

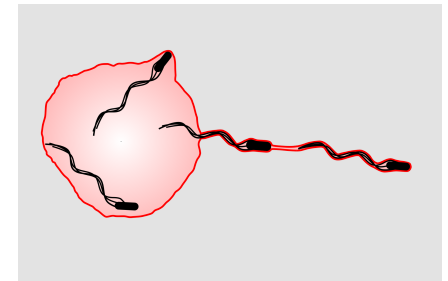
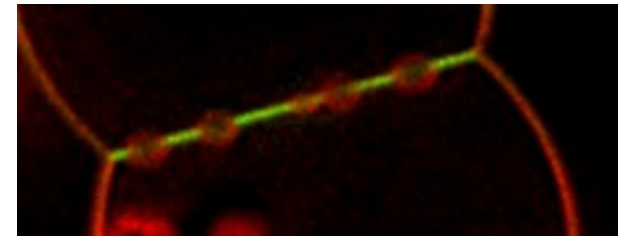
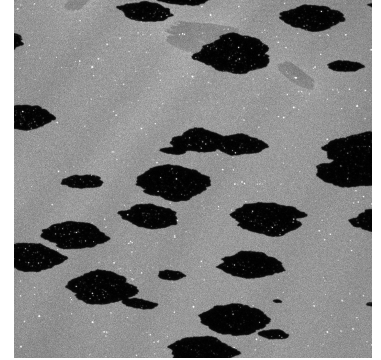
# Stress and confinement in shaping lipid membranes

**Margarita Staykova**  
Department of Physics,  
Durham University, UK



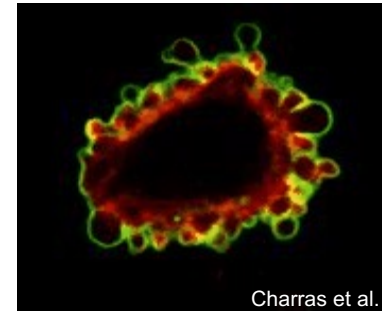
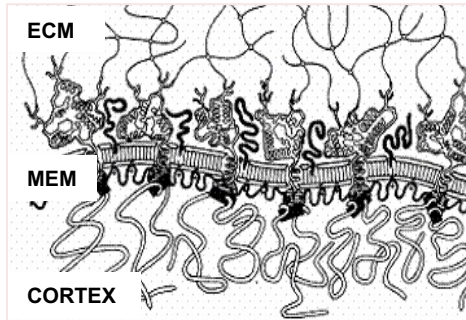
# Content

1. Friction dominated response of fluid supported membranes to lateral stretch
2. Hydraulic fracturing of membrane adhesion
3. Propulsion of GUVs enclosing with active particles



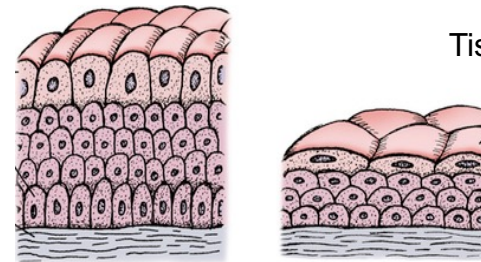
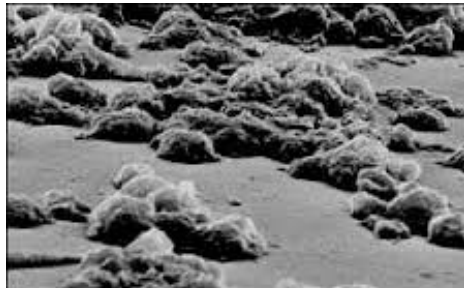
# Membranes are coupled to dynamic structures

Sub-cellular



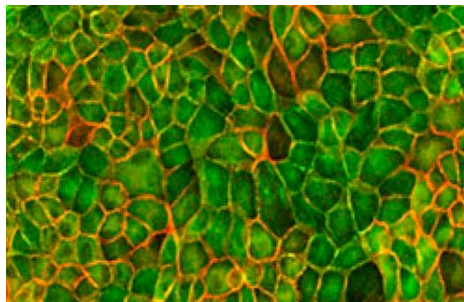
Membrane blebs

Cell-Substrate

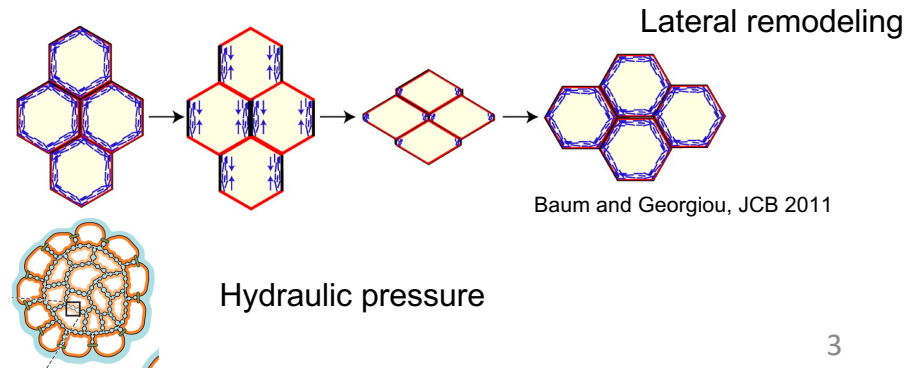


Tissue/organ deformations

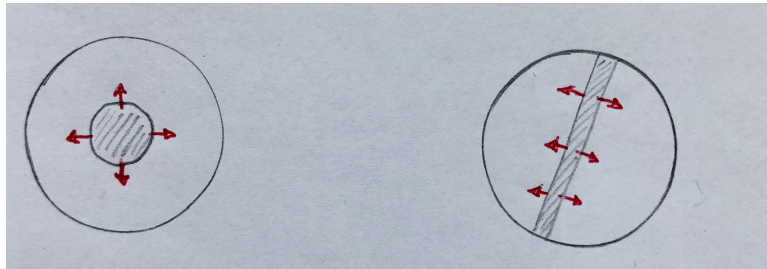
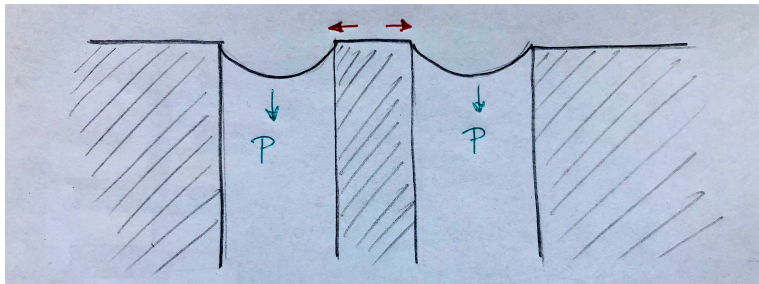
Cell-cell



Ladoux's Lab

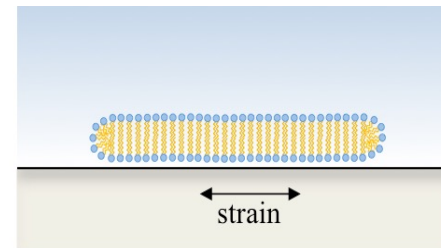
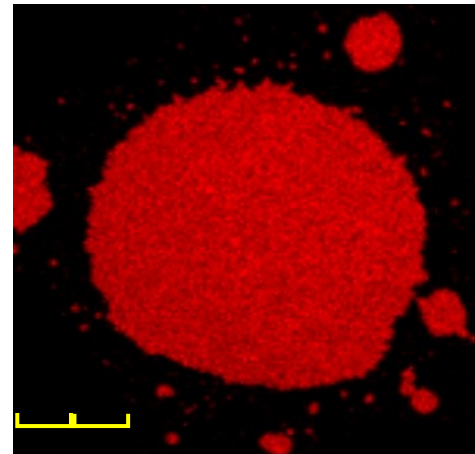


# Stretching experiments



bi-axial

uni-axial

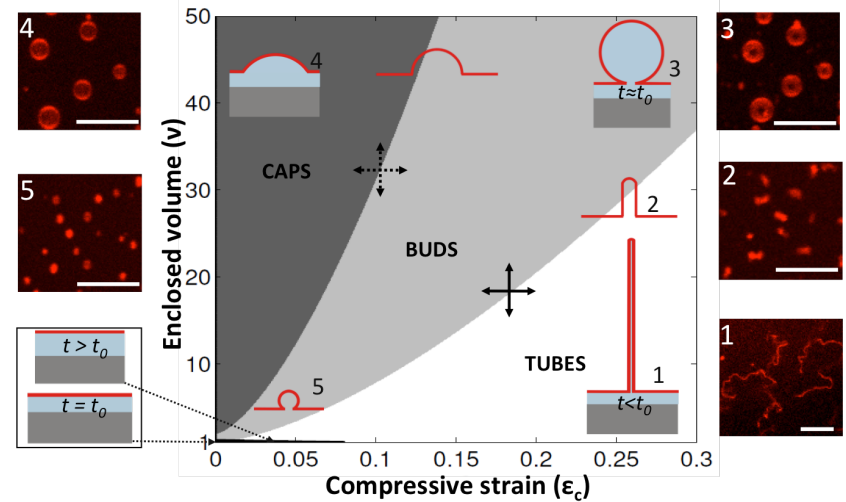
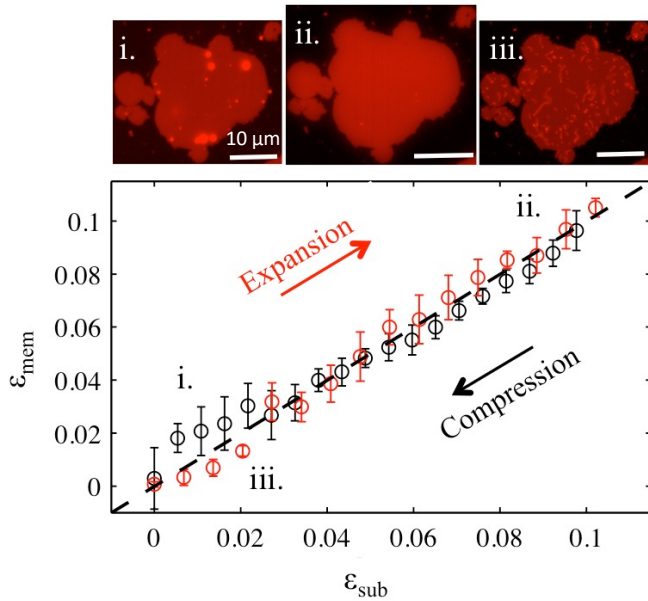


DOPC/  
Rh-DPPE

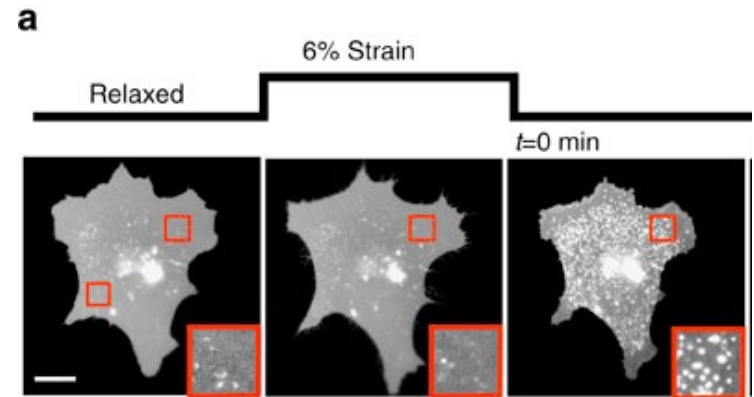
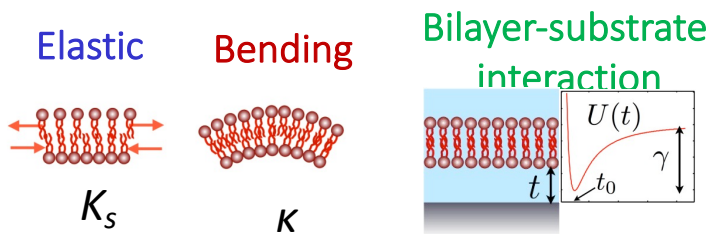
# Membrane buckling upon compression

(substrates with hydrophobic pinning points)

PNAS 108 (2011);  
PRL 110 (2013);  
Soft matter 32 (2017)

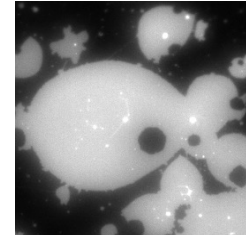
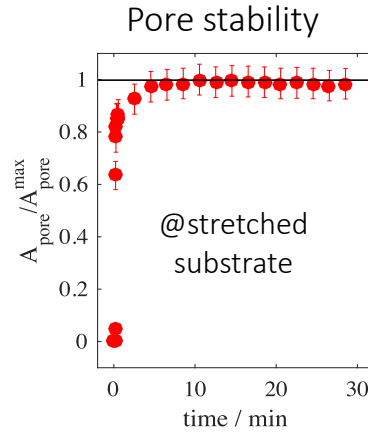
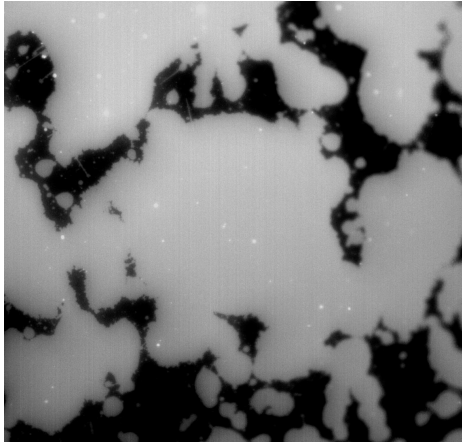


$$f = \frac{K_s}{2} (\phi^{+2} + \phi^{-2}) + \frac{\kappa}{2} H^2 + U(t)$$

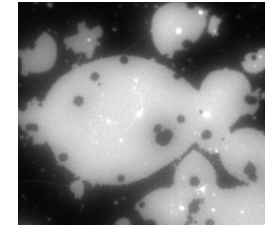


# Pores upon *bi-axial* stretch

(hydrophilic substrates)

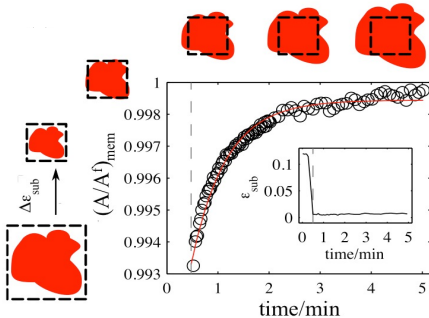
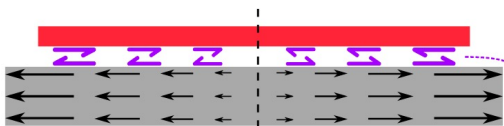


$\dot{\epsilon} \sim 0.05 \% s^{-1}$



$\dot{\epsilon} \sim 0.4 \% s^{-1}$

## Characteristic length-scales



**Characteristic length** over which tension propagates:

$$L_c = \sqrt{\frac{K_s}{b\dot{\epsilon}}}$$

Stretching modulus  
 $K_s = 0.1 \text{ Nm}^{-1}$   
 b- friction coefficient

When  $R_{\text{patch}} > L_c$   
 multiple pores open

$$\tau = \frac{bR_{\text{pore}}^3 e}{\gamma}$$

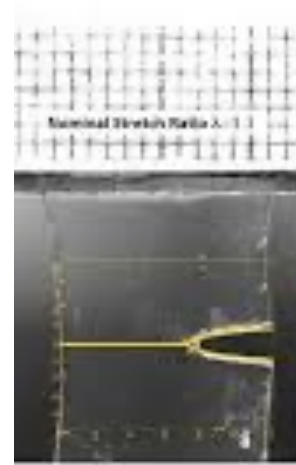
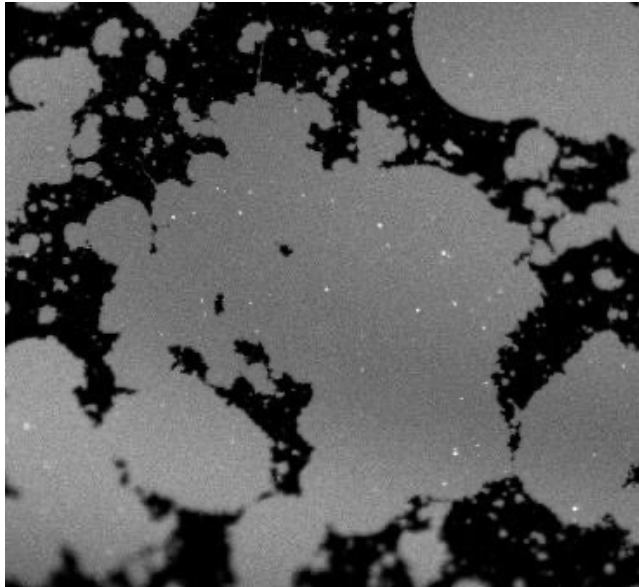
Edge tension  
 $\gamma = 10 \text{ pN}$

Takes tens of hours to reseal the pores

Sliding is opposed to dynamic friction

# Elliptic pores upon *uni-axial* stretch.

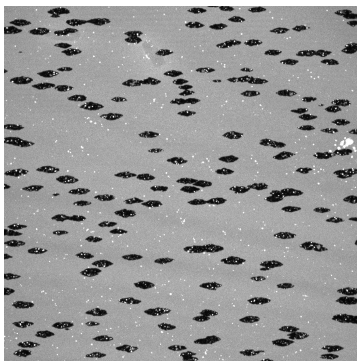
## Mechanism?



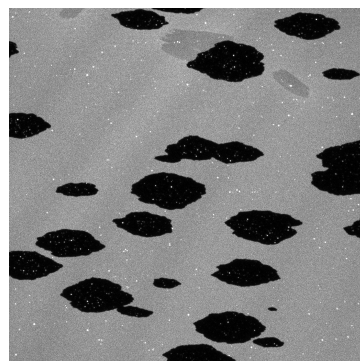
Akin to elastic fracture of solid materials (hydrogels)

(a)

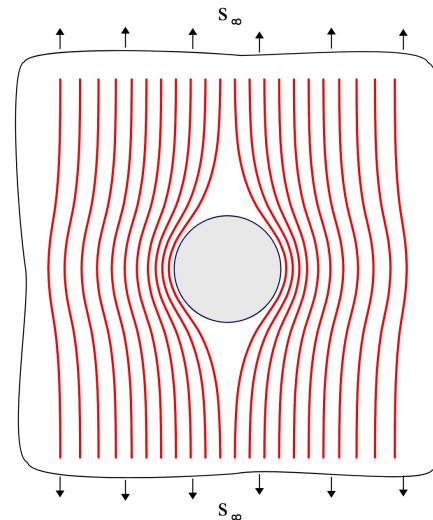
Guo et al., JMPC '18



$\dot{\epsilon} \sim 0.3 \% s^{-1}$



$\dot{\epsilon} \sim 0.01 \% s^{-1}$



Stress concentration around holes in solid materials



Marino Arroyo



Céline Dinet

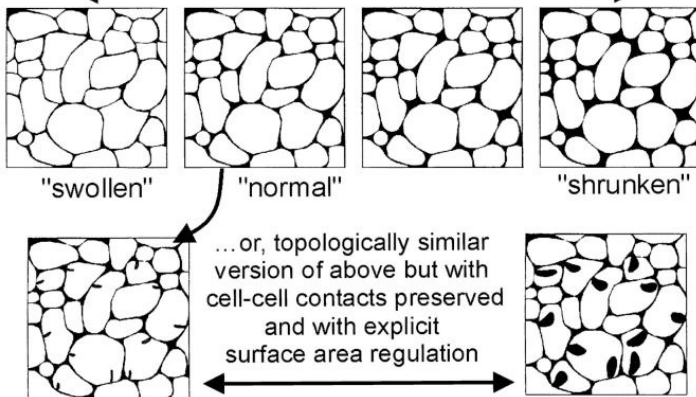


Alejandro Torres-Sánchez

# Hydraulic Fracturing at Membrane interfaces

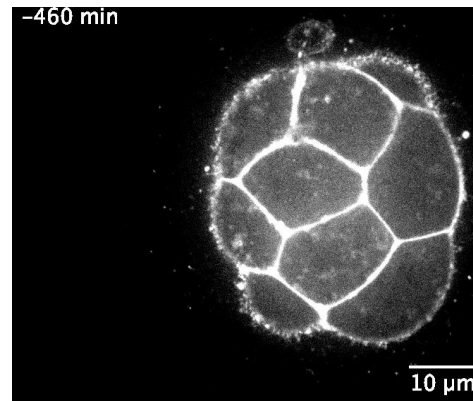
Brain tissue tortuosity?

Chen & Nicholson (2000) model



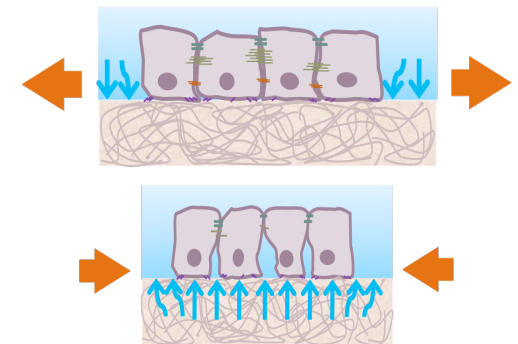
Morris et al.,  
Biophys J 1999

Formation of embryo lumen



Dumortier et al.,  
Science 2019

Fracking in epithelial sheets

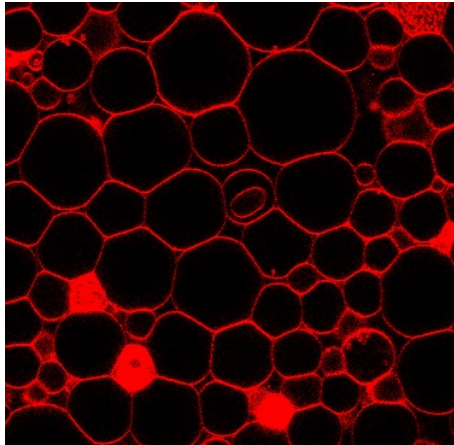


Casares et al.,  
*Nat Mat* 2015

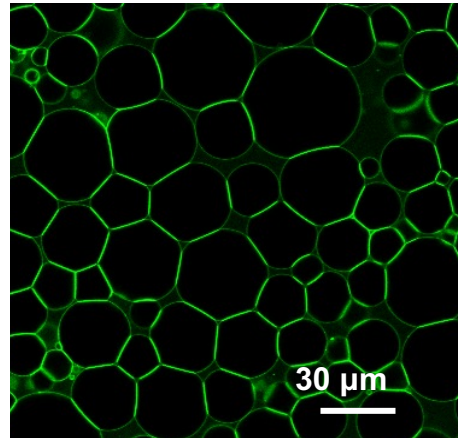


# Experimental system

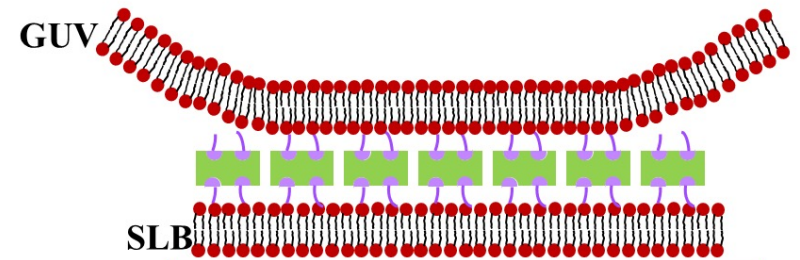
Artificial tissue made of vesicles







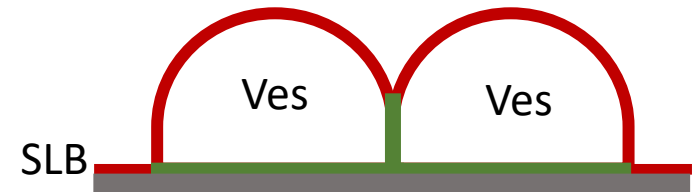
Membrane channel  
(Rhodamine)



Protein linker channel  
(Neutravidin-Dy488)



-  Phospholipids
-  Fluorescent Neutravidin
-  Biotinylated lipid
-  Plasma treated glass cover-slide



We image:

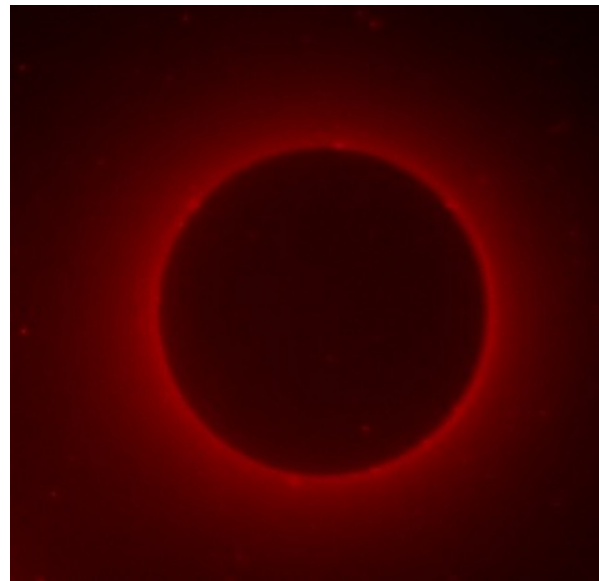
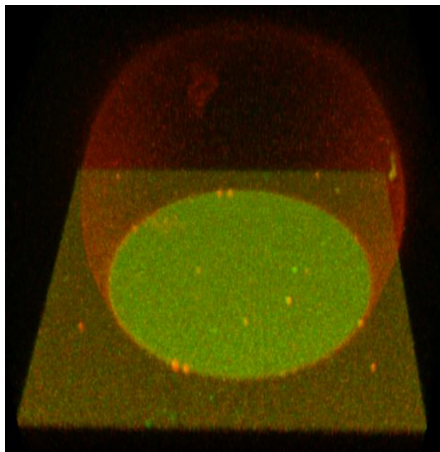
- Vesicle-SLBplane
- Vesicle-Vesicle plane

We vary:

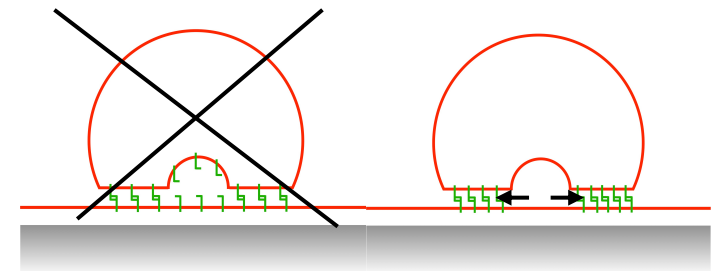
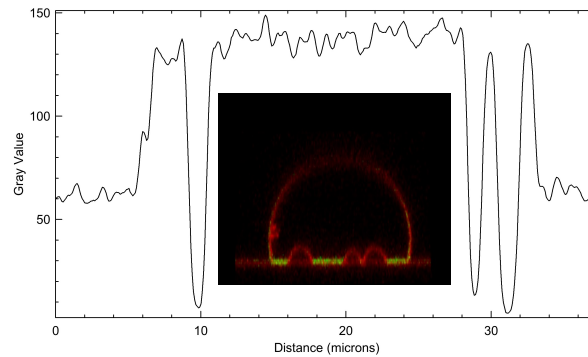
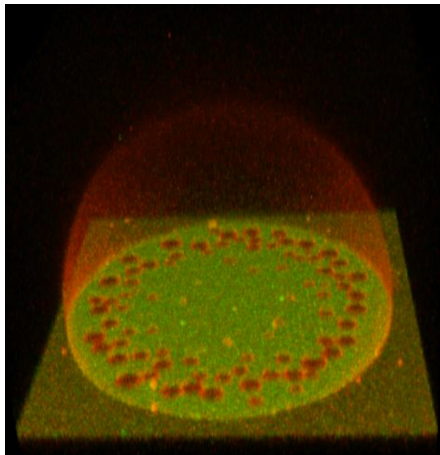
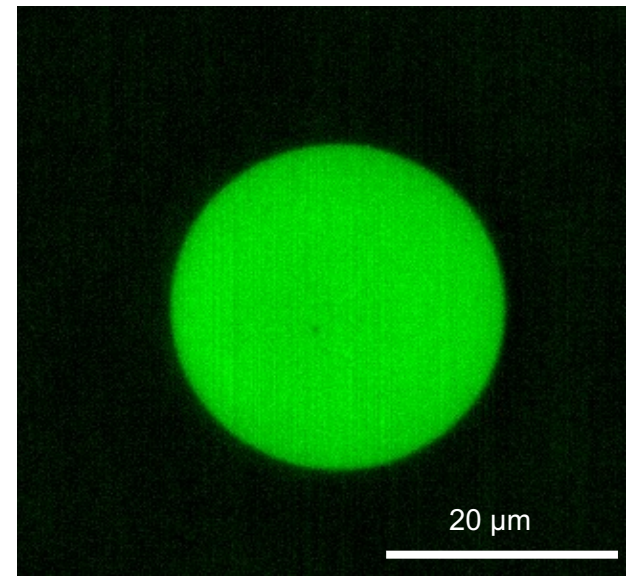
- Magnitude of the osmotic shock:  
(25-100mM)
- Linker density: 0.2 - 4mol %
- Linker type: NaV, DNA, E-cadherins

# Hydraulic fractures at membrane adhesion contacts

Lipid Membrane



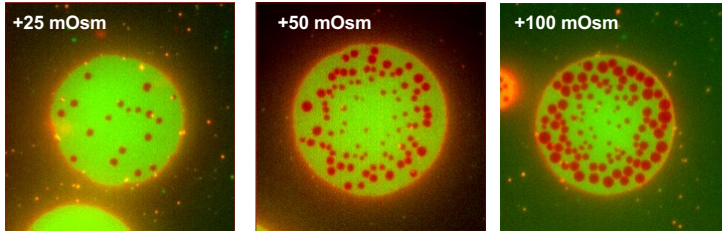
Neutravidin



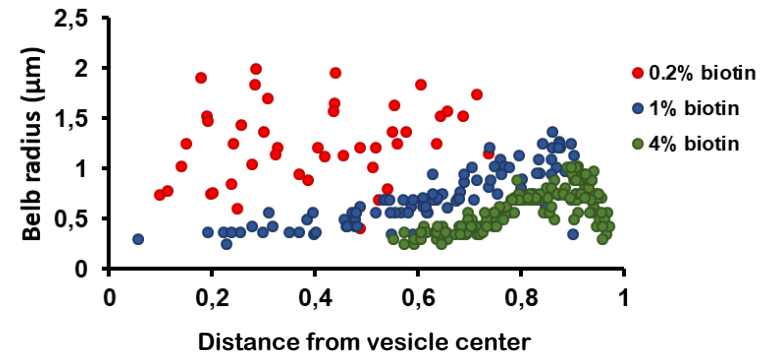
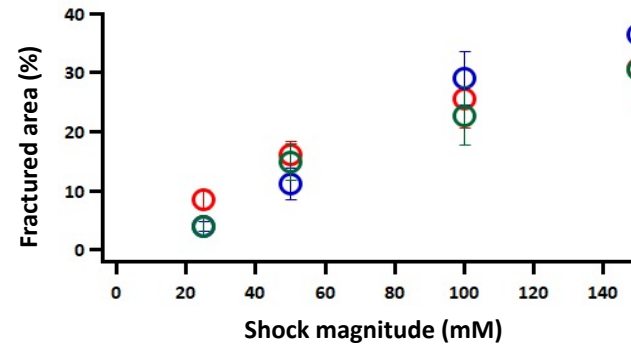
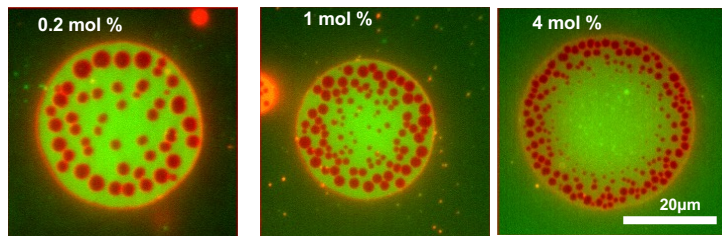
Belbs- by fast redistribution of linkers

# Biotin-Neutravidin

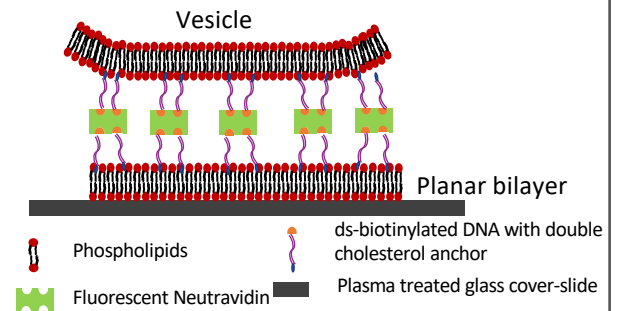
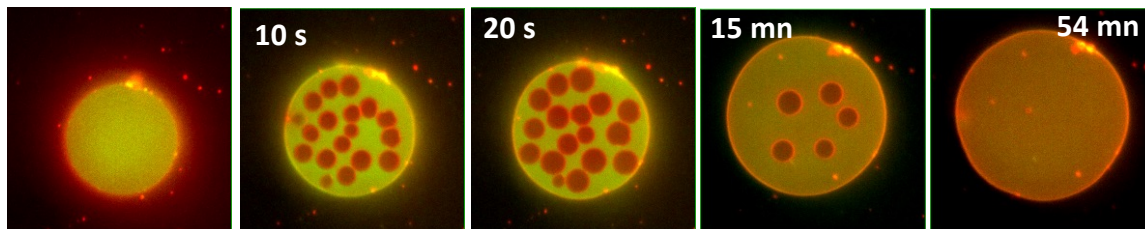
1 mol % biotin



+100 mM

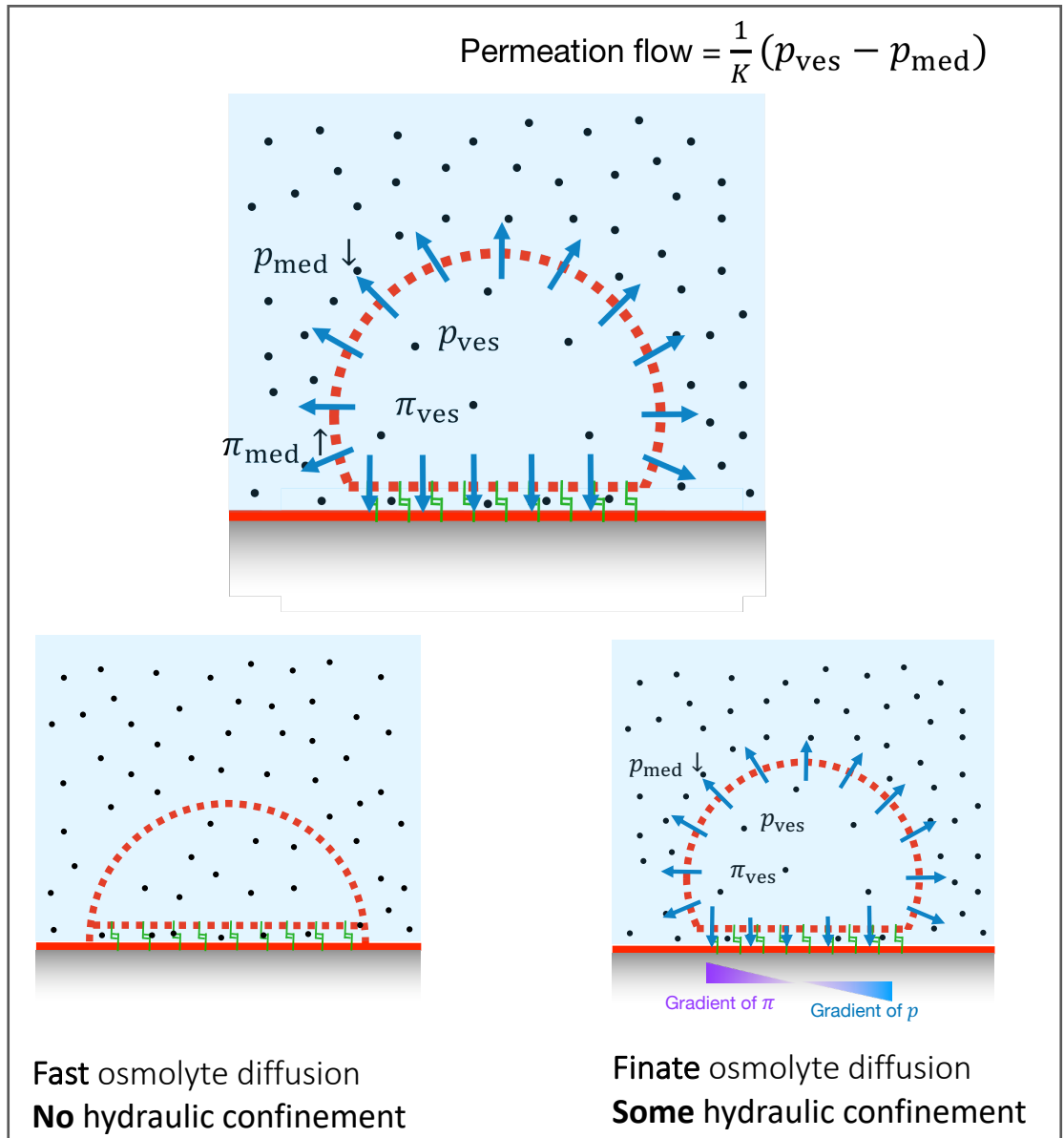
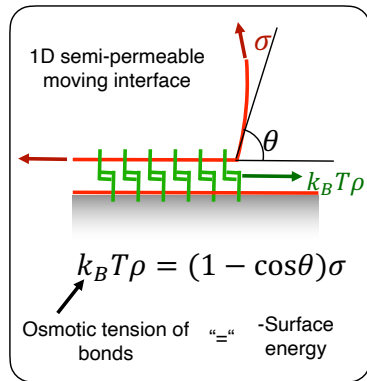
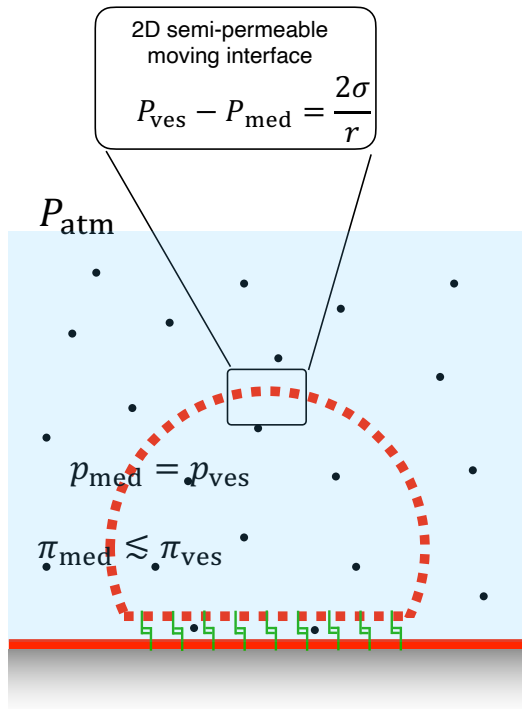


# DNA linkers

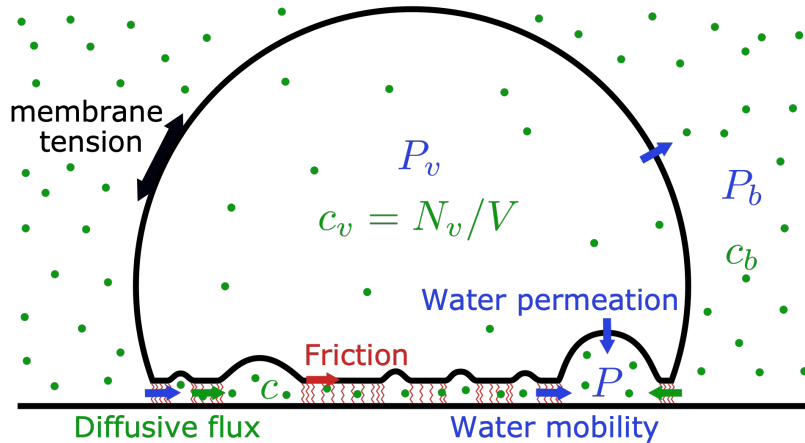


# Mechanism

Water partial pressure  $p$   
 Osmotic pressure  $\pi$   
 Mechanical pressure  $P = p + \pi$



# Model



## Ingredients:

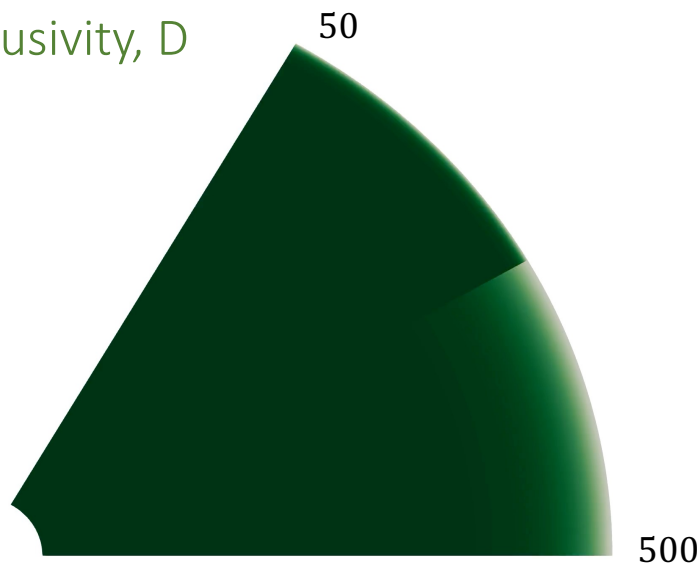
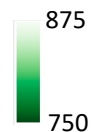
- Mechanics of fluid membrane in/out-of-plane.
- Water transport
- Osmolyte transport
- Adhesion molecule dynamics (advection, reaction, diffusion)

- Size of vesicle/patch
- Number of linkers
- Osmolarity and magnitude of shock

- Membrane viscosity
- Membrane permeability
- Length of bonds
- Stiffness of bonds

- Membrane friction
- Darcy permeability of interstitial space
- Diffusivity of osmolytes in interstitial space

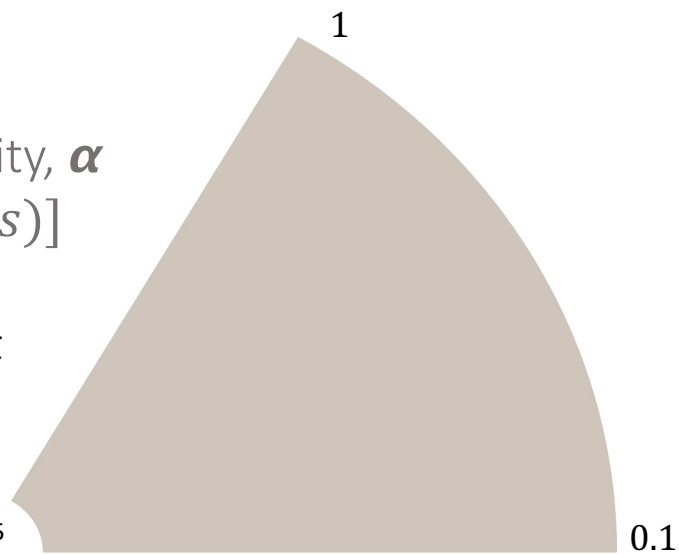
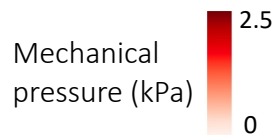
Osmolyte diffusivity,  $D$   
[ $\mu\text{m}^2/\text{s}$ ]



Osmotic pressure  
(kPa)

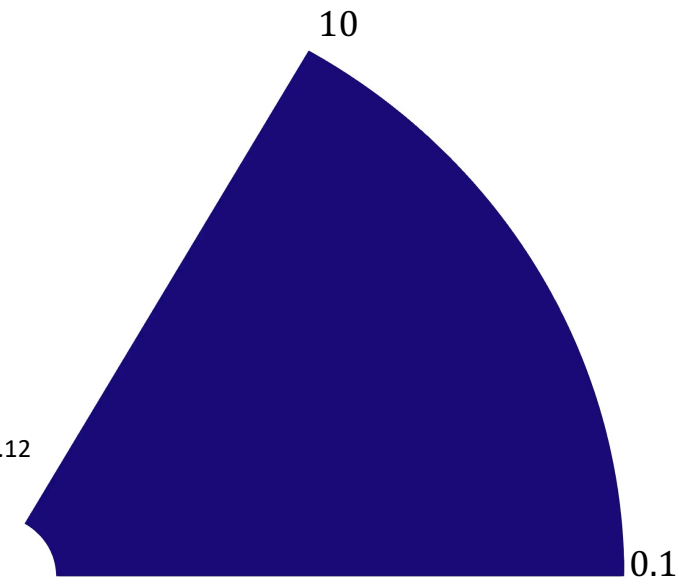
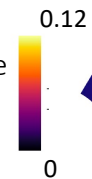
Water Mobility,  $\alpha$   
[ $\mu\text{m}^2/(\text{kPa}\cdot\text{s})$ ]

$$\ell_{\text{scr}} = \sqrt{K\alpha z}$$

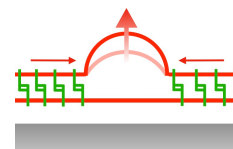
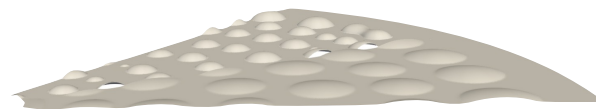


Mechanical pressure (kPa)

Membrane friction  
 $\text{kPa}\cdot\text{s}/\mu\text{m}$

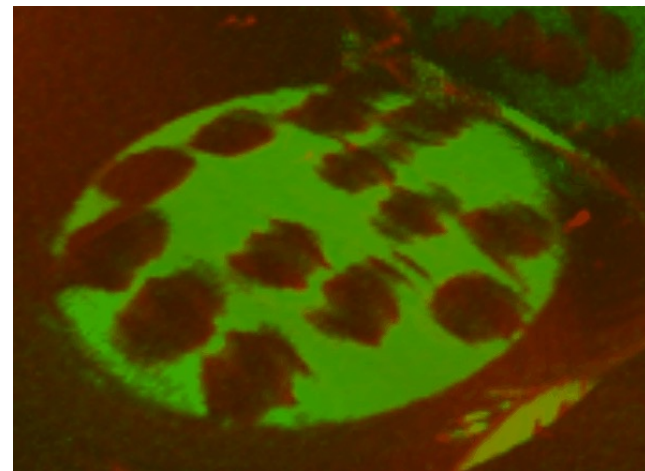
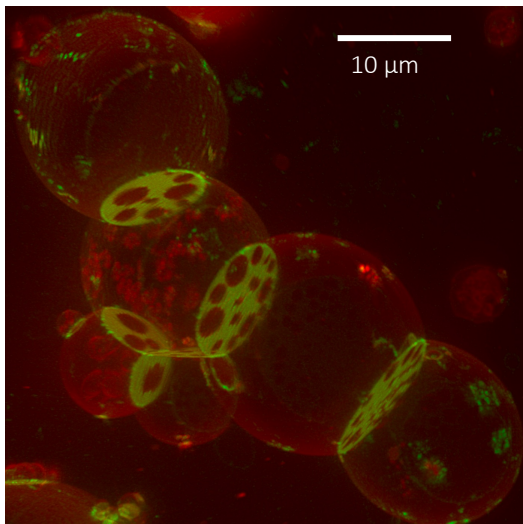
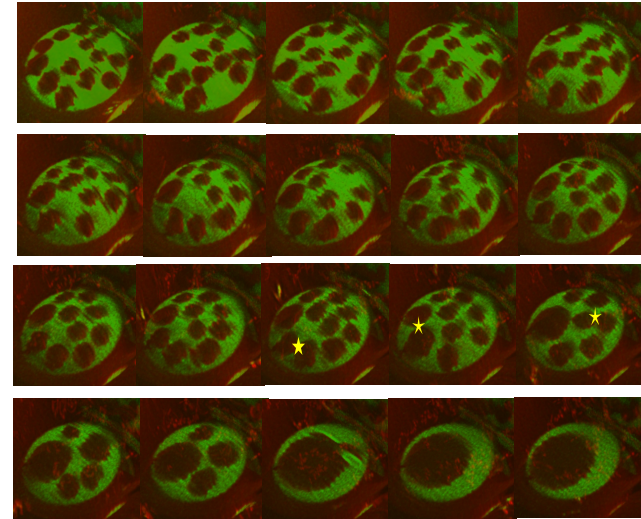
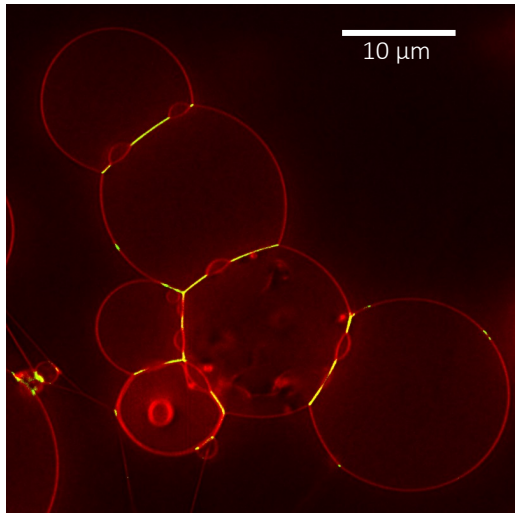


Membrane tension  
(mN/m)



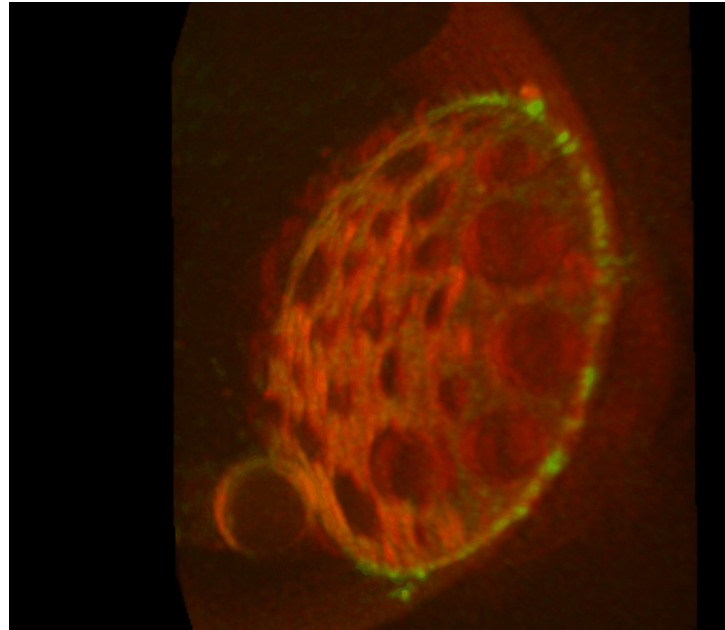
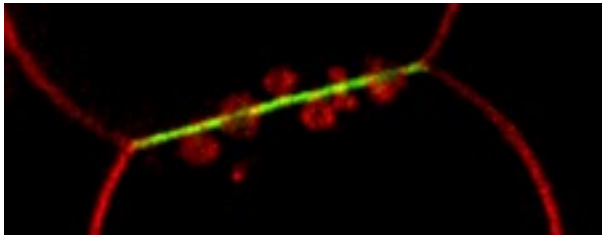
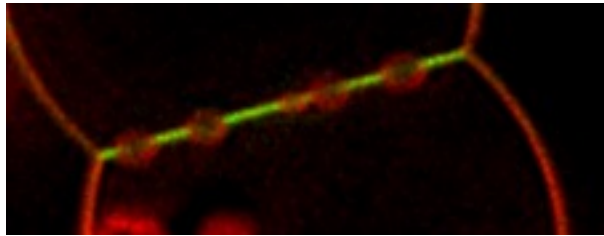
Membrane  
slippage flow

# Fast dynamics at membrane-membrane interface

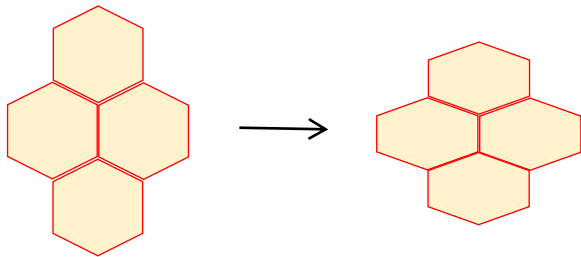


# 'Endocytosis'

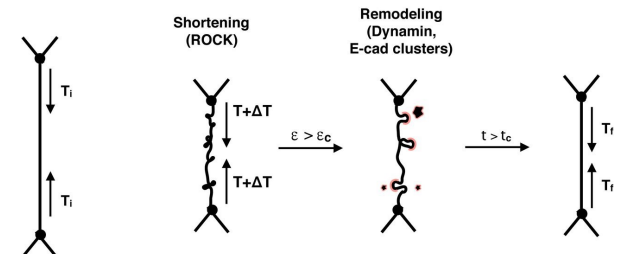
Higher linker density  
Pulling apart the two vesicles



? Passive mechanism for shortening of cell contacts



.. a relevant mechanism  
for the reduction of  
junctional membrane  
area during tissue  
elongation



Cavanaugh et al'20



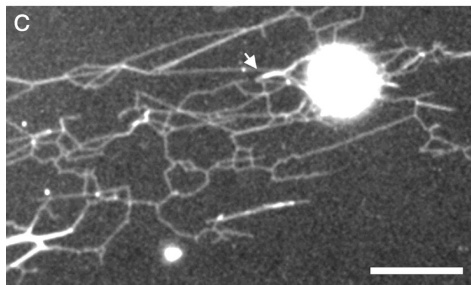


Lucas le Nagard

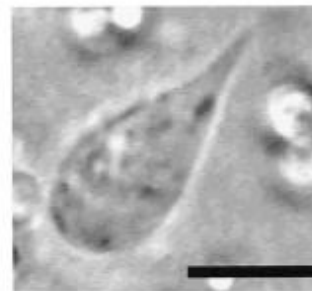
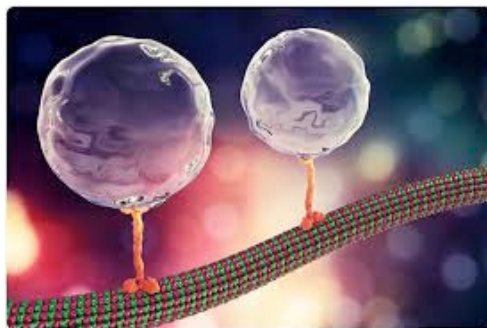
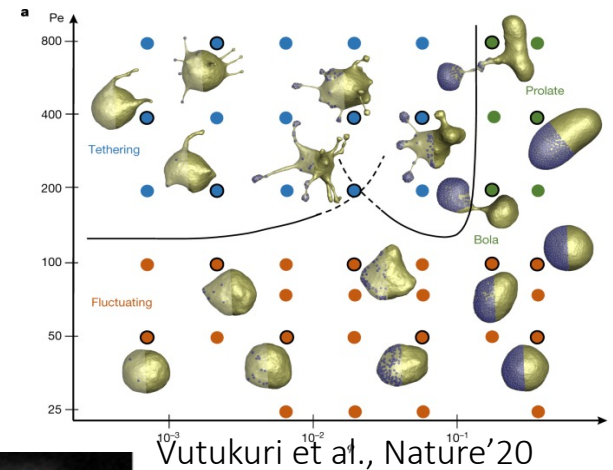
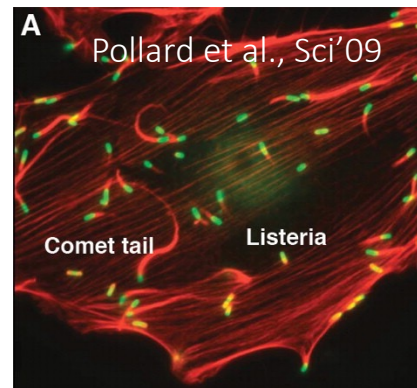


Wilson Poon

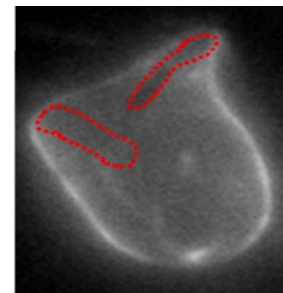
# Swimming vesicles powered by bacteria



Koester, PNAS'03



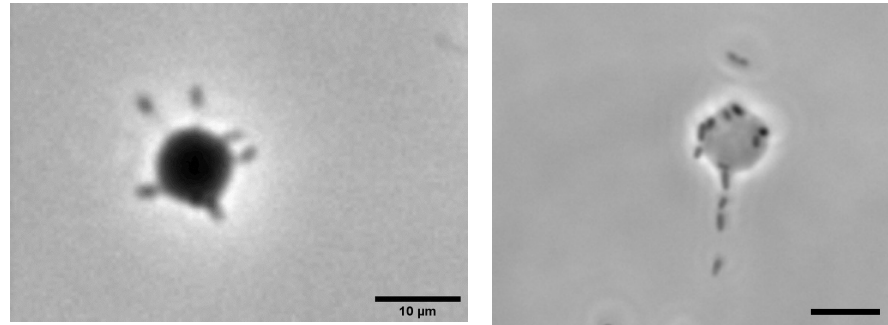
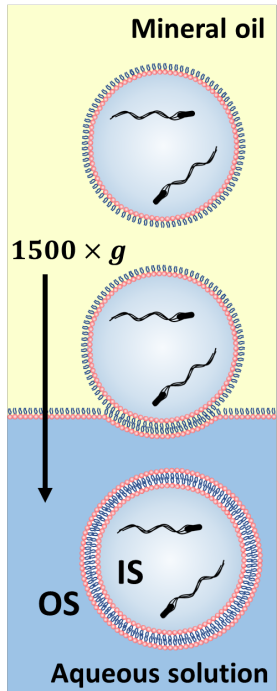
Miyata et al., PNAS'99



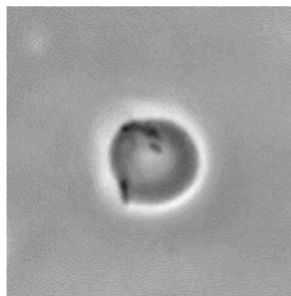
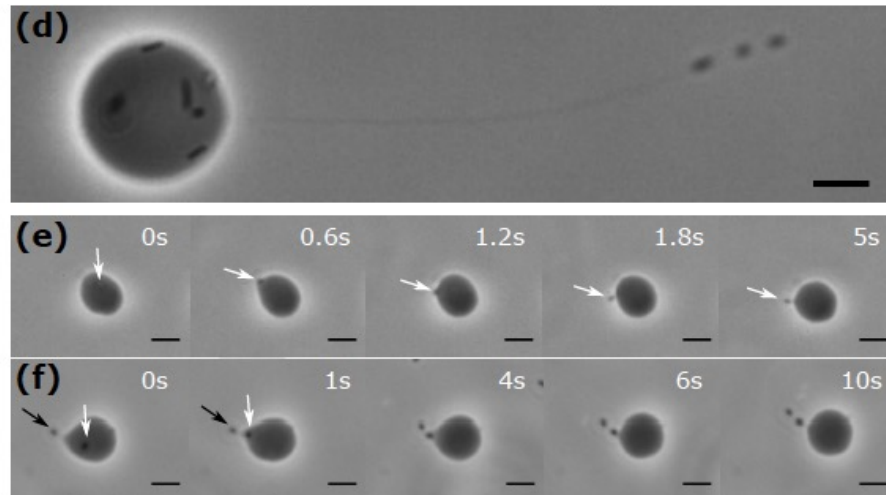
Takatori et al., PRL'20

# Bacteria push lipid tubes

*E. coli* in POPC GUVs

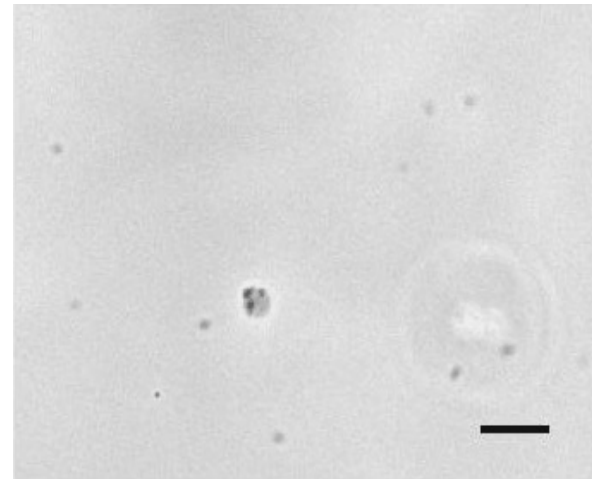
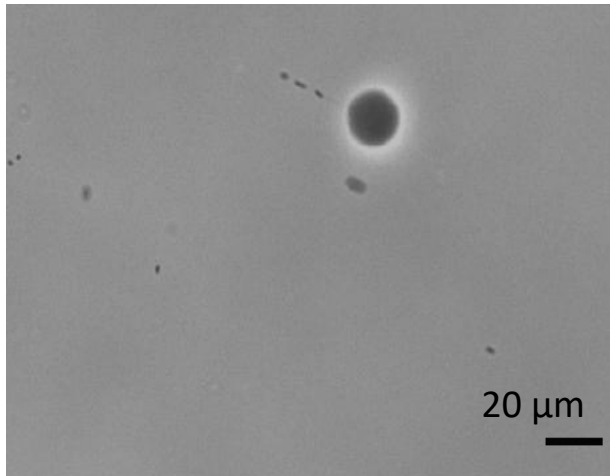


Low membrane tension allows bacteria to extrude tubes

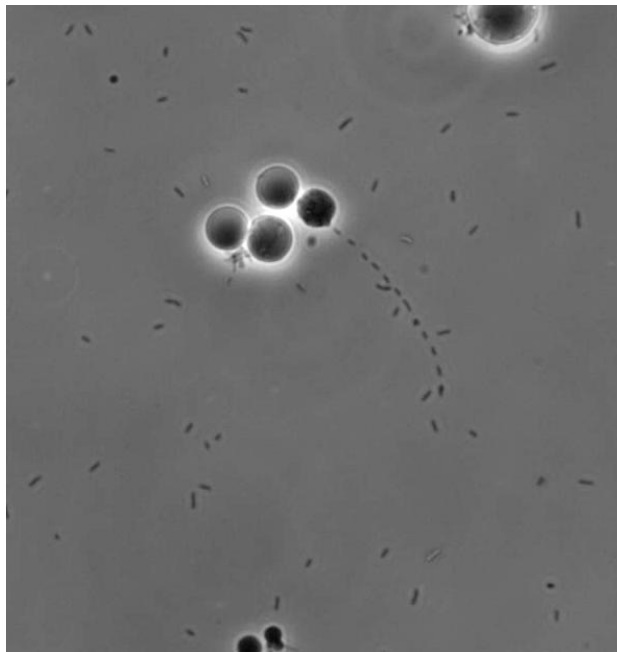


Tense vesicles

# Vesicles propelled by bacteria



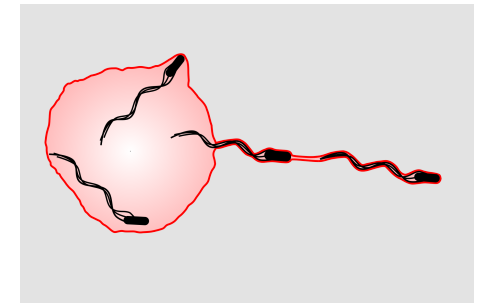
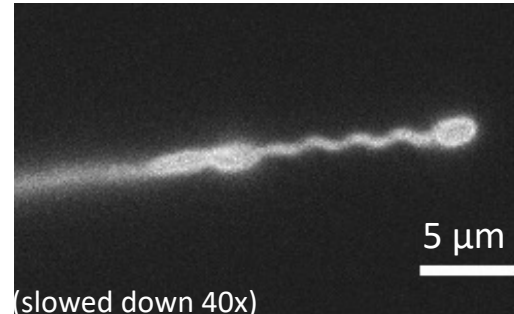
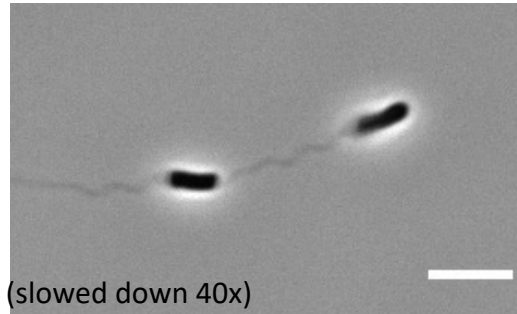
(accelerated 10x)



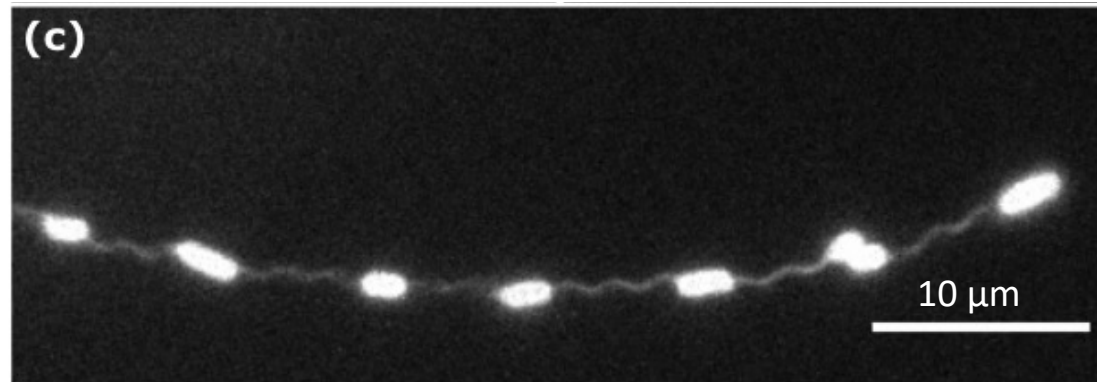
(accelerated 50 x)

Typical speed of a GUV  
propelled by one  
bacteria :  $1 \mu\text{m}\cdot\text{s}^{-1}$

# Tube act as a flagellum



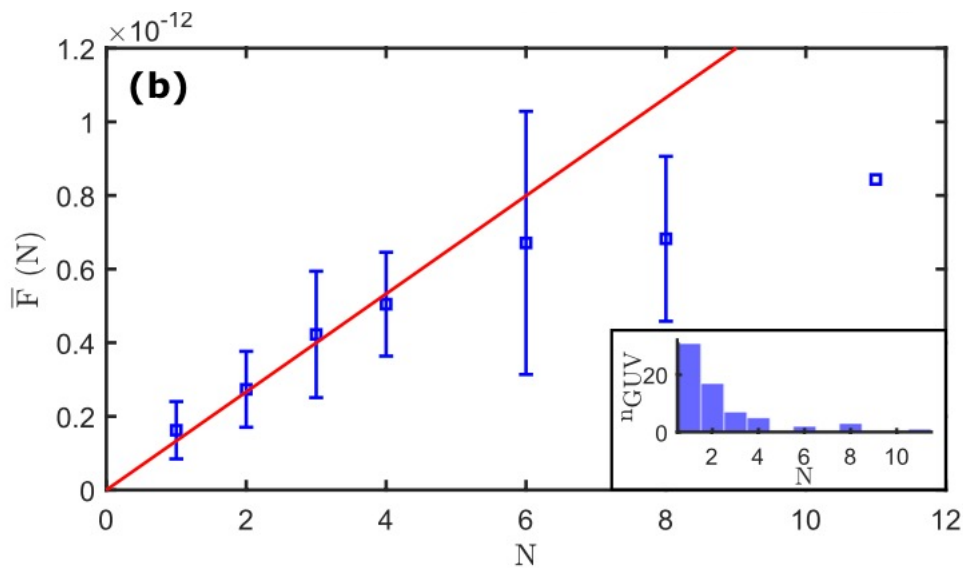
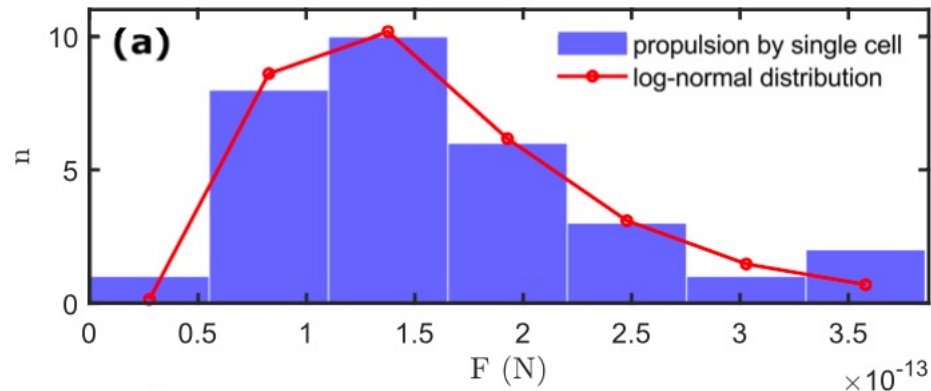
Lipid tube act as a flagellum for the propulsion of vesicle



Tube characteristics correspond to those of the flagella bundle:

- Rotation speed  $\sim 60 - 100$  Hz
- Helix pitch  $\sim 2.3 \mu\text{m}$
- Diameter  $\sim 0.4 \mu\text{m}$

# Propulsive force



Force-free swimmer at low Reynolds number: propulsive force  $F$  exactly balanced by drag force on the swimmer.

$$F = (\xi_{GUV} + N_b \xi_b) v$$

$$N_b = 1, n = 31$$

$$\langle F \rangle = (1.6 \pm 0.5) \times 10^{-13} \text{ N}$$

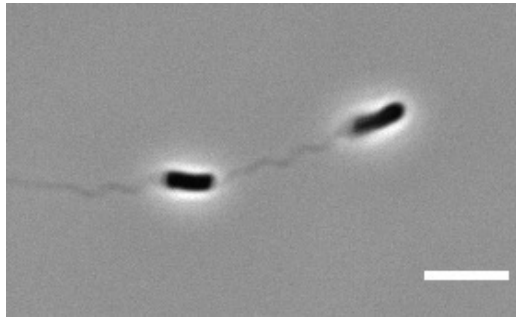
3x smaller than thrust force in bulk

$$\bar{F} = 1.3 \times 10^{-13} N_b N$$

Each additional cell in the tube contributes to increasing the resulting force

# Questions

## 1. Why are tubes so thin?



Symmetric membrane,  
no spontaneous curvature

$$f = 2\pi\sqrt{2\kappa\sigma}$$

$$R = \sqrt{\frac{\kappa}{2\sigma}}$$

$$f \sim 4.5^{-13} \text{ N}$$

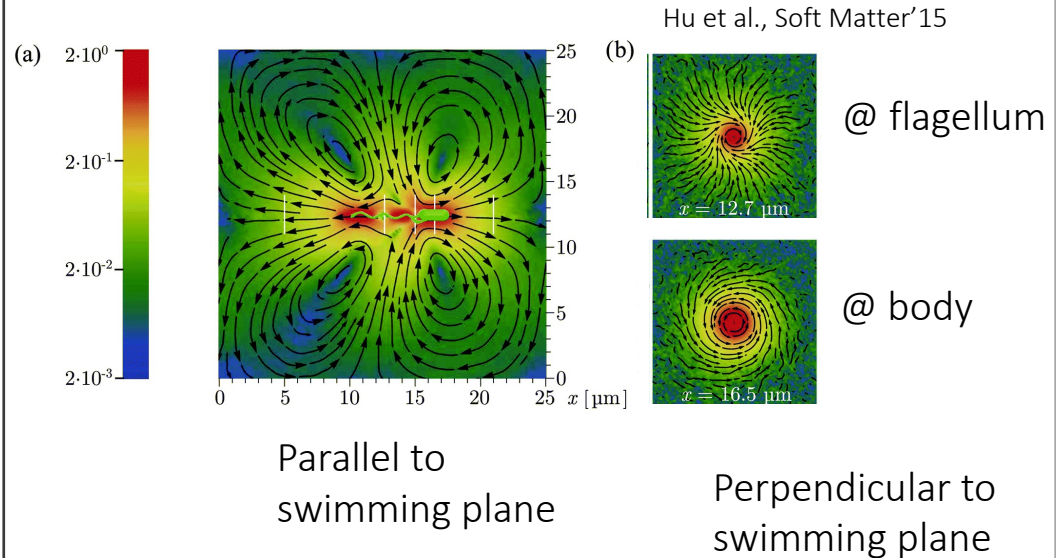
Bacteria thrust force

$$\kappa \sim 10^{-19} \text{ J}$$

Bending rigidity of  
POPC membrane

$$R_{min} \sim 1.4 \mu\text{m}$$

## 2. Stability of tubes with large in plane shear?



## 3. Swimming of bacteria in membrane confinement?

- Vibrio species with membrane sheath
- Intracellular pathogens, such as Salmonella, deforming cell membranes

