Modeling lipid bilayer membranes, Modand vesicles as model cellsicles

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lipid macromolecules and lipid bilayer membranes

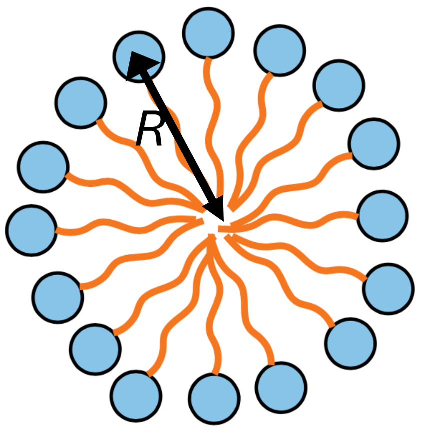
$$4\pi R^2 = N a, \quad \frac{4\pi R^3}{3} = N v$$

$$R = \frac{3v}{a}, \quad l \geq R = \frac{3v}{a}$$

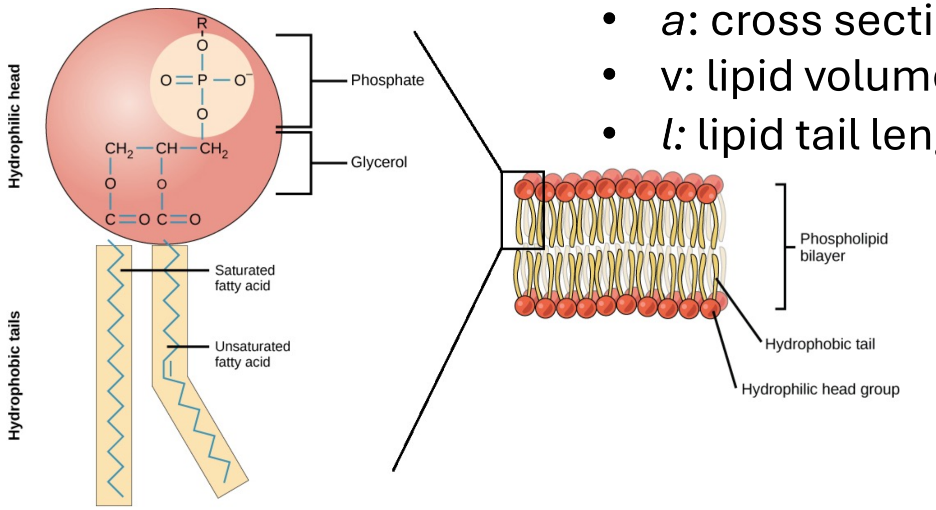
Packing parameter: $p = \frac{v}{la} \leq \frac{1}{3}$

(Israelachvili *et al.*, J Chem Soc. 1976)

A spherical micelle of radius *R and N lipids*



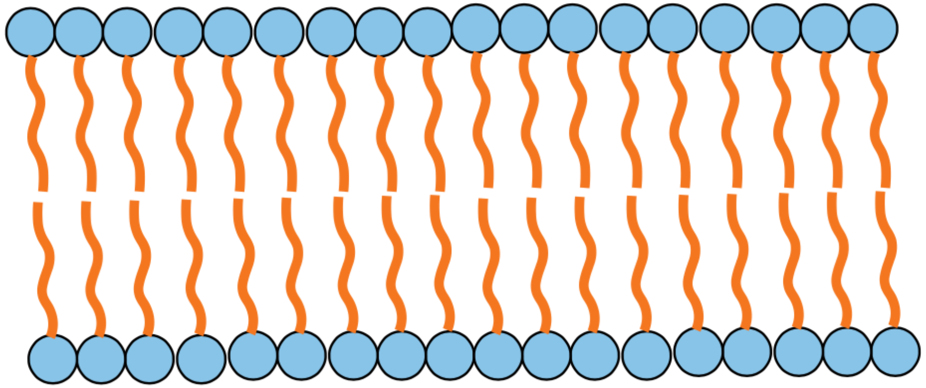
Micelles



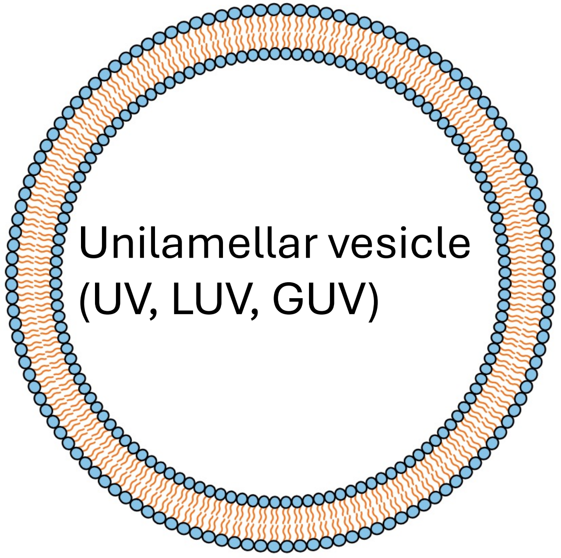
- *a*: cross sectional area of lipid head (0.6-0.7 nm^2)
- v: lipid volume
- *l:* lipid tail length (1.5-3 nm)

- A candidate of protocell for the origin of life (Babu *et al.*, Nature, 2022)

- Lipids are amphiphilic macromolecules



Planar bilayer $\frac{1}{2} \leq p = \frac{v}{la} \leq 1$



Vesicles

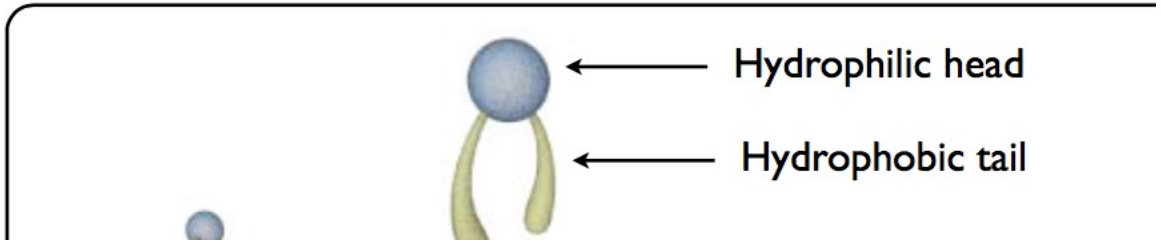
Excess area: $\Delta = \frac{A}{r^2} - 4\pi$

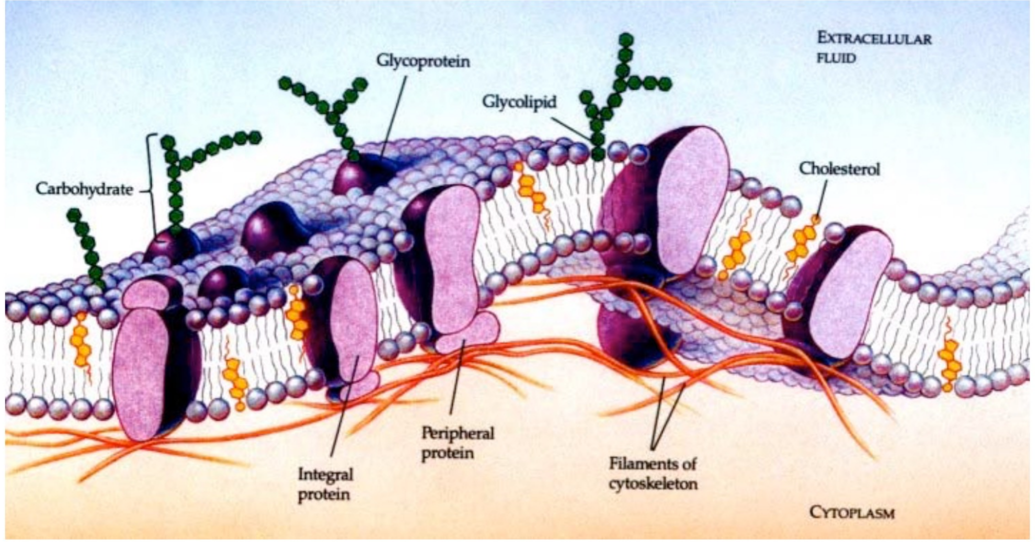
Excess length: $\delta = \frac{L}{l} - 2\pi$

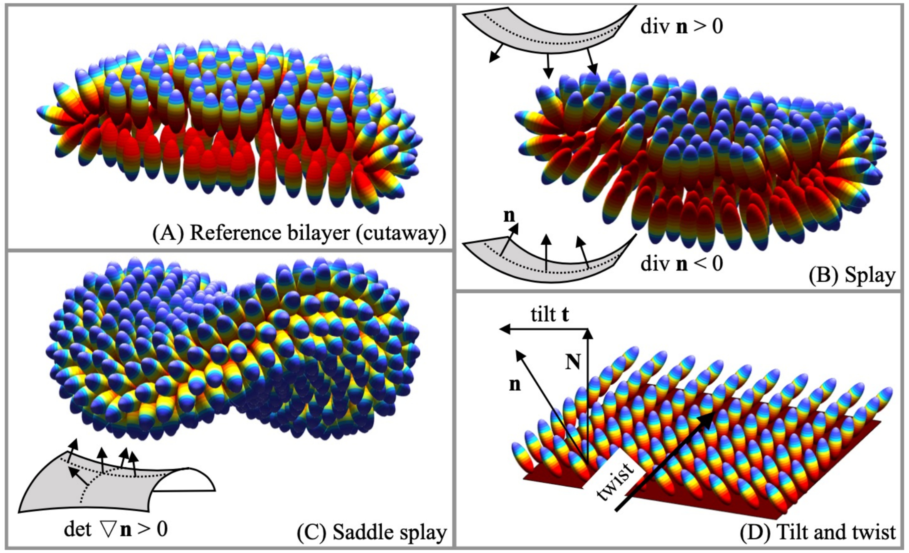
Reduced volume: $V^* = \left(1 + \frac{\Delta}{4\pi}\right)^{-3/2}$

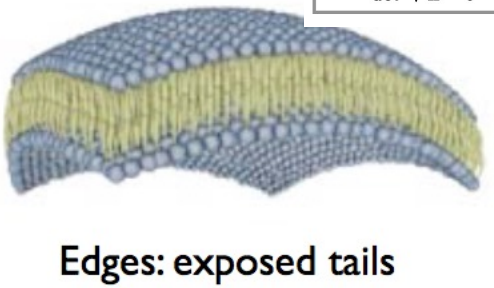
Reduced area: $A^* = \left(1 + \frac{\delta}{2\pi}\right)^{-2}$

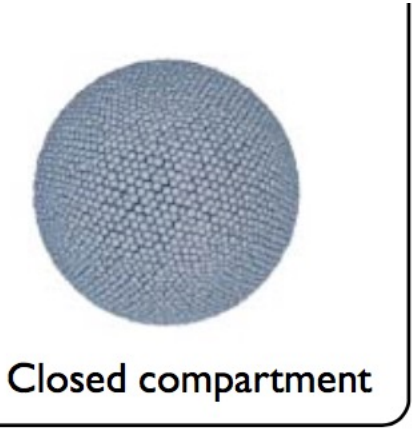
Mechanics of lipid bilayer membranes











$$\mathcal{W} \equiv \int_\Sigma \tfrac{1}{2}k_\mathrm{B}\left[(\operatorname{div}\mathbf{n}+k_0)^2 - k_0^2\right] + \tfrac{1}{2}k_\mathrm{T}(\operatorname{curl}\mathbf{n})^2 + k_\mathrm{G}\det\nabla\mathbf{n} + \tfrac{1}{2}k_\theta|\mathbf{t}|^2\,dA.$$

- k_B: bending modulus
- k_T: twist modulus
- k_G: saddle-splay modulus
- k_θ: tilt modulus

- Bilayer of thickness $2d \sim 4$ nm with a bending modulus κ, area stretching modulus K, membrane conductance σ_m and permittivity ε_m (membrane capacitance $c_m = \varepsilon_m / 2d$)

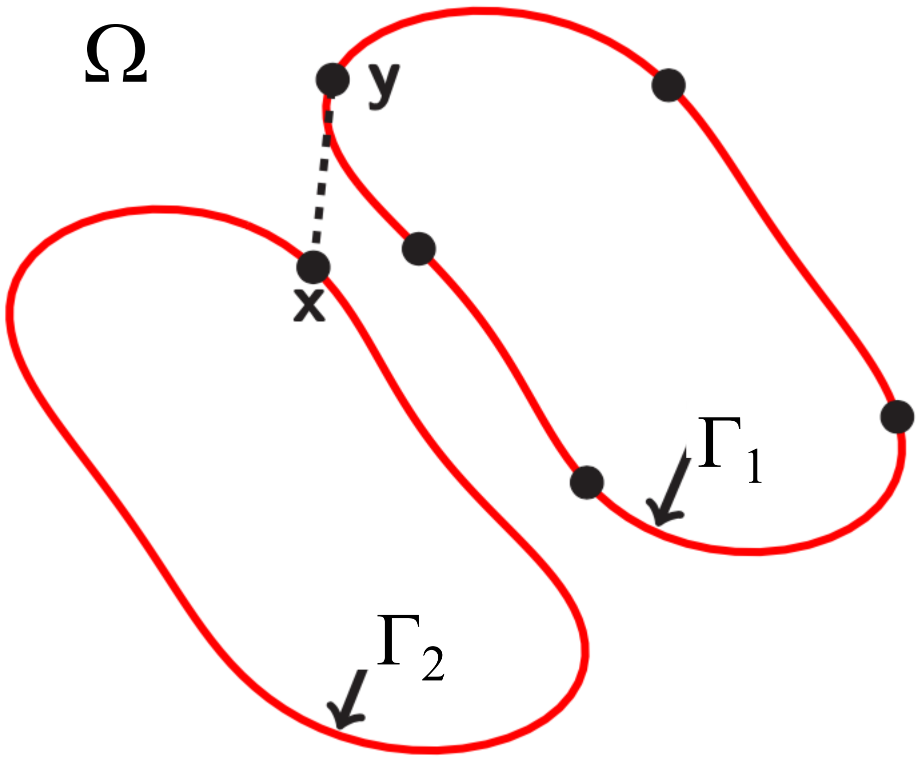
Vesicle hydrodynamics as a problem of fluid-structure interaction

- For $\boldsymbol{x}$ in Ω

$$\mu\Delta\boldsymbol{u} = \nabla p,$$
$$\nabla\cdot\boldsymbol{u} = 0,$$
$$\boldsymbol{u} \to \boldsymbol{u}_\infty \text{ as } |\boldsymbol{x}| \to \infty$$

- For $\boldsymbol{x}$ on Γ_i

$$\boldsymbol{u}(\mathbf{x} \text{ on } \Gamma_i) = \dot{\mathbf{x}}_{\boldsymbol{i}}$$
$$[\boldsymbol{\tau}\cdot\widehat{\boldsymbol{n}}] = \boldsymbol{f}_{mem}$$
$$\nabla_s\cdot\boldsymbol{u}_s = 0$$
$$\boldsymbol{\tau} = -p\mathbf{I} + \mu(\nabla\boldsymbol{u} + (\nabla\boldsymbol{u})^T)$$
$$\boldsymbol{f}_{mem} = -\kappa_b\boldsymbol{x}_{ssss} + (\sigma\boldsymbol{x}_s)_s$$



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$$[\![\boldsymbol{\tau}\cdot\widehat{\boldsymbol{n}}]\!] = \boldsymbol{\xi} = \boldsymbol{f}_{mem} + \mathcal{A}$$
$$\nabla_s\cdot\boldsymbol{u}_s = 0$$
$$\boldsymbol{\tau} = -p\mathbf{I} + \mu(\nabla\boldsymbol{u} + (\nabla\boldsymbol{u})^T)$$
$$\boldsymbol{f}_{mem} = -\kappa_b\boldsymbol{x}_{ssss} + (\sigma\boldsymbol{x}_s)_s$$

$$\dot{\mathbf{x}} = \mathbf{u}_\infty(\mathbf{x}) + \mathcal{S}[\boldsymbol{\xi}](\mathbf{x}), \qquad \mathbf{x}_s\cdot\dot{\mathbf{x}}_s = \mathbf{0},$$

$$\mathcal{S}[\boldsymbol{\xi}](\mathbf{x}) = \frac{1}{4\pi\mu}\int_\gamma\left(-\ln\|\mathbf{x}-\mathbf{y}\| + \frac{(\mathbf{x}-\mathbf{y})\otimes(\mathbf{x}-\mathbf{y})}{\|\mathbf{x}-\mathbf{y}\|^2}\right)\boldsymbol{\xi}(\mathbf{y})ds_{\mathbf{y}},$$

$$\mathbf{x}^{N+1} - \Delta t\mathcal{S}^N\mathcal{B}^N\mathbf{x}^{N+1} - \Delta t\mathcal{S}^N\mathcal{T}^N\sigma^{N+1} = \mathbf{x}^N + \Delta t\mathcal{S}^N\mathcal{A}^N\mathbf{x}^N,$$

$$\mathcal{B}[\mathbf{f}](\mathbf{x}) = -\kappa_b\mathbf{f}_{ssss},\ \mathcal{T}[\sigma](\mathbf{x}) = (\sigma\mathbf{x}_s)_s,$$

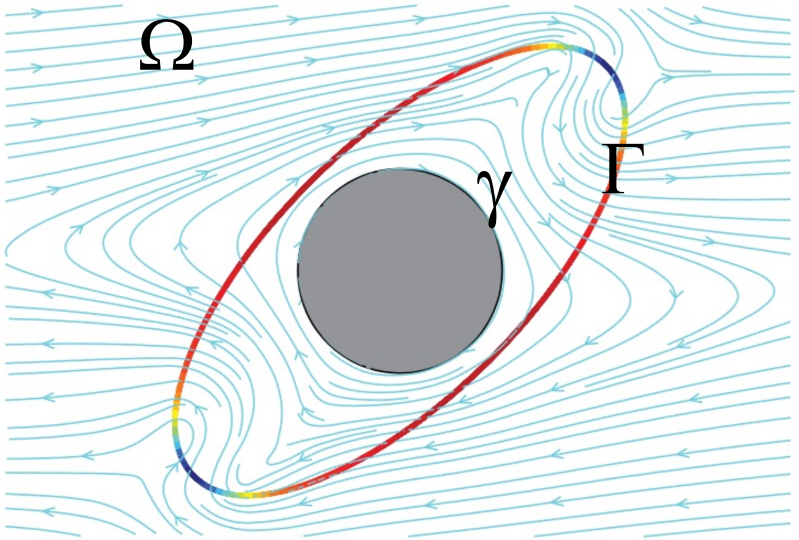
$$\mathbf{x}_s^N\cdot\mathbf{x}_s^{N+1} = 1.$$

- Error in length and/or error in area can be used to adjust the time-step size. (Quaife and Biros, JCP, 2016)

- Error in length varies with the vesicle dynamics and often increases deformation.

Vesicle hydrodynamics as a problem of fluid-structure interaction

$$\mathbf{u}(\mathbf{x}) = \mathbf{u}_\infty(\mathbf{x}) + \mathcal{S}_\Gamma[\boldsymbol{\xi}](\mathbf{x}) + \mathcal{S}_\gamma[\boldsymbol{\eta}](\mathbf{x}) + \mathcal{D}_\gamma[\boldsymbol{\eta}](\mathbf{x}) + \boldsymbol{\phi}(\mathbf{x},\mathbf{c})\cdot\mathbf{F} + \mathbf{R}(\mathbf{x},\mathbf{c})\cdot T,$$



$$\boldsymbol{\phi}(\mathbf{x},\mathbf{c}) = \frac{1}{4\pi}\left(-\mathbf{I}\log|\mathbf{r}| + \frac{\mathbf{r}\otimes\mathbf{r}}{|\mathbf{r}|^2}\right), \quad \mathbf{R}(\mathbf{x},\mathbf{c}) = \frac{1}{4\pi}\frac{\mathbf{r}^\perp}{\rho^2},$$

$$\mathcal{D}_\gamma[\boldsymbol{\eta}](\mathbf{x}) = \int_\gamma \frac{1}{\pi}\frac{(\mathbf{x}-\mathbf{y})\cdot\hat{\mathbf{n}}_\mathbf{y}}{|\mathbf{x}-\mathbf{y}|^2}\frac{(\mathbf{x}-\mathbf{y})\otimes(\mathbf{x}-\mathbf{y})}{|\mathbf{x}-\mathbf{y}|^2}\boldsymbol{\eta}(\mathbf{y})ds_\mathbf{y},$$

$$\mathbf{x}^{N+1} - \Delta t\mathcal{S}_\Gamma^N[\boldsymbol{\xi}^{N+1}] - \Delta t\mathcal{S}_\gamma^N[\boldsymbol{\eta}^{N+1}] - \Delta t\mathcal{D}_\gamma^N[\boldsymbol{\eta}^{N+1}]$$
$$= \mathbf{x}^N + \Delta t\boldsymbol{\phi}(\mathbf{x}^N,\mathbf{c}^N)\cdot\mathbf{F} + \Delta t\mathbf{R}(\mathbf{x}^N,\mathbf{c}^N)\cdot T$$

$$\mathbf{v} + \omega(\mathbf{x}-\mathbf{c})^\perp - \mathcal{S}_\Gamma^N[\boldsymbol{\xi}^{N+1}] - \frac{1}{2}\boldsymbol{\eta}^{N+1} - \mathcal{S}_\gamma^N[\boldsymbol{\eta}^{N+1}] - \mathcal{D}_\gamma^N[\boldsymbol{\eta}^{N+1}],$$
$$= -v_\theta\mathbf{e}_\theta + \boldsymbol{\phi}(\mathbf{x}^N,\mathbf{c}^N)\cdot\mathbf{F}$$

$$\int_\gamma \boldsymbol{\eta}^{N+1}\,ds = 0, \quad \int_\gamma \boldsymbol{\eta}^{N+1}\cdot(\mathbf{x}^N-\mathbf{c}^N)^\perp\,ds = 0$$

- A rigid particle (γ) inside a vesicle (Γ) under linear shear flow (Veerapaneni, YY, Vlahovska, Blawzdziewicz, PRL, 2011)
- For $\boldsymbol{x}$ on γ $\quad \mathbf{u}(\mathbf{x}) = \mathbf{v} + \boldsymbol{\omega}\times(\mathbf{x}-\mathbf{c})$

$$\int_\gamma \boldsymbol{\tau}\cdot\hat{\mathbf{n}}\,ds = \mathbf{F}, \qquad \mathbf{x}\in\gamma,$$
$$\int_\gamma (\mathbf{x}-\mathbf{c})^\perp\cdot\boldsymbol{\tau}\cdot\hat{\mathbf{n}}\,ds = T, \qquad \mathbf{x}\in\gamma,$$

Vesicle hydrodynamics

- Vesicle hydrodynamics and electrohydrodynamics in free space
  (Vlahovska, Ann. Rev. Fluid Mech.,2019; Kaoui, Biros, Misbah, PRL, 2009; Zhao and Shaqfeh, JFM, 2013;
  Spann, Zhao, Shaqfeh, PF, 2014; Narsimhan, Spann, Shaqfeh, JFM, 2015;
  Gounley, Boedec, Jaeger, Leonetti, JFM, 2016;)

  Nganguia, YY, PRE, 2013

  YY, Veerapaneni, Miksis, JFM 2014

  Quaife, Veerapaneni, YY, PRF, 2019

- Vesicle hydrodynamics in confinement
  (Agarwal and Biros, PRF, 2020, 2022; Kahali, Panigrahi and Chakraborty, Flow, 2024)

  Pak, YY, Marple, Veerapaneni, Stone, PNAS, 2015

  Quaife, Gannon, YY, PRF, 2021

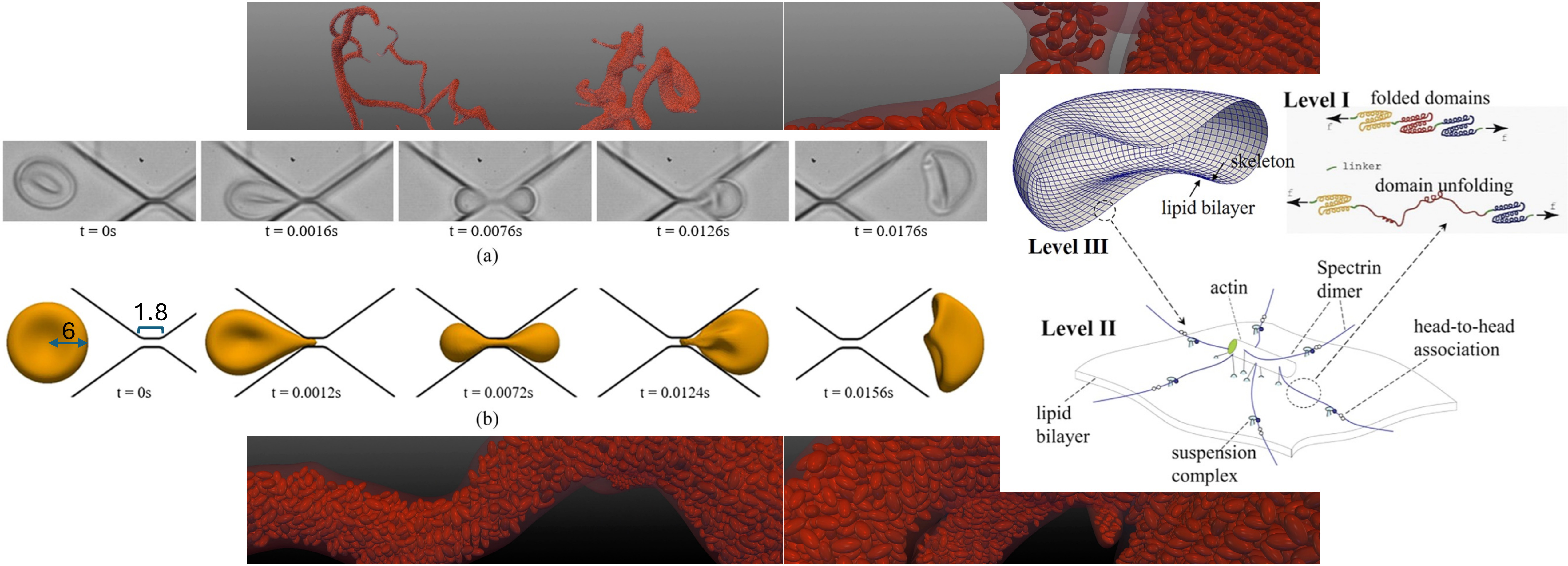
  Gannon, Quaife, YY, Soft Matter, 2024

  Peng, Viallat, YY, Ann. Rev. Fluid Mech., in preparation for 2026 issue

- Vesicle interacting with inclusions (passive, externally forced, active)

  Veerapaneni, YY, Vlahovska, Blawzdziewicz, PRL, 2011

Application 1: Vesicles as model red blood cells



Lu, Morse, Rahimian, Stadler, Zorin, 2019, SC
Lu, Peng, 2019, Phys. Fluids

A multicomponent vesicle under strong confinement

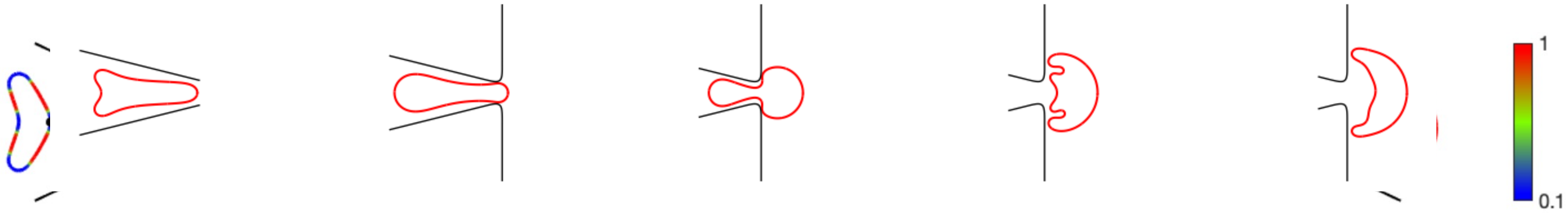
(Gannon, Quaife, YY, Soft Matter, 2024)

$$E_b = \frac{1}{2}\int_\gamma b(u)\kappa^2\, ds, \qquad E_t = \int_\gamma \sigma\, ds, \qquad E_p = \frac{a}{\varepsilon}\int_\gamma \left(f(u) + \frac{\varepsilon^2}{2}|\nabla_\gamma u|^2 \right) ds,$$

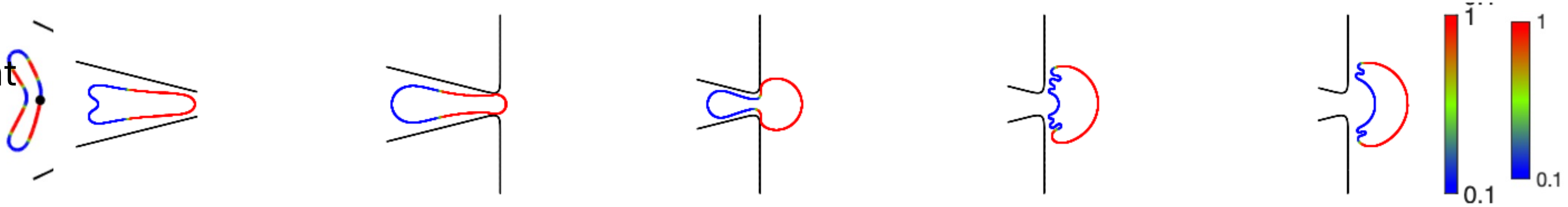
$$\mathbf{f}_b = -(b(u)\kappa\mathbf{n})_{ss} - \frac{3}{2}\left(b(u)\kappa^2\mathbf{s}\right)_s, \quad \mathbf{f}_t = (\sigma\mathbf{s})_s, \quad \mathbf{f}_p = \left(\frac{a}{\varepsilon}\left(f(u) - \frac{\varepsilon^2}{2}u_s^2\right)\mathbf{s}\right)_s$$

$$b(u) = \frac{\beta-1}{2}\tanh\left(3\left(u-\frac{1}{2}\right)\right) + \frac{\beta+1}{2} \qquad f(u) = \frac{1}{4}u^2(1-u)^2$$

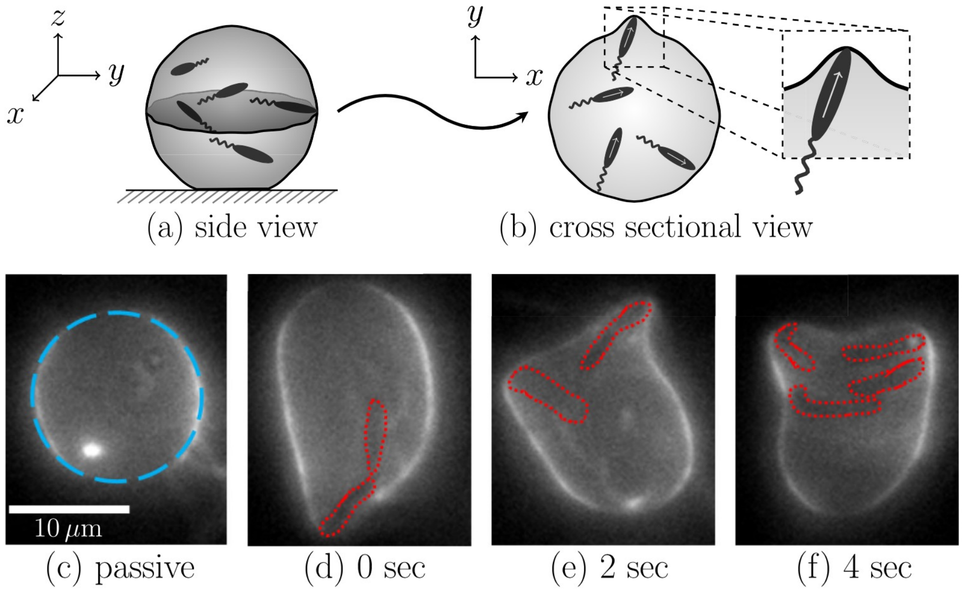
- Single component
- Reduced area = 0.6

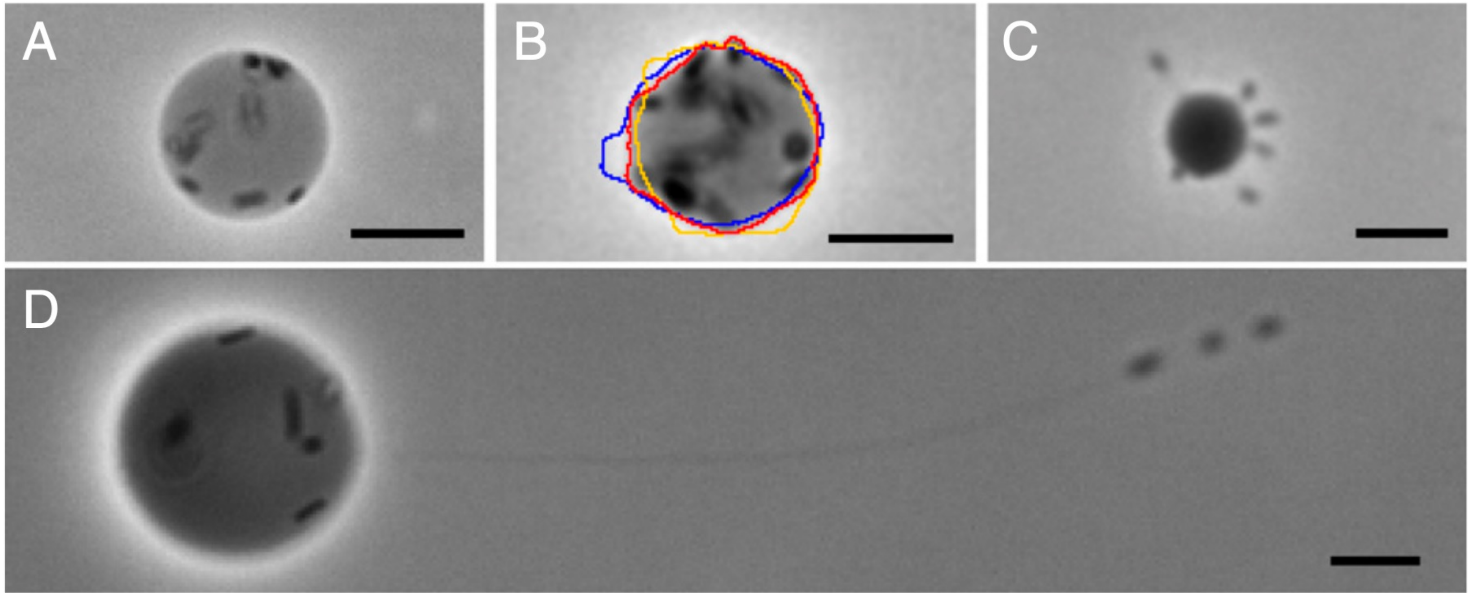


- 45% floppy component
- Reduced area = 0.4



Application 2: vesicle enclosing a suspension of microswimmers

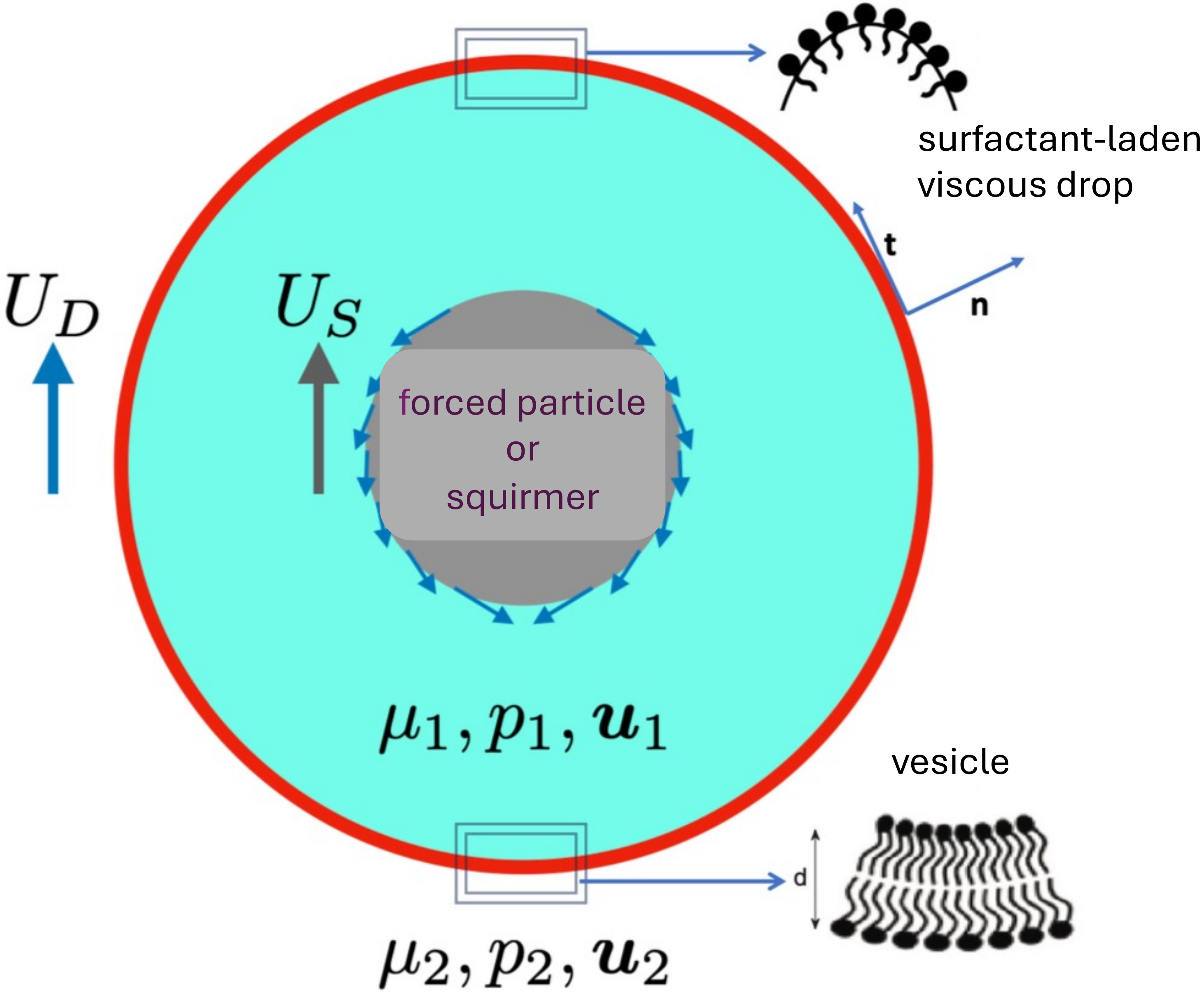


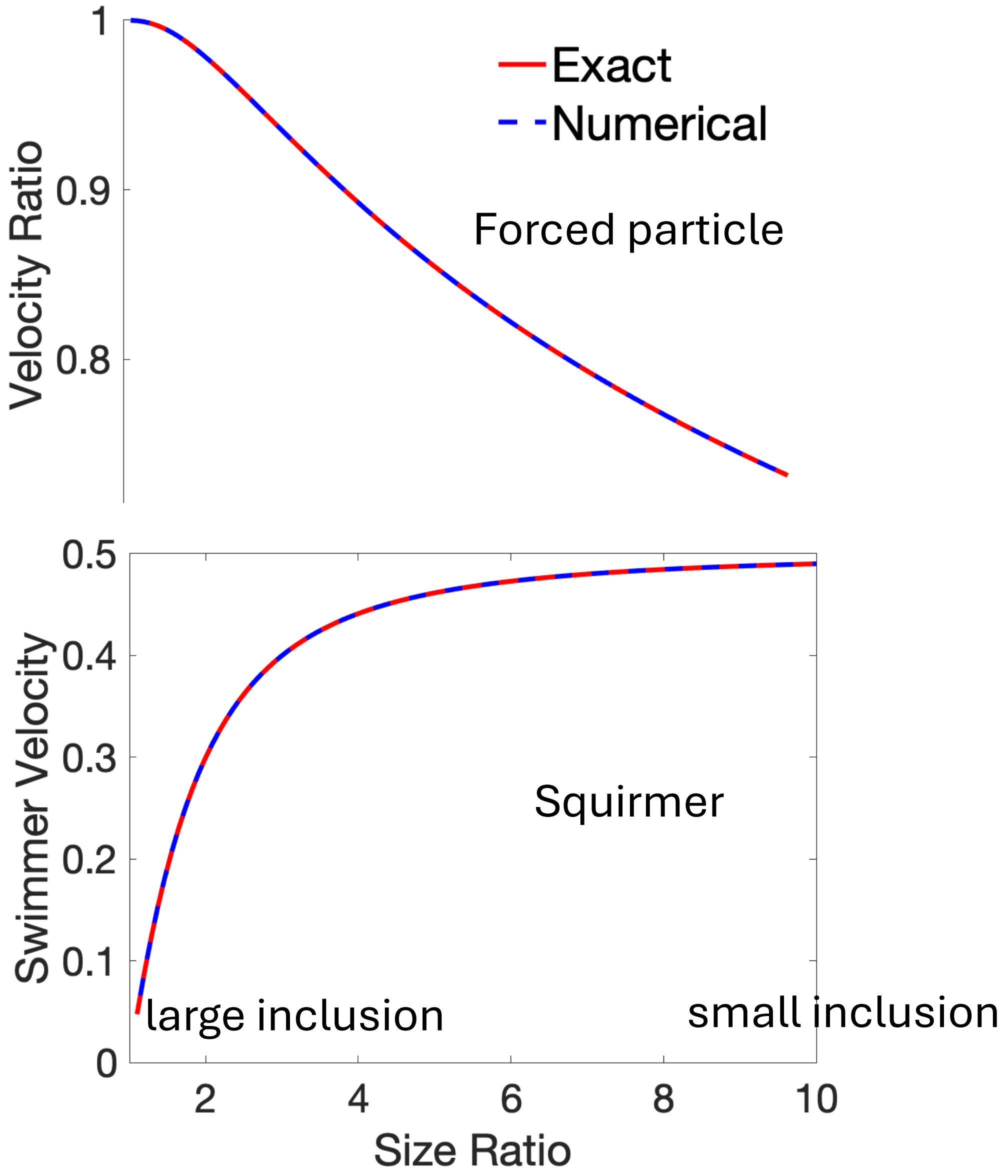


- Giant unilamellar vesicle (GUV) enclosing a suspension of *Bacillus subtilis* PY79 (Takatori and Sahu, PRL, 2020)
- GUV is undeformed when bacteria are non-motile in (c).
- GUV deforms and flattens when bacteria interact with the membrane.

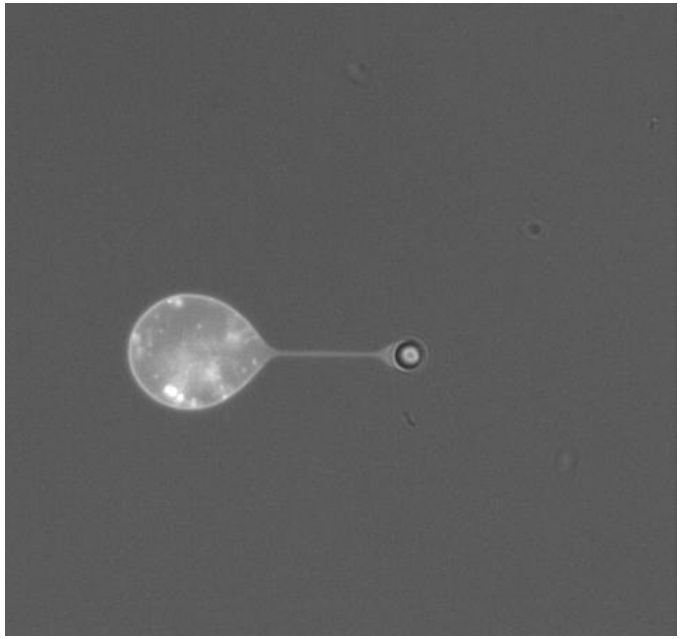
- GUV containing a suspension of *Escherichia coli* bacteria (Nagard *et al*., PNAS, 2022)
- GUV is undeformed when it is tense in A.
- Once deflated in B, C, and D, GUV deforms to various degrees, from mild fluctuations in B to tubular formation in C and D.

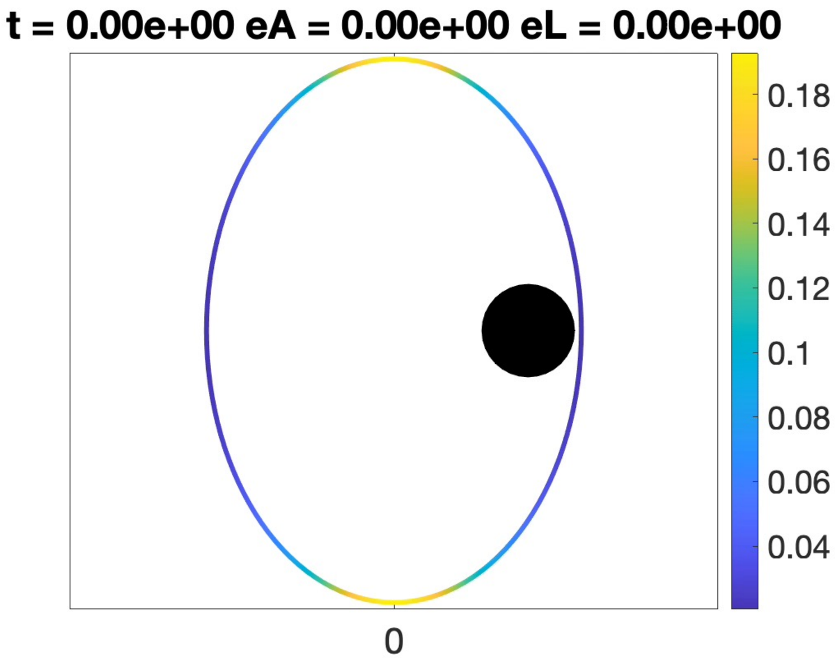
Hydrodynamics of a vesicle enclosing a rigid particle

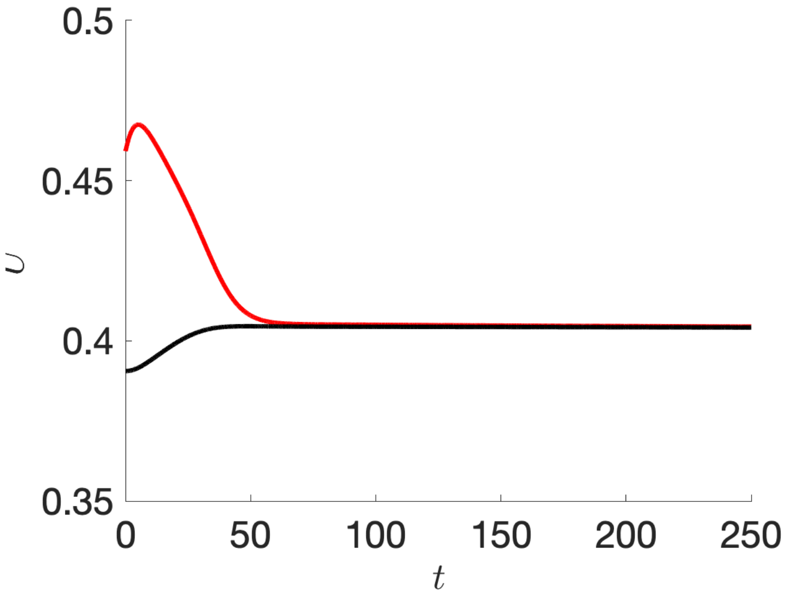




Hydrodynamics of a vesicle enclosing a rigid particle under a magnetic field

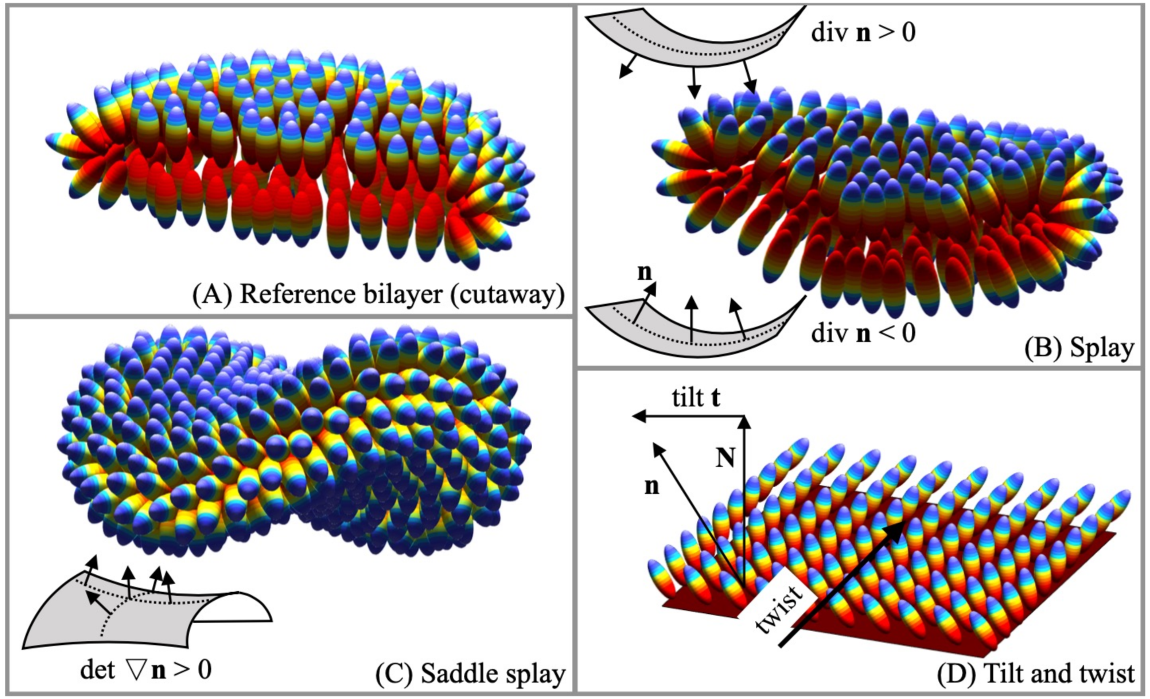


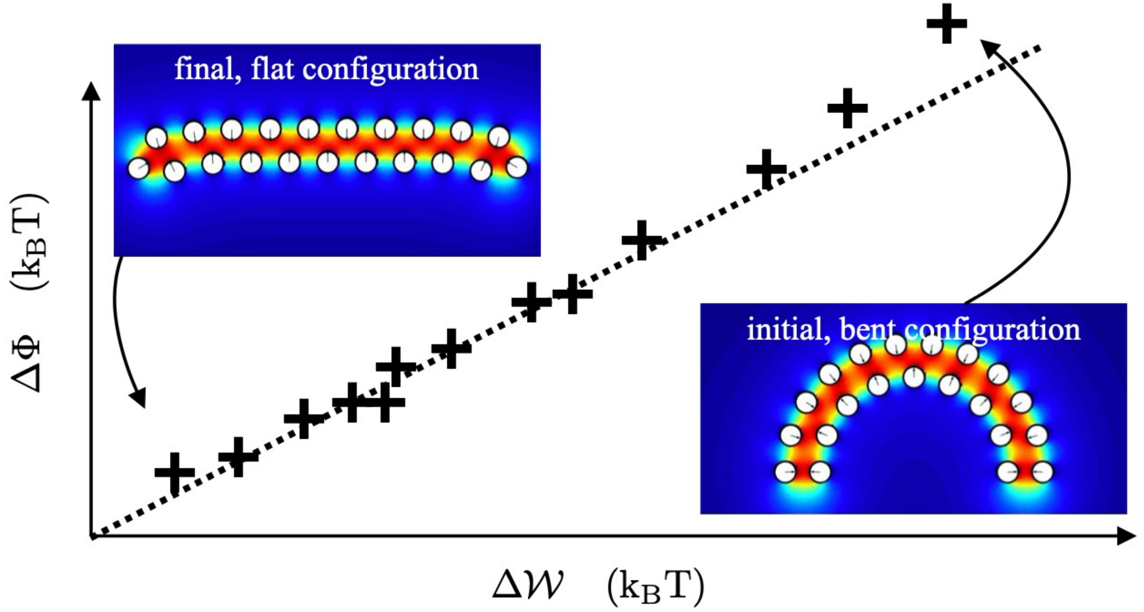




- Vesicle and particle move in unison
- Particle is extremely close to vesicle membrane
- Long tube forms and elongates

Hydrophobic attraction potential between amphiphilic particles





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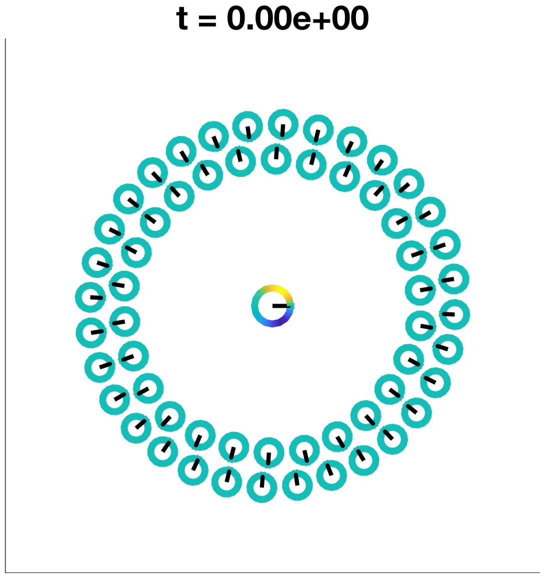
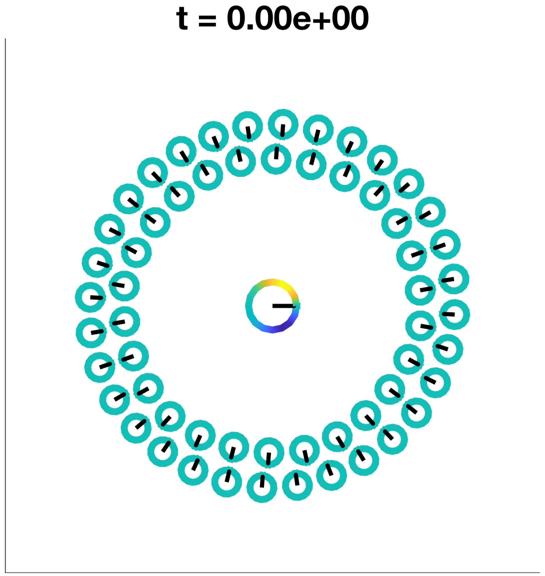
Fu, Ryham, Klockner, Wala, Jiang, YY, SIAM MMS, 2020
Fu, Quaife, Ryham, YY, JFM, 2022
Fu, Ryham, Quaife, YY, PRF, 2023

	HAP	experiment
k_B	$11 \pm 2.5\ \mathrm{k_BT}$	$10\ \mathrm{k_BT}$
k_A	$34\ \mathrm{k_BT}\ \ \mathrm{nm}^{-2}$	30–$40\ \mathrm{k_BTnm}^{-2}$
k_θ	$12\ \mathrm{k_BT}\ \ \mathrm{nm}^{-2}$	$10\ \mathrm{k_BTnm}^{-2}$

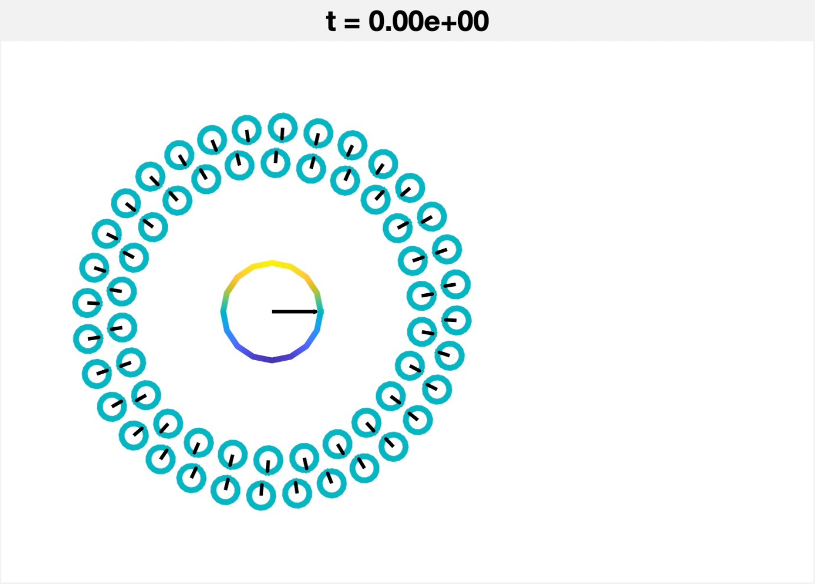
A squirmer inside a janus-particle (JP) vesicle



- Squirmer circling along the (JP) membrane

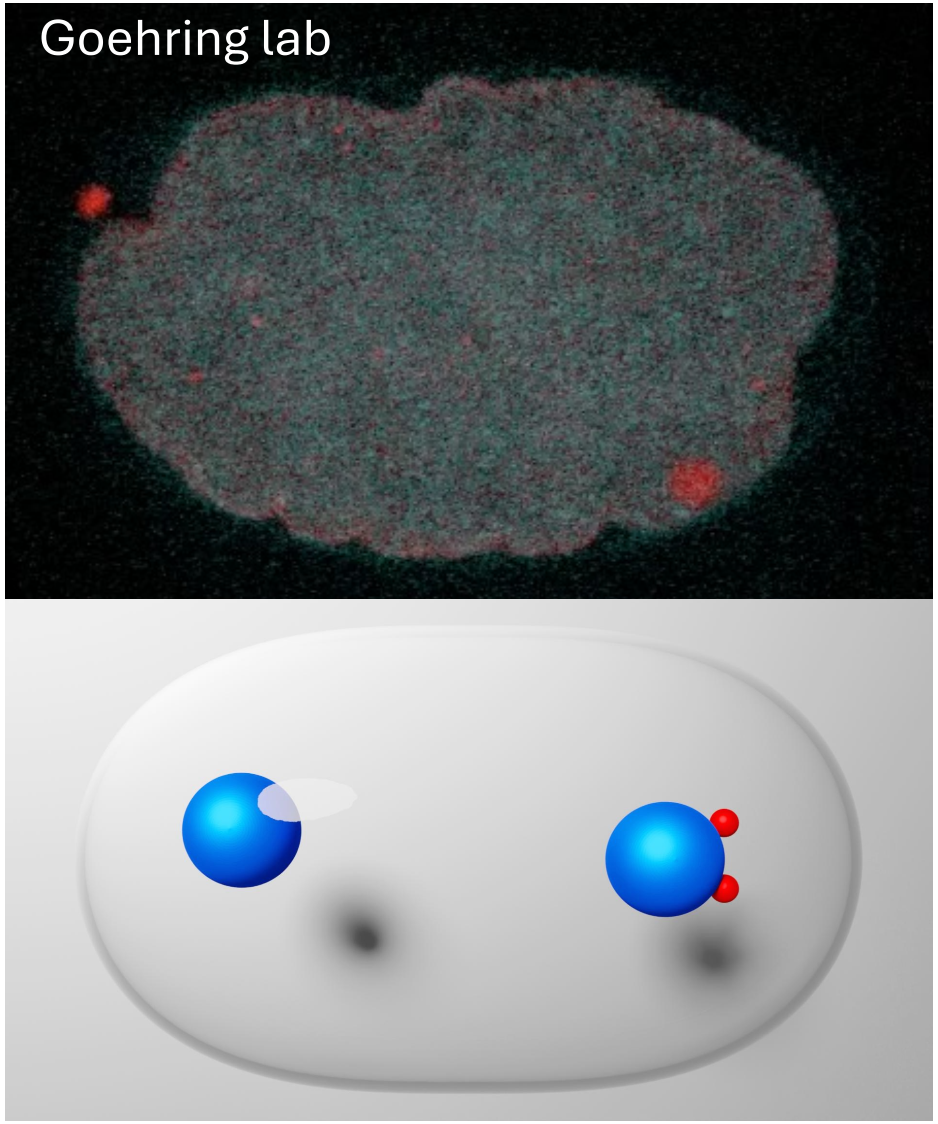


- JP vesicle opens up

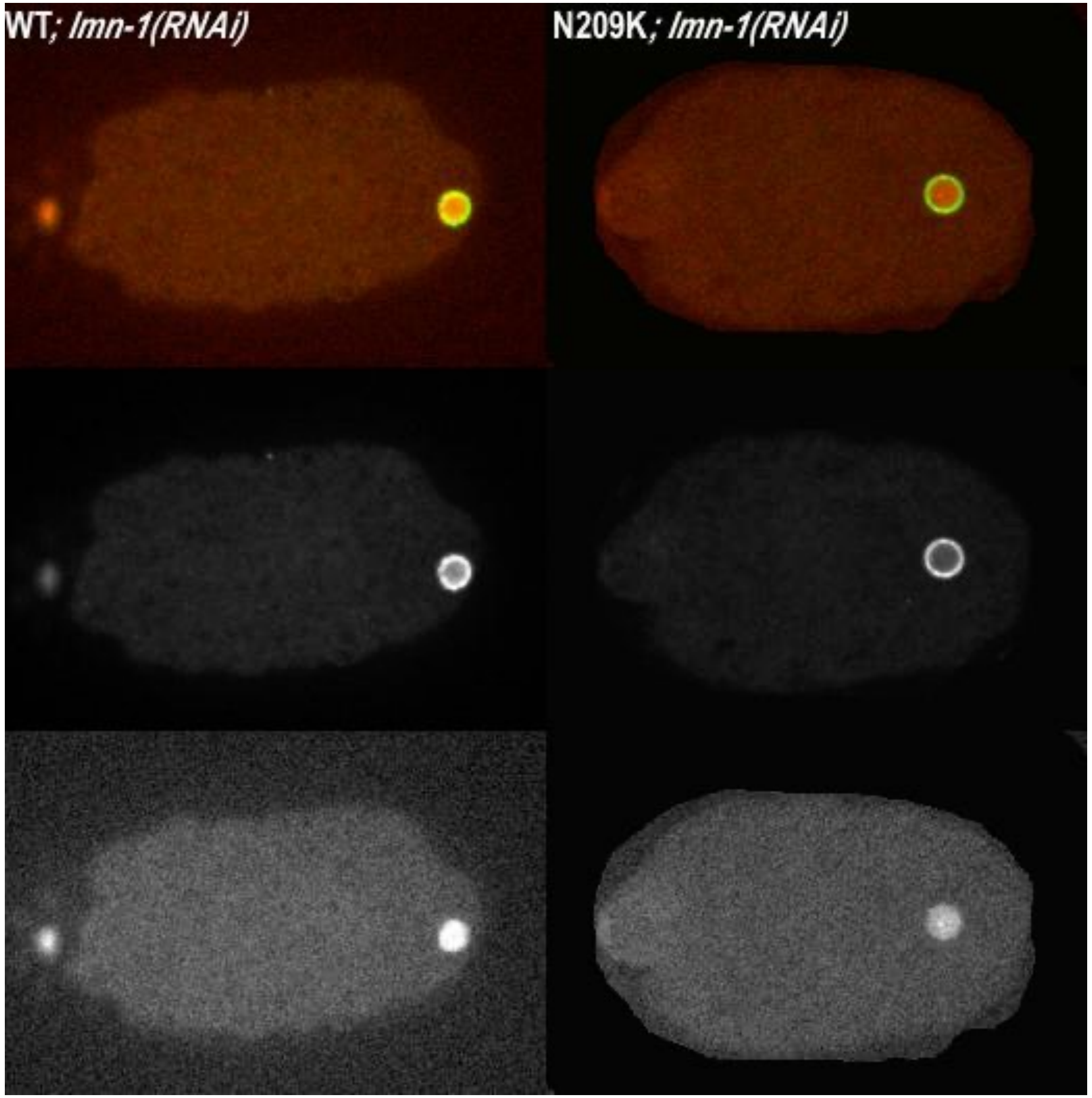


- Squirmer escapes and the JP vesicle reseals

Application 3: deformation of a pronucleus

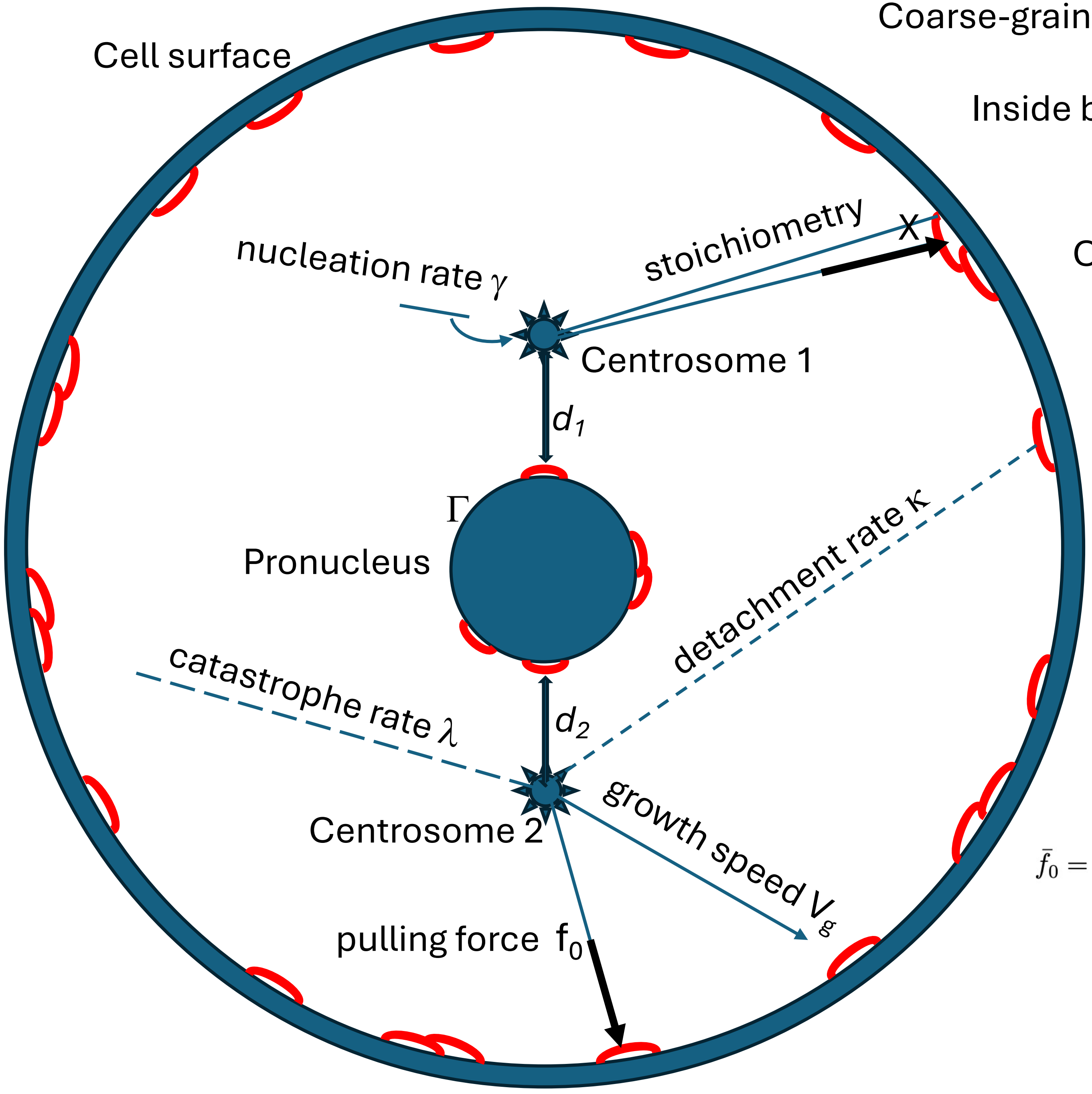


Pronuclei migration in *C. Elegans* embryo
Farhadifar, YY, Shelley



Penfield et al., MBoC, 2018

Coarse-grained stoichiometric model and fluid-structure interactions



Inside bulk:

$$\Delta \mathbf{u} = \nabla p, \quad \nabla \cdot \mathbf{u} = 0,$$

$$\bar{\eta}\dot{\mathbf{X}}_c = \bar{f}_0 \int cP\hat{\boldsymbol{\xi}} da,$$

On Γ:

$$\frac{\partial P}{\partial t} = \left[\left(\dot{\mathbf{X}}_c + \hat{\boldsymbol{\xi}}\right)\cdot\hat{\mathbf{n}}\right]_+ \bar{\gamma}\chi e^{-D/\bar{l}_c}\frac{1-e^{-\bar{\alpha}c(1-P)}}{\bar{\alpha}c} - \bar{\kappa}P,$$

$$\partial_t c + \nabla_s \cdot \left[\left(\mathbf{v}_m + (\mathbf{I}-\hat{\mathbf{n}}\hat{\mathbf{n}})\cdot\frac{-\bar{f}_0 cP\hat{\boldsymbol{\xi}}}{\bar{\eta}_m}\right)c\right] + (\mathbf{u}\cdot\hat{\mathbf{n}})\,(\nabla_s\cdot\hat{\mathbf{n}})c = \frac{1}{Pe}\nabla_s^2 c,$$

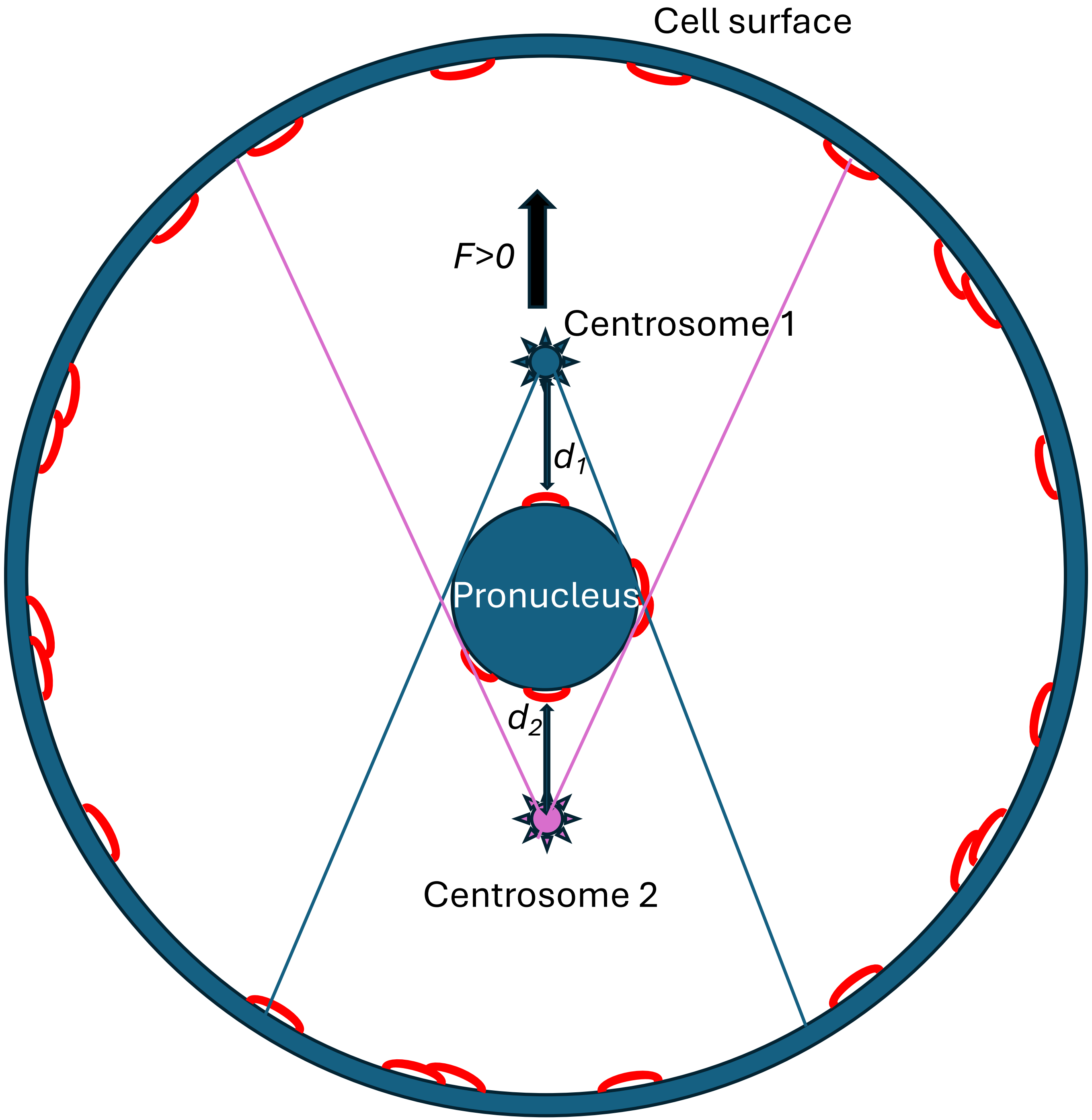
$$[\![\mathbf{T}]\!]\cdot\hat{\mathbf{n}} = -\bar{k}_b\mathbf{x}_{ssss} + (\sigma\mathbf{x}_s)_s + \bar{f}_0\left(-cP\hat{\boldsymbol{\xi}}\right),$$

$$\frac{d\mathbf{x}(\Gamma)}{dt} = \mathbf{u}|_\Gamma + \bar{\beta}\left[\left(-\bar{k}_b\mathbf{x}_{ssss} + (\sigma\mathbf{x}_s)_s + \left(-\bar{f}_0 cP\hat{\boldsymbol{\xi}}\right)\right)\cdot\hat{\mathbf{n}}\right]\hat{\mathbf{n}},$$

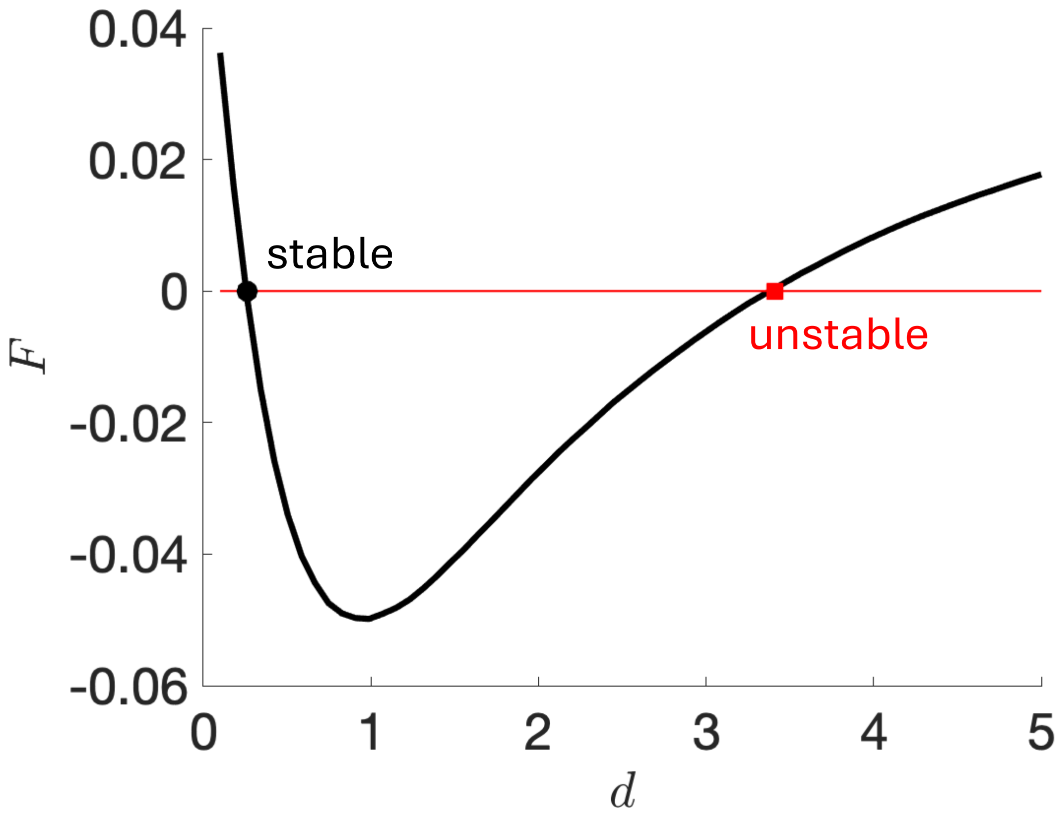
$$\bar{\eta} = \frac{\eta}{\mu R}, \quad \bar{k}_b = \frac{k_b}{\mu V_g R^2}, \quad \bar{\beta} = \frac{\beta\mu}{R},$$

$$\bar{f}_0 = \frac{f_0 c_0}{\mu V_g/R}, \quad \bar{\gamma} = \frac{\gamma}{R/V_g}, \quad \bar{\kappa} = \frac{\kappa}{R/V_g}, \quad \bar{\eta}_m = \frac{\eta_m}{\mu R}, \quad Pe = \frac{V_g R}{D_s}, \quad \bar{l}_c = \frac{l_c}{R}, \quad \bar{\alpha} = c_0\pi r_m^2.$$

Lu, Barnett, YY, Farhadifar and Shelley



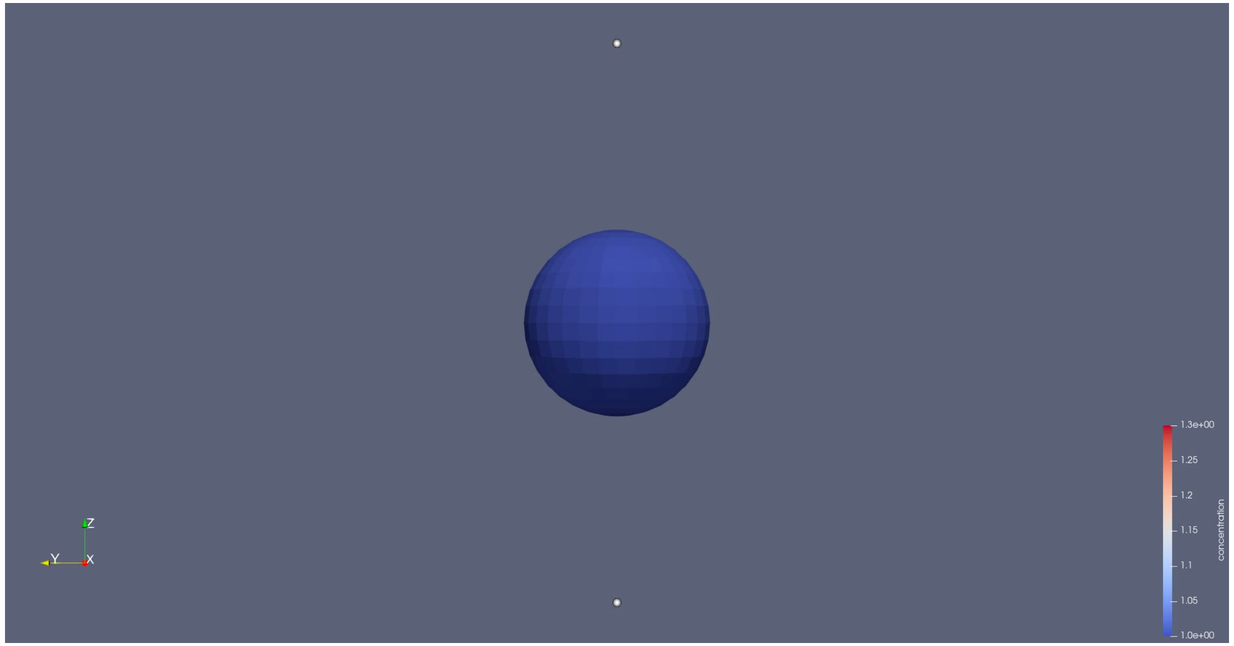
- 100 motors on the cell surface, and parameter values from previous works on centrosome dynamics



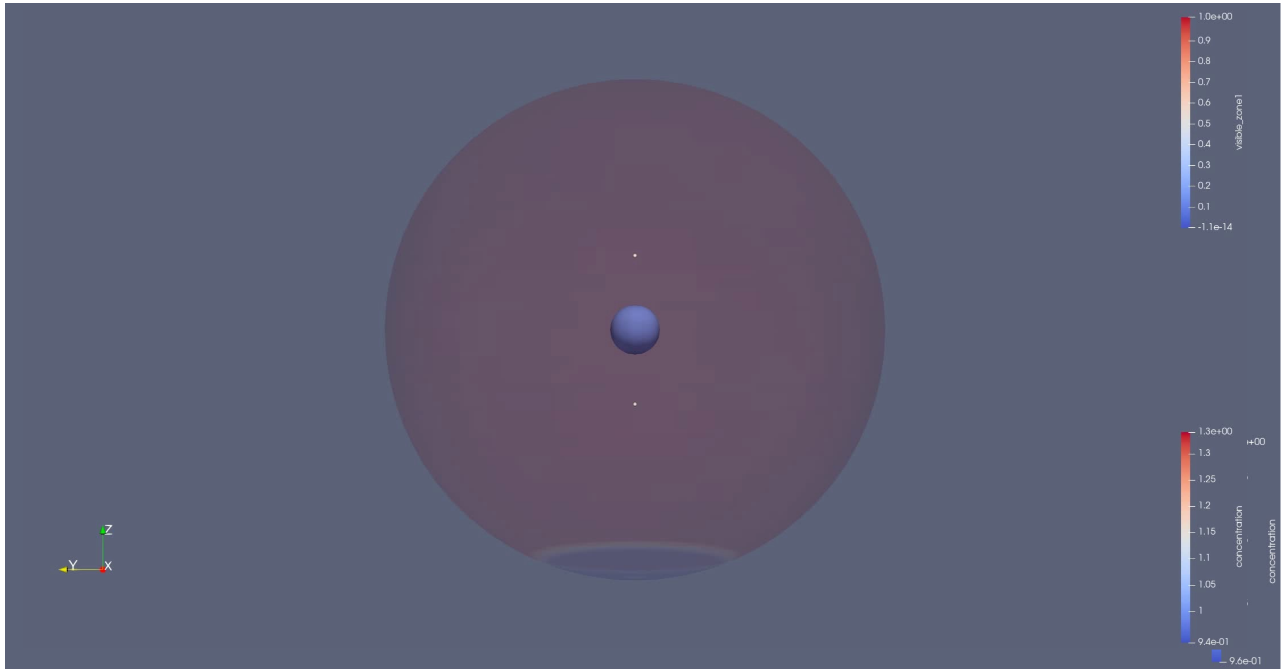
Lu, Barnett, YY, Farhadifar and Shelley

Spherical vesicle (inextensible)

- With permeability β=0, a spherical vesicle stays spherical
- CFG distribution stays nearly uniform for large CFG drag η_m in the membrane



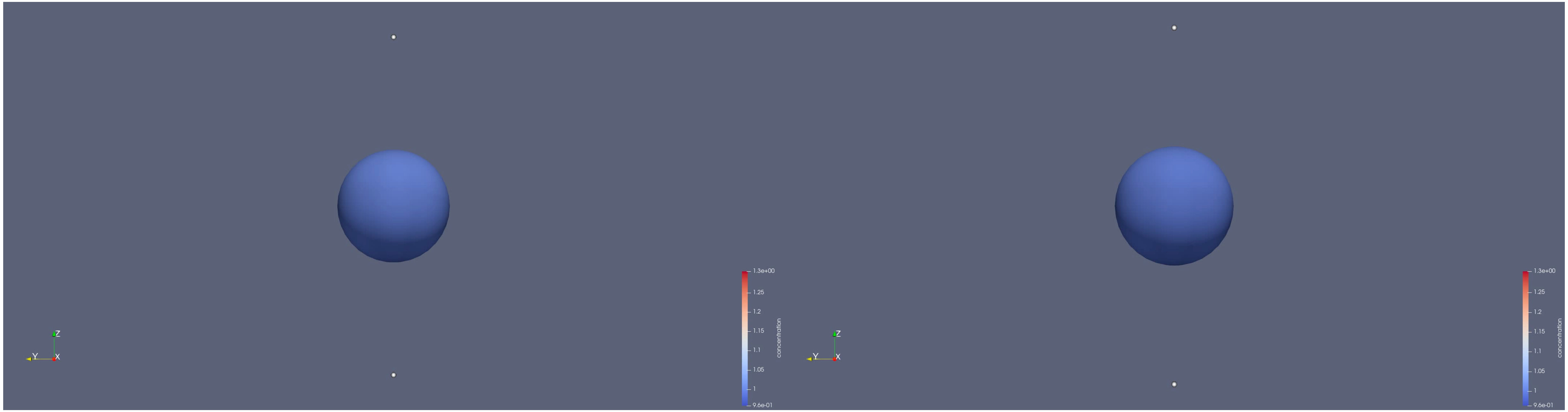
(nearly) uniform distribution of CFGs



CFGs pulled to the poles for small drag η_m

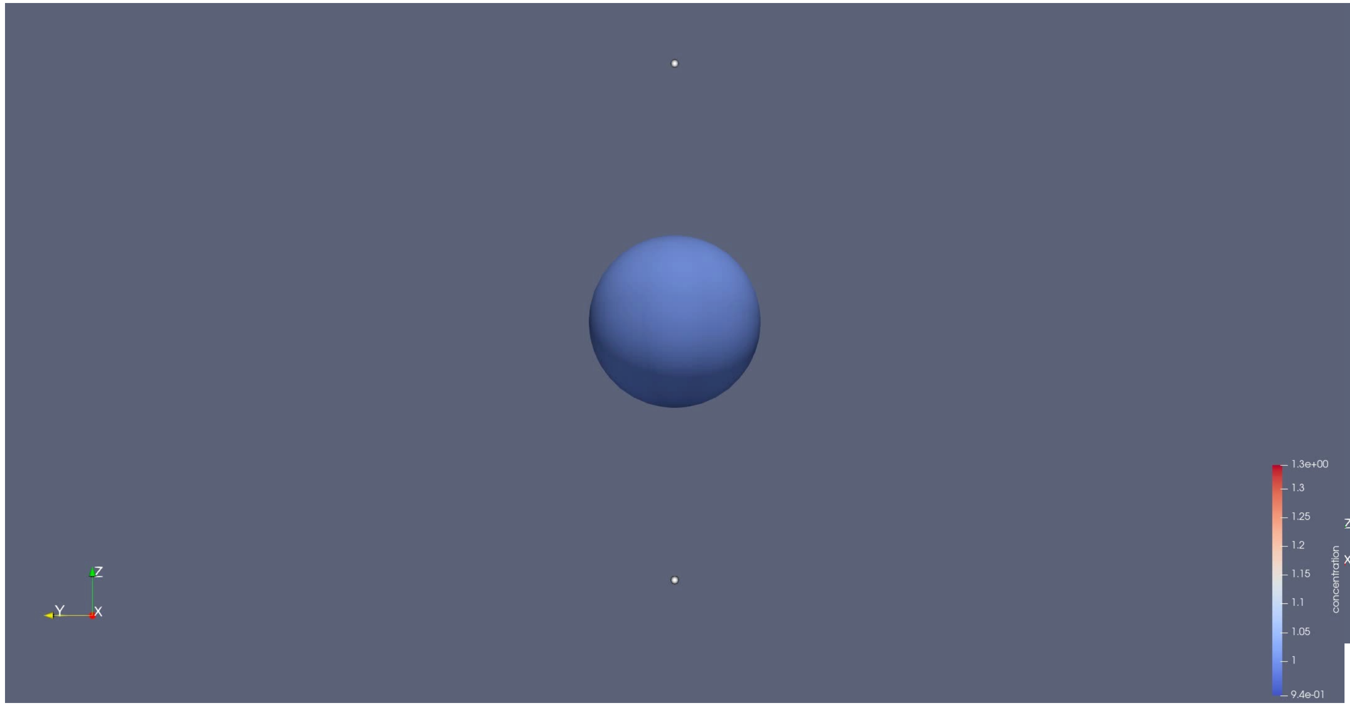
Semi-permeabile membrane deforms by pulling forces ($\beta = 10^{-5}$ and $\eta_m = 10^2$)

$\kappa_b = 10^{-2}$ $\kappa_b = 10^{-1}$

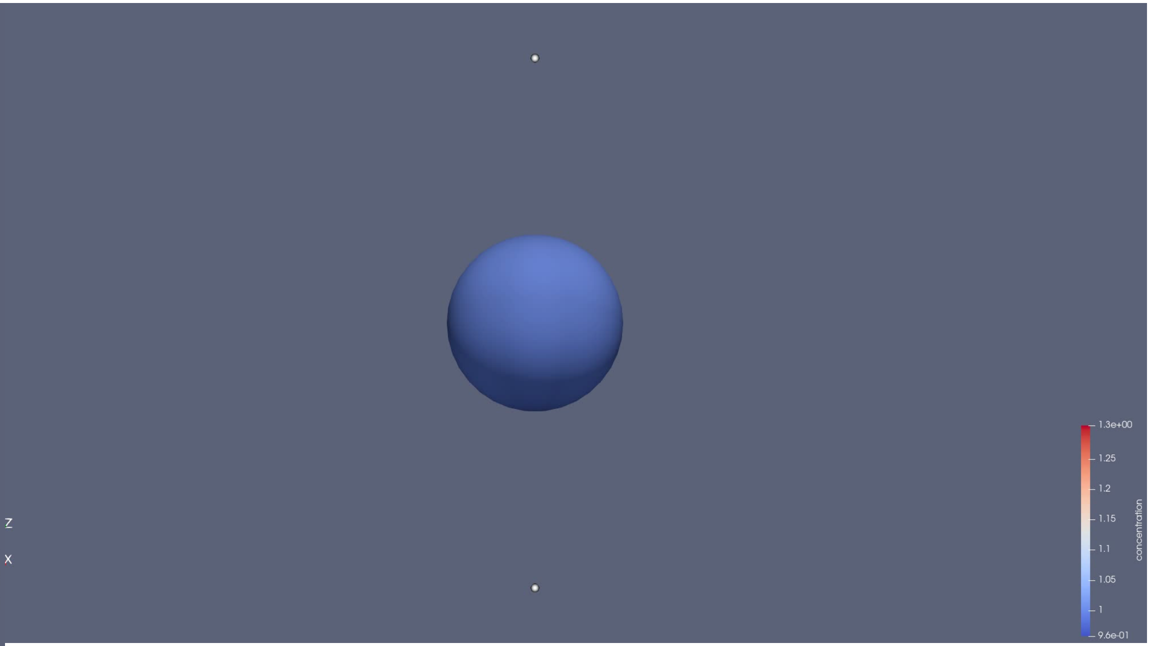


Semi-permeabile membrane deforms by pulling forces ($\kappa_b = 10^{-2}$ and $\eta_m = 10^2$)

$\beta=10^{-3}$



$\beta=10^{-5}$



Questions for the workshop:

For fluid-structure interactions in Stokes flow,

Q1:....how do we resolve near contact when a rigid particle is actively moving toward a lipid bilayer membrane...

Q2:....how do we model/simulate a rupturing/open lipid bilayer membrane...

Q3:....how do we address surface transport on an extremely deformed lipid bilayer membrane...

in the boundary integral framework?