protrusions by streamlining actin polymerization in one specific direction [Batchelder et al. PNAS 2011]
- How the elastic interactions in a flexible membrane influence the mechanism of protrusion formation?
- Implications for a wider class of systems where elastic deformation of a membrane is involved

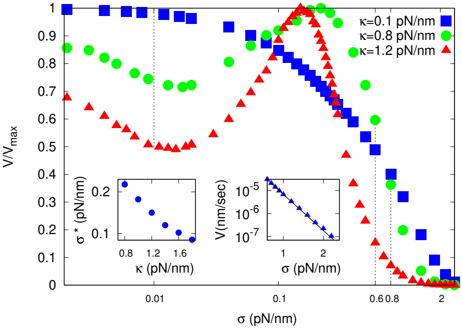
# Model description

- $1d$ membrane modelled by Helfrich Hamiltonian
- $\mathcal{H} = \sigma \sum_i (h_i')^2 + \kappa \sum_i (h_i'')^2$
- Rigid rod-like filaments pushing the membrane from below
- Filaments grow by creating local protrusions which have energy cost



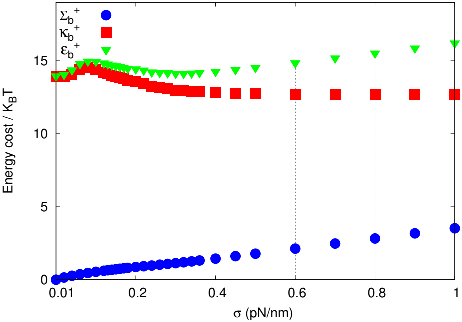
# Peak and dip in $V - \sigma$ curve

- Pushed by the growing filaments, the membrane develops an average velocity
- With increasing $\sigma$ it should become more difficult for the filaments to push the membrane
- But for intermediate or large $\kappa$ velocity shows growth with $\sigma$

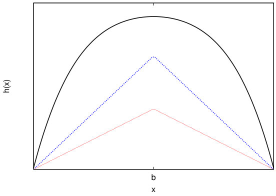


# Bending energy cost shows a peak with $\sigma$

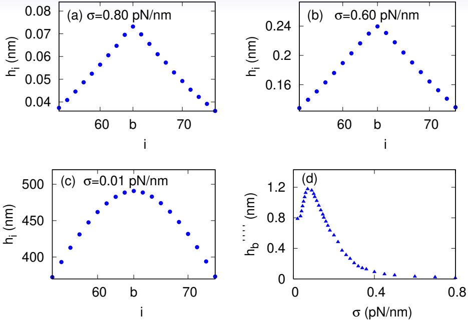
- Energy cost for creating a protrusion at the binding site $\mathcal{E}_b^+$
- Surface energy cost and bending energy cost: $\mathcal{E}_b^+ = \Sigma_b^+ + \mathcal{K}_b^+$
- For large $\kappa$, variation of $\mathcal{E}_b^+$, $\Sigma_b^+$ and $\mathcal{K}_b^+$ with $\sigma$
- $\Sigma_b^+$ increases with $\sigma$ but $\mathcal{K}_b^+$ shows a peak
- Decrease in $\mathcal{E}_b^+$ with $\sigma$ shows that it is indeed easier to push the membrane as $\sigma$ increases



# Qualitative change in protrusion shape

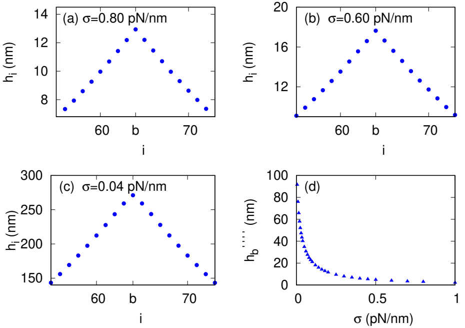



- A simple explanation from membrane shape near binding site
- For very large $\sigma$ and $\kappa$, an almost linear height variation
- As we lower $\sigma$, the qualitative shape remains similar but the magnitude of height gradient is larger: very high bending energy cost at the binding site
- As $\sigma$ is lowered further, such membrane shape becomes unsustainable
- Height gradient now varies more slowly in space and this shape stores less bending energy




- Bending energy cost depends on $h''''$
- $h''$ has a sharp minimum at the binding site for small $\sigma$: large curvature $h''''$
- When membrane shape changes, $h''$ varies more slowly around the binding site
- $h''$ minimum is not as sharp: curvature $h''''$ decreases

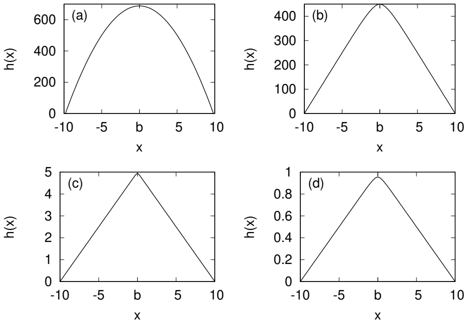
# For small $\kappa$ shape does not change




- For small $\kappa$ bending energy is not significant enough to bring about this change
- Here membrane height profile remains linear around the binding site for all $\sigma$ values and the fourth derivative drops monotonically

# Analytical calculation of membrane shape

- Time-evolution equation of height field in presence of an external point force
  $\partial_t h(x,t) = \sigma \partial_x^2 h(x,t) - \kappa \partial_x^4 h(x,t) + F\delta(x) + \eta(x,t)$
- In the long time limit $\langle h(x) \rangle \sim -\frac{F}{2\sigma}\left(\sqrt{\frac{\kappa}{\sigma}} e^{-\sqrt{\frac{\kappa}{\sigma}}|x|} + |x|\right)$
- Similar change in membrane shape as seen in simulations



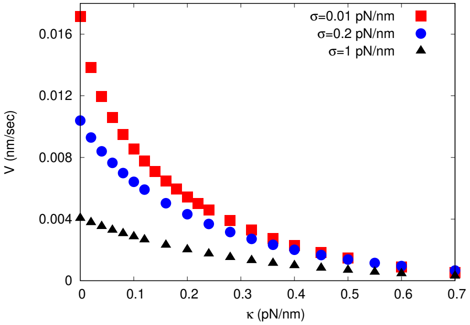

(a) $\sigma = 0.001,\ \kappa = 1.0$
(b) $\sigma = 0.01,\ \kappa = 0.01$
(c) $\sigma = 1.0,\ \kappa = 0.01$
(d) $\sigma = 5.0,\ \kappa = 1.0$

# Quantitative explanation for full $V - \sigma$ curve

- $V$ results from both upward and downward movement of the membrane
- Energy cost $\mathcal{E}_i^{\pm}$ for changing height from $h_i$ to $h_i \pm \delta$
- $\mathcal{E}_i^{\pm} = \sigma\{2\delta^2 \mp 2\delta h_i''\} + \kappa\{6\delta^2 \pm 2\delta h_i''''\}$
- At steady state average velocity is same everywhere on the membrane
- $V_b = \delta[U_0 p_0 e^{-\beta\mathcal{E}_b^+} + e^{-\beta\mathcal{E}_b^+} - (1-p_0)e^{-\beta\mathcal{E}_b^-}]$
- $h_b$ can increase due to bound filament polymerization or membrane thermal flutuations but can decrease only when filament is not bound
- For large $\kappa$ and small $\sigma$ surface energy cost can be neglected and $\mathcal{E}_b^{\pm} \approx \mathcal{K}_b^{\pm}$
- $V \approx e^{-6\beta\delta^2\kappa}\delta\{(U_0+1)p_0 e^{-2\beta\delta\kappa h_b''''} - 2(1-p_0)Sinh(2\beta\delta\kappa h_b'''')\}$

- As $h_b''''$ increases with $\sigma$, reaches a peak and decreases, $V$ decreases with $\sigma$, reaches a minimum and starts increasing again
- But for large $\sigma$ it is not possible to neglect surface energy cost anymore
- However, in this limit of large $\kappa$ and large $\sigma$ magnitude of $h_b''$ and $h_b''''$ are negligible
- $V \simeq \delta(U_0 + 1)p_0 e^{-6\beta\delta^2\kappa} e^{-2\beta\delta^2\sigma}$
- $V$ decreases exponentially with $\sigma$: verified from simulations
- When $\kappa$ is held fixed at a larger value, height derivatives become negligible at smaller $\sigma$
- Peak position $\sigma^*$ shifts leftward with increasing $\kappa$: consistent with simulations

# $V - \kappa$ curves are monotonic for all $\sigma$




- Peak in $V$ was associated with peak in $\mathcal{E}_b^+$
- As $\kappa$ increases, $\mathcal{K}_b^+$ goes up and magnitude of $h_b''$ decreases
- $\Sigma_b^+ = \sigma\{2\delta^2 - 2\delta h_b''\}$ increases with $\kappa$
- $\mathcal{E}_b^+$ always increases with $\kappa$ and $V$ drops steadily

# Outlook

- Non-monotonic variation in velocity and bending energy
- What happens in higher dimension or in presence of nonlinearity?
- For a $2d$ membrane bending energy cost is much higher
- Moderate or large $\kappa$ values remain numerically inaccessible in $2d$
- Possible experimental verification
- Results obtained in a simple and general model: opens up the possibility of wider application
- Ref: R.K. Sadhu and S. Chatterjee, Phys Rev E **100** 020401(R) (2019)