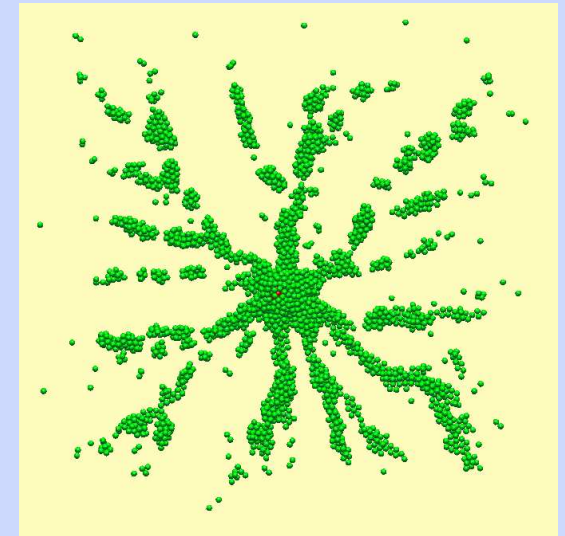
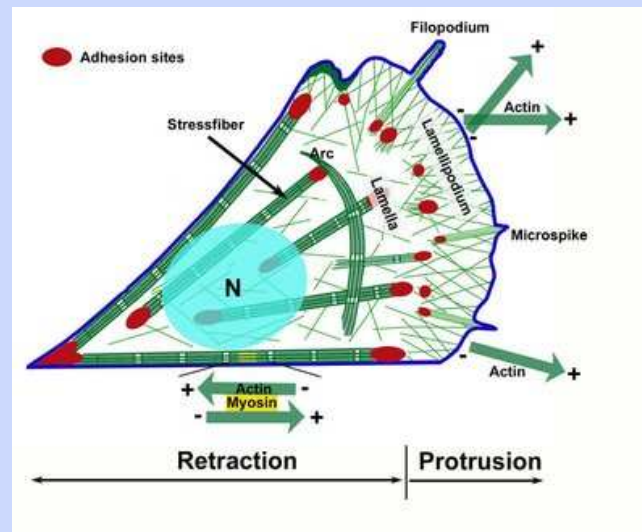
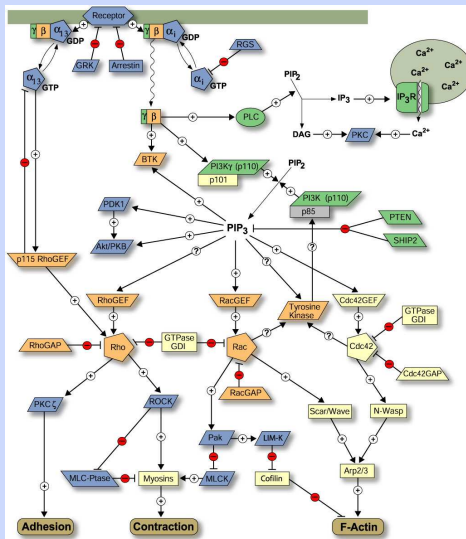


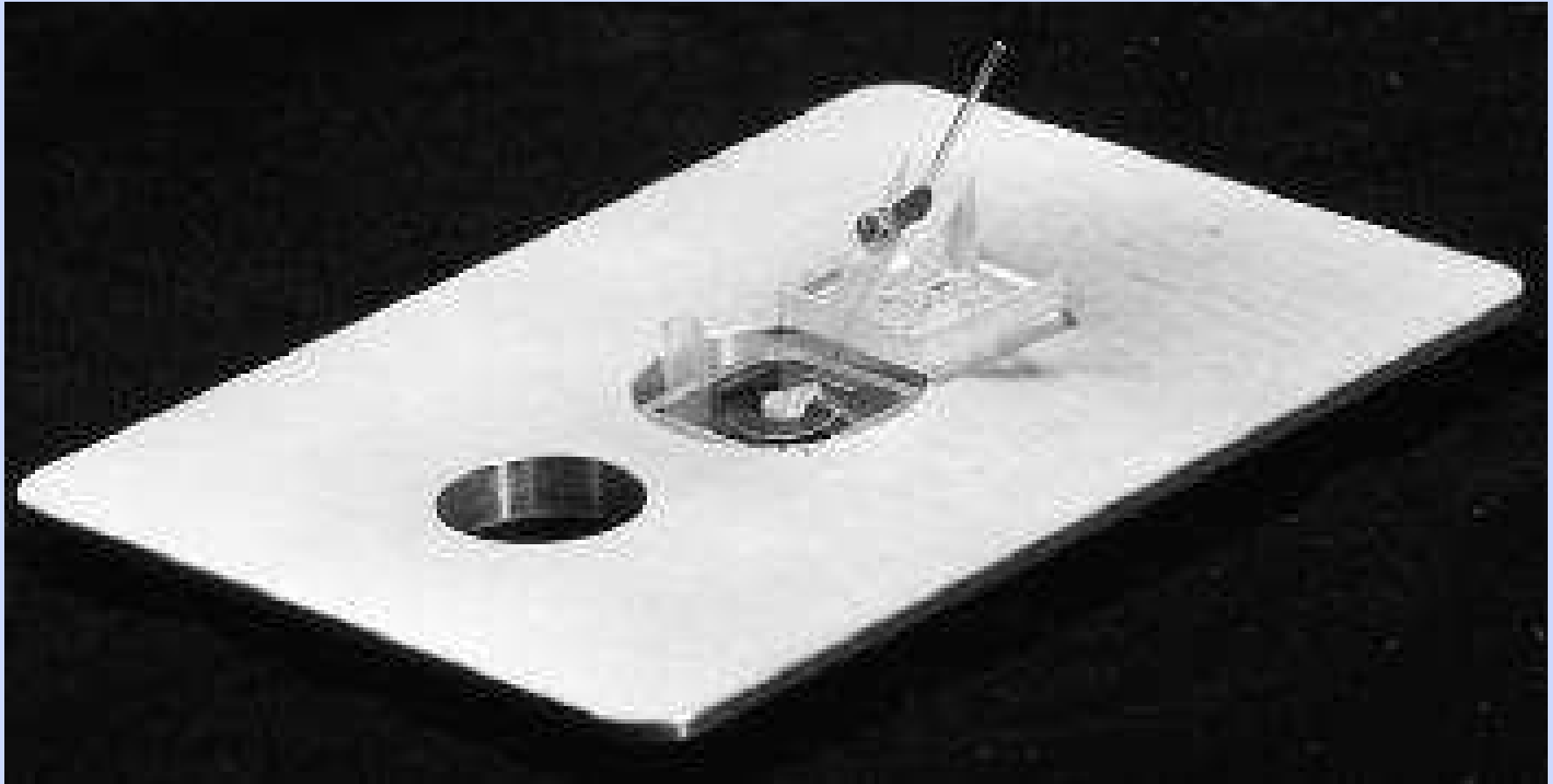
From Crawlers to Swimmers- Mathematical and Computational Problems in Cell Motility

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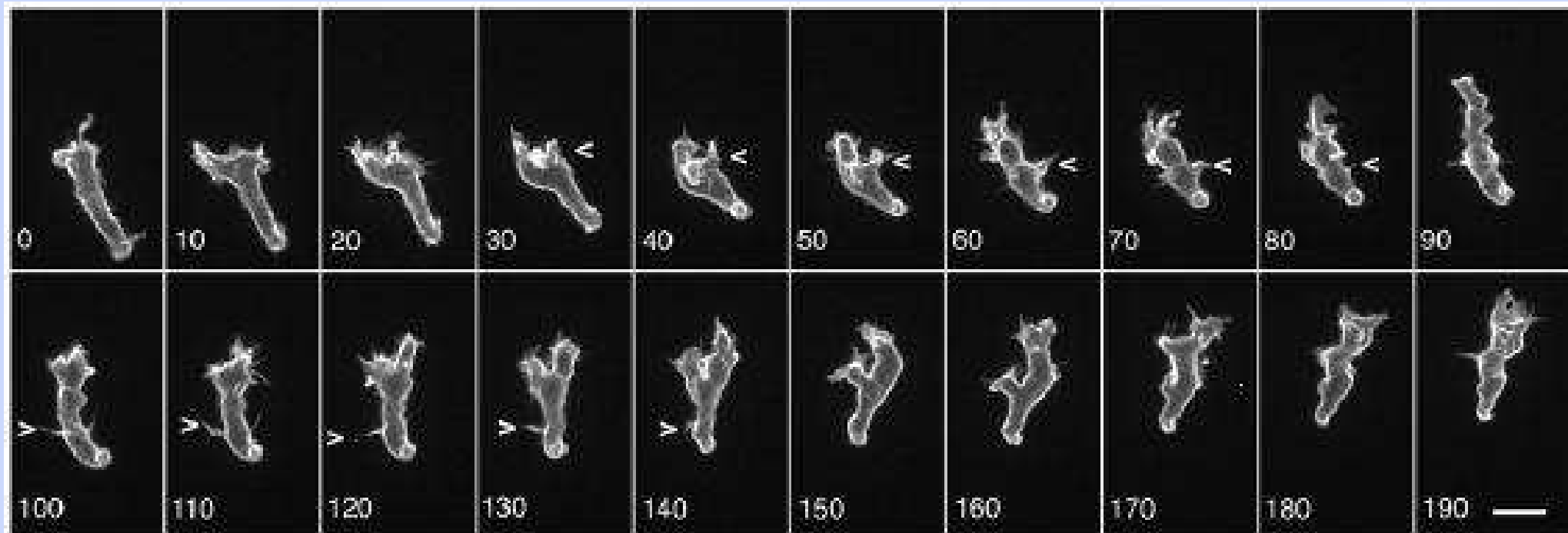


Edinburgh – Oct. 2017 – Lecture 2

Dicty can also swim ..



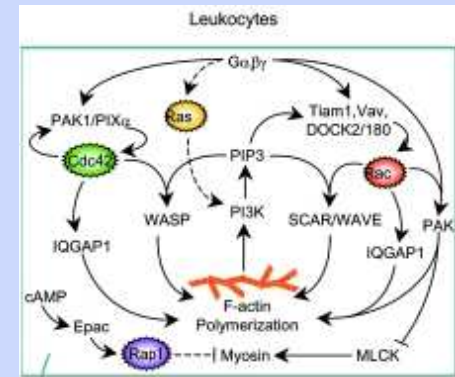
.. and they undergo big shape changes in swimming



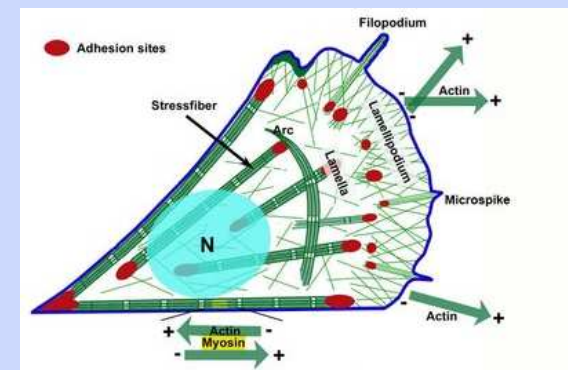
Dictyostelium amoebae and neutrophils can swim N. P. Barry and M. S. Bretscher, PNAS, 2010, 107 11376-11380

Recall the three three major problems ...

- The transduction problem — how are extracellular signals transduced into intracellular signals that can be used to control the shape changes. (Module I)



- The interior problem — how does the cell control the shape changes that give rise to motion. (Module II)



- The exterior problem — how do the shape changes give rise to motion, how fast do they move, and how efficient is the motion. (Module III)



Today we do the exterior problem ..

The governing equations for motion in an incompressible Newtonian fluid of density ρ , viscosity μ , and velocity \mathbf{u} , are

$$\rho \frac{\partial \mathbf{u}}{\partial t} + \rho(\mathbf{u} \cdot \nabla) \mathbf{u} = \nabla \cdot \boldsymbol{\sigma} + \mathbf{f} = -\nabla p + \mu \Delta \mathbf{u} + \mathbf{f},$$
$$\nabla \cdot \mathbf{u} = 0$$

$\boldsymbol{\sigma} = -p\boldsymbol{\delta} + \mu(\nabla \mathbf{u} + (\nabla \mathbf{u})^T)$ is the viscous stress tensor and \mathbf{f} is the external force field.

Consider the effects of controlled changes in the shape of a swimmer moving through such a fluid, neglect body forces (or absorb them in the pressure) and scale the Navier-Stokes equations to obtain

$$\text{Re} \left[\text{Sl} \frac{\partial \mathbf{u}}{\partial t} + (\mathbf{u} \cdot \nabla) \mathbf{u} \right] = -\nabla p + \nabla^2 \mathbf{u}$$
$$\nabla \cdot \mathbf{u} = 0$$

where $\text{Re} = \rho L V / \mu$ is the Reynolds number, $\text{Sl} = \omega L / U$ is the Strouhal number and ω is a characteristic frequency of the shape changes.

Characteristic Reynolds numbers are ..

	<i>Reynolds Number</i>
A large whale swimming at 10 m s^{-1}	300,000,000
A tuna swimming at the same speed	30,000,000
A duck flying at 20 m s^{-1}	300,000
A large dragonfly going 7 m s^{-1}	30,000
A copepod in a speed burst of 0.2 m s^{-1}	300
Flapping wings of the smallest flying insects	30
An invertebrate larva, 0.3 mm long, at 1 mm s^{-1}	0.3
A sea urchin sperm advancing the species at 0.2 mm s^{-1}	0.03
A bacterium, swimming at 0.01 mm s^{-1}	0.00001

The small size and slow speed of cells considered here leads to LRN flows, and in this regime cells move by exploiting the viscous resistance of the fluid.

For example, Dd amoebae have a typical length $L \sim 25 \mu\text{m}$ and can swim at $U \sim 3 \mu\text{m}/\text{min}$,

Assuming the medium is water ($\rho \sim 10^3 \text{ kg m}^{-3}$, $\mu \sim 10^{-3} \text{ Pa} \cdot \text{s}$), and the deformation frequency $\omega \sim 1/s$, $Re \sim \mathcal{O}(10^{-6})$ and $Sl \sim \mathcal{O}(10^{-4})$.

The Stokes problem for LRN flows

Thus the problem is to solve the Stokes equations

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

for a specified sequence of shape changes of the boundary. Notice that time does not appear in these equations, and therefore if (\mathbf{u}, p) is a solution then so is $(-\mathbf{u}, -p)$.

- When can the swimmer propel itself by shape deformations?

It's easier to say when it can't – this is Purcell's *scallop theorem* —

If the sequence of shapes in a cyclic time-periodic stroke is identical when viewed under time-reversal, then there is no net motion per cycle.

- Thus if a scallop can only open and close its valves, it cannot swim.

E. Purcell, Life at low Reynolds number, Amer. J. Physics, 1977.



Swimming at low Reynolds number

Let $\mathcal{B}(t)$ and \mathbf{V} be the boundary and velocity of the swimmer. Set $\mathbf{V} = \mathbf{v} + \mathbf{U}$ where \mathbf{v} defines the intrinsic shape deformation and \mathbf{U} is the rigid motion.

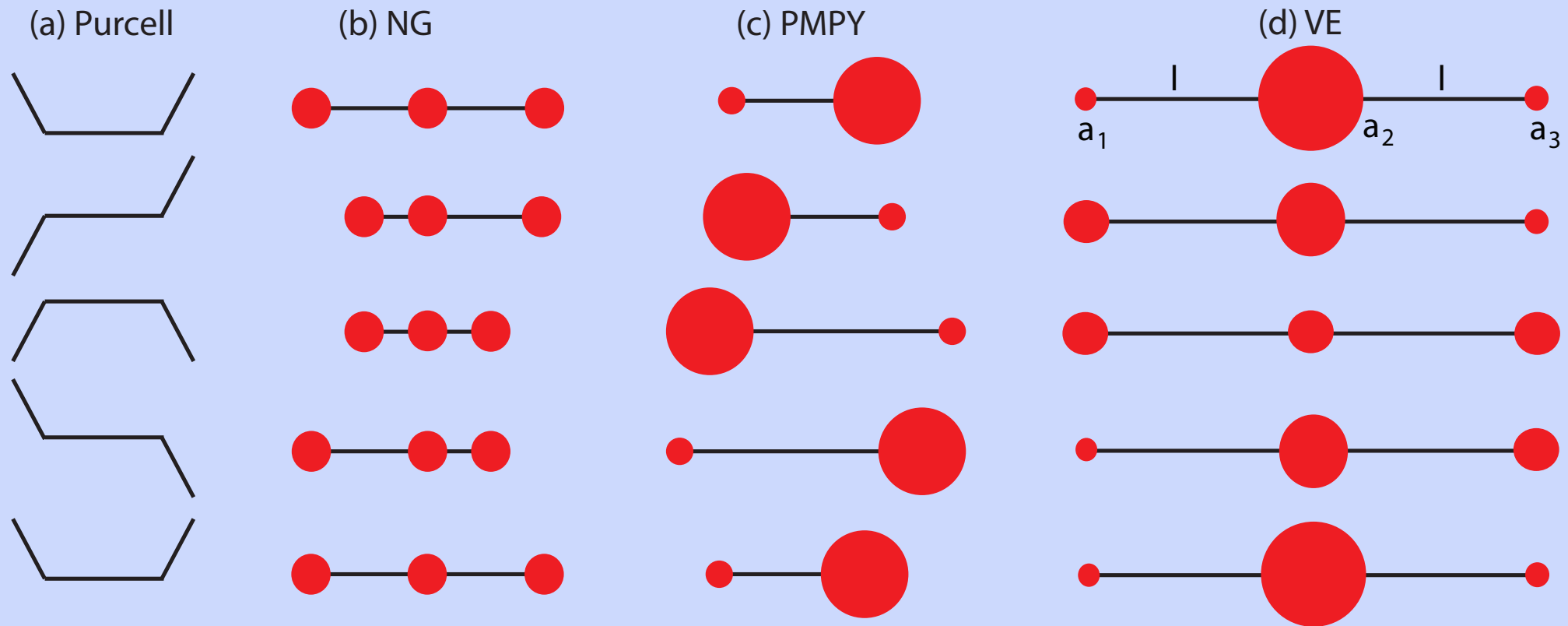
A *cyclic swimming stroke* is a T-periodic sequence of shapes.

The canonical LRN self-propulsion problem is: *given a cyclic shape deformation by specifying \mathbf{v} , solve the Stokes equations subject to*

$$\sum \mathbf{F}_i = 0, \quad \sum \mathbf{\Gamma}_i = 0, \quad \mathbf{u}|_{\mathcal{B}} = \mathbf{V}, \quad \mathbf{u}|_{\mathbf{x} \rightarrow \infty} = \mathbf{0}, \quad (1)$$

- A general sequence $\mathcal{S}(t)$ of shape changes is not an admissible motion, since it will produce forces and torques, but the swimmer has to be force and torque free.
- An admissible motion will also include rigid translations and rotations that generate counter flows that exactly cancel the forces and torques.

Discrete models of swimmers



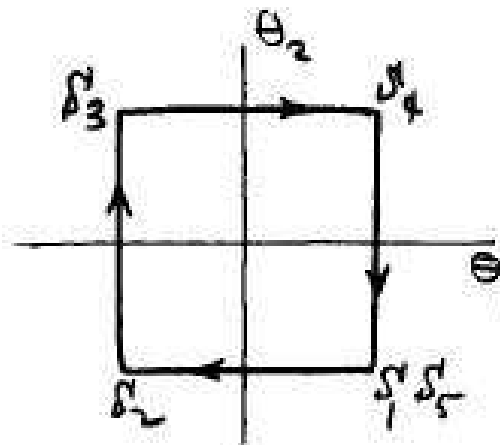
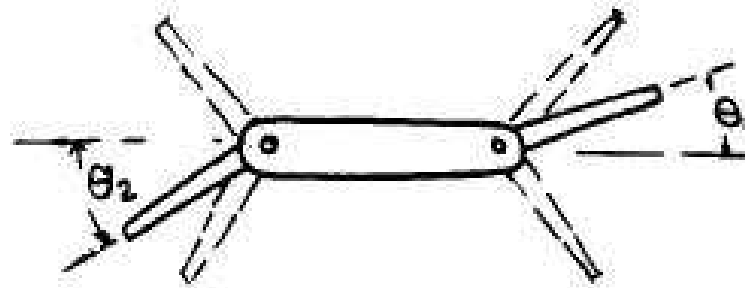
(a) Purcell's 3-link swimmer

(b) Najafi-Golestanian's 3-sphere model (NG)

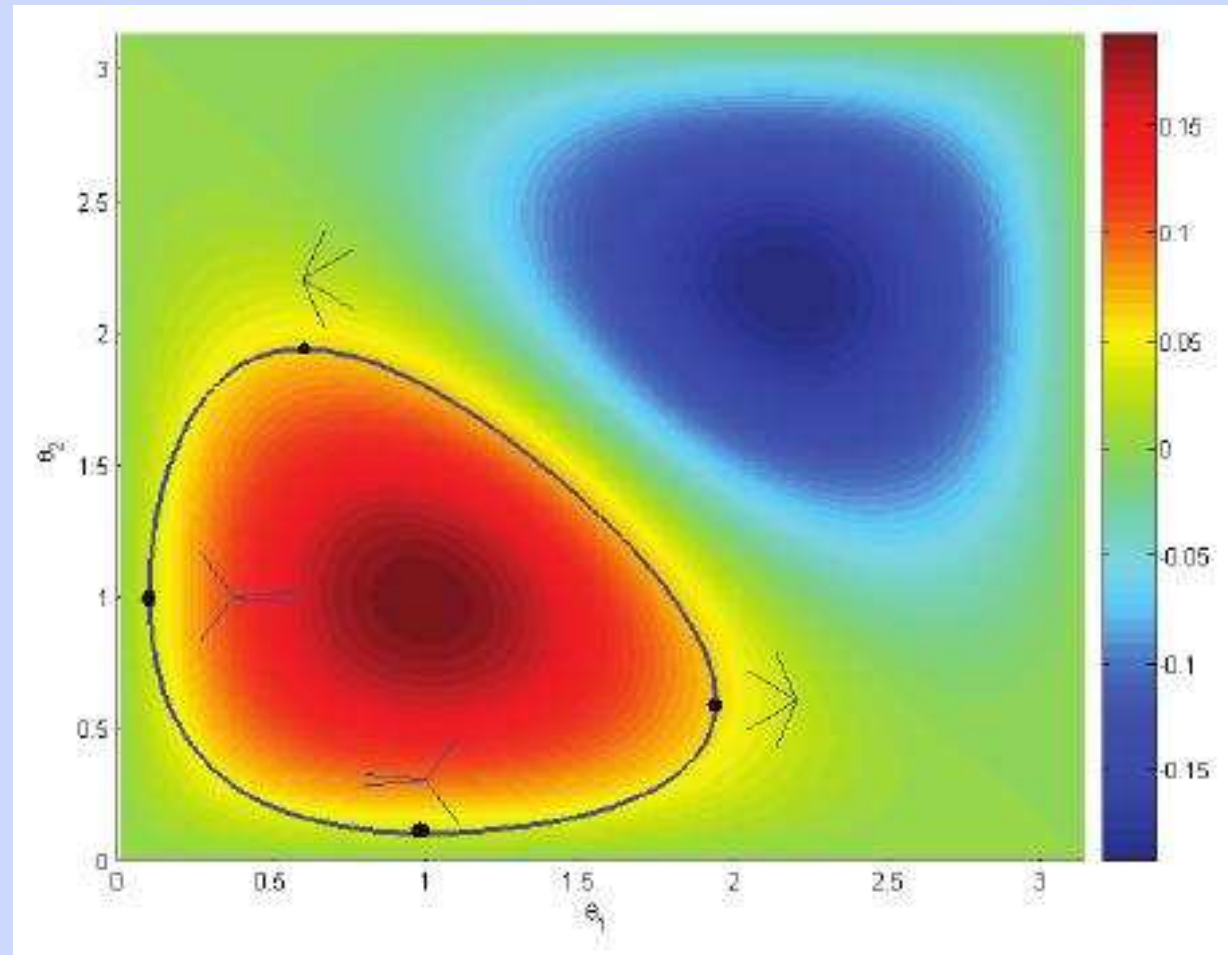
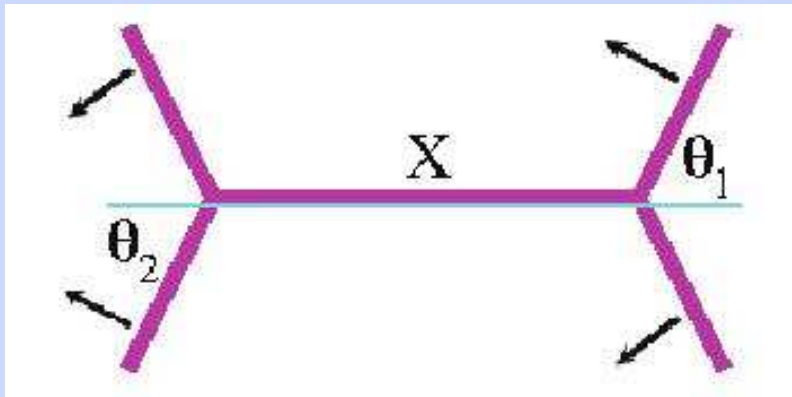
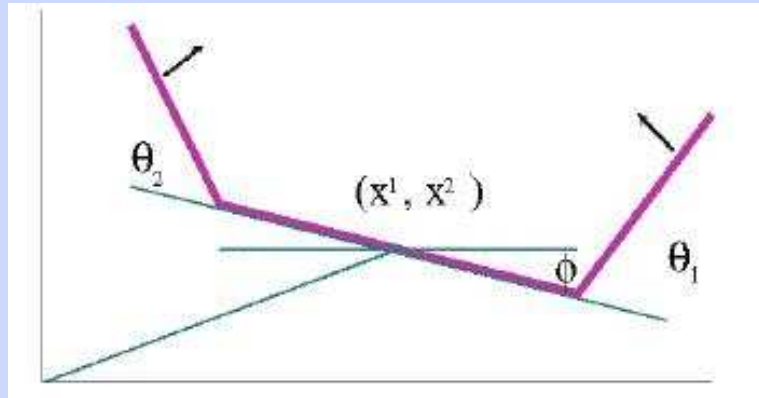
(c) Pushmepullyou (PMPY)

(d) The 3-sphere volume-exchange model (VE)

Purcell's swimmer



Analysis of Purcell's swimmer



A geometric theory of swimming: Purcell's swimmer and its symmetrized cousin, Avron and Raz, New J. Phys, (2008).

The free-space Greens function

Thus the problem is to solve the Stokes equations

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

Take the divergence of the momentum equation and apply the continuity equation to show that p is harmonic

$$\nabla^2 p = 0$$

and take the Laplacian to show that \mathbf{u} is biharmonic

$$\nabla^4 \mathbf{u} = \mathbf{0}.$$

The free space Green's function or Stokeslet, and the pressure vector have the form

$$\mathbf{G}(\mathbf{x}, \mathbf{x}_0) = \frac{1}{r} \left[\mathbf{I} + \frac{\mathbf{r}\mathbf{r}}{r^2} \right] \quad \mathbf{p} = 2 \frac{\mathbf{r}}{r^3}$$

where \mathbf{I} is the unit second-rank tensor, $\mathbf{r} = \mathbf{x} - \mathbf{x}_0$, and $r = |\mathbf{x} - \mathbf{x}_0|$. Thus the velocity and pressure fields generated by a point force \mathbf{f} at the origin are

$$\mathbf{u}(\mathbf{x}) = \frac{\mathbf{G}(\mathbf{x}, \mathbf{0})}{8\pi\mu} \cdot \mathbf{f} \quad p = \frac{1}{8\pi} \mathbf{p}(\mathbf{x}, \mathbf{0}) \cdot \mathbf{f}.$$

$\mathbf{G}(\mathbf{x}, \mathbf{0})/(8\pi\mu)$ is called the *Stokeslet* or the Oseen tensor.

Some basic solutions of the Stokes problem

Other basic solutions that are needed are those for a rigid sphere pulled through a quiescent fluid, for a radially expanding or contracting sphere, and for the interaction between two spheres.

When a sphere of radius a is pulled through a quiescent fluid with a steady force \mathbf{F} under no-slip conditions at the surface, the resulting flow field is given by

$$\mathbf{u}(\mathbf{r}) = \mathbf{F} \cdot \left(1 + \frac{a^2}{6} \nabla^2\right) \frac{\mathbf{G}(\mathbf{x}, \mathbf{x}_s)}{8\pi\mu} = \frac{\mathbf{F}}{8\pi\mu r} \cdot \left[\mathbf{I} + \frac{\mathbf{r}\mathbf{r}}{r^2} + \frac{a^2}{3r^2} \left[\mathbf{I} - 3\frac{\mathbf{r}\mathbf{r}}{r^2}\right]\right] \quad (2)$$

where \mathbf{x}_s is the position of the center of the sphere and $\mathbf{r} = \mathbf{x} - \mathbf{x}_s$. The second term represents the degenerate quadrupole needed to satisfy the no-slip boundary condition at $r = a$, but it is small when $a/r \ll 1$. The resulting velocity of the sphere is given by Stoke's law

$$\mathbf{F} = 6\pi\mu a \mathbf{U}. \quad (3)$$

S. Kim and S. J. Karrila, Microhydrodynamics: Principles and Selected Applications, 1991

C. Pozrikidis", Boundary Integral and Singularity Methods for Linearized Viscous Flow, 1992

Some basic solutions of the Stokes problem ...

A second basic solution is the velocity field \mathbf{u} produced by a radially expanding sphere, which can be generated by a point source at the center \mathbf{x}_0 of the sphere. The corresponding velocity is

$$\mathbf{u} = \alpha \frac{\mathbf{r}}{r^3} \quad (4)$$

where $\mathbf{r} = \mathbf{x} - \mathbf{x}_s$ and α is a constant given by $\alpha = \dot{a}a^2$, and

$$\mathbf{u} = \dot{a} \left(\frac{a}{r} \right)^2 \frac{\mathbf{r}}{r} = \frac{\dot{v}}{4\pi r^2} \hat{\mathbf{r}}, \quad (5)$$

where $v = 4\pi a^3/3$ is the volume of the sphere and $|\hat{\mathbf{r}}| = 1$.

By combining the previous solutions we obtain the velocity field for the combination of the pulled and expanding sphere, namely

$$\mathbf{u}(\mathbf{r}; a, \mathbf{F}, \dot{v}) = \frac{1}{24\pi\mu r} \left[\left(3 + \frac{a^2}{r^2} \right) \mathbf{F} + 3 \left(1 - \frac{a^2}{r^2} \right) (\mathbf{F} \cdot \hat{\mathbf{r}}) \hat{\mathbf{r}} \right] + \frac{\dot{v}}{4\pi r^2} \hat{\mathbf{r}}. \quad (6)$$

Performance measures for swimmers

The total force on a swimmer is

$$\mathbf{F} = \int_{\partial\mathcal{B}(t)} (\boldsymbol{\sigma} \cdot \mathbf{n}) dS$$

and this must vanish, but there's no free lunch, so the work done or the power expended is not necessarily zero. The latter is given by

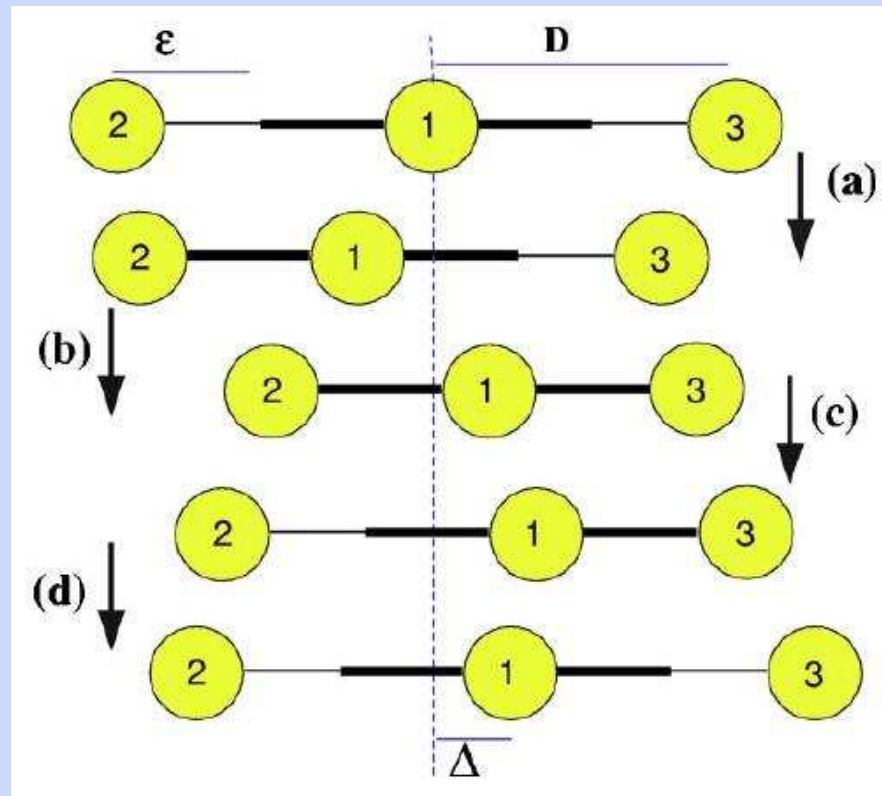
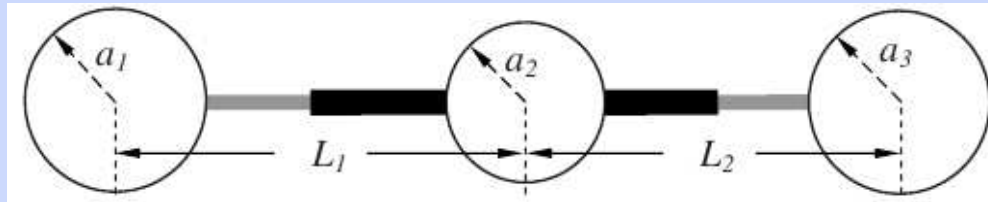
$$P = \int_{\partial\mathcal{B}(t)} (\boldsymbol{\sigma} \cdot \mathbf{n}) \cdot \mathbf{v} dS$$

and we define the performance measure

$$e = \frac{\int_0^T U dt}{\int_0^T P(t) dt} = \frac{\mathbf{X}}{\int_0^T \int_{\partial\mathcal{B}(t)} (\boldsymbol{\sigma} \cdot \mathbf{n}) \cdot \mathbf{v} dS}$$

e has units of 1/power, and measures how much power is expended to achieve the translation \mathbf{X} in one cycle.

Three linked spheres – the accordion model



Analysis of the NG model

Since the Stokes equations are linear and we assume well-separated spheres, we use the Oseen tensor and pressure vector to relate forces and velocities

$$\mathbf{v}_i(\mathbf{x}) = G(\mathbf{x} - \boldsymbol{\xi})\mathbf{F}_i \quad p(x) = H(\mathbf{x} - \boldsymbol{\xi})\mathbf{F}$$

$$G(\mathbf{r}) = \frac{1}{8\pi\eta} \left(\frac{\delta}{r} + \frac{\mathbf{r}\mathbf{r}}{r^3} \right) \quad H(\mathbf{r}) = \frac{\mathbf{r}}{4\pi r^3}$$

This leads to

$$v_1 = \frac{f_1}{6\pi\mu a_1} + \frac{f_2}{6\pi\mu L_1} + \frac{f_3}{6\pi\mu(L_1 + L_2)}.$$

There are similar equations for v_2 and v_3 . The leading order approximation V_0 to the speed V is the mean speed $V_0 = \sum_i v_i/3$. After specifying the L'_i and using the force-free condition, one can eliminate the forces, and when all spheres have the same radius a one finds that and to a first approximation

$$V_0 = \frac{1}{3}(v_1 + v_2 + v_3) = \frac{a}{6} \left[\left(\frac{L'_2 - L'_1}{L_1 + L_2} \right) + 2 \left(\frac{L'_1}{L_2} - \frac{L'_2}{L_1} \right) \right]$$

plus terms that average to zero over a cycle.

The PMPY model

The PMPY swimmer consists of two spheres with radii $a_i(t)$ ($i = 1, 2$) and one connecting arms with length $l(t)$. When $a_i/l \ll 1$, the velocities of the spheres (U_i) are related to the forces exerted on the spheres (F_i) via the Oseen tensor

$$U_1 = \frac{F_1}{6\pi\mu a_1} + \frac{a_1^2}{l^2}\dot{a}_1 \quad U_2 = \frac{F_2}{6\pi\mu a_2} + \frac{a_2^2}{l^2}\dot{a}_2.$$

The velocities are related via the following relation.

$$U_2 - U_1 = \dot{l}$$

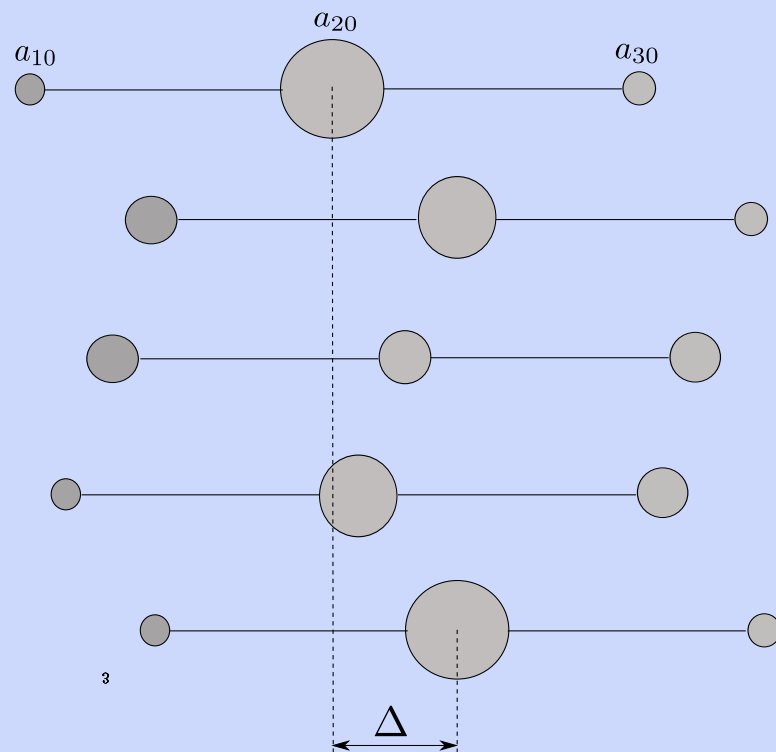
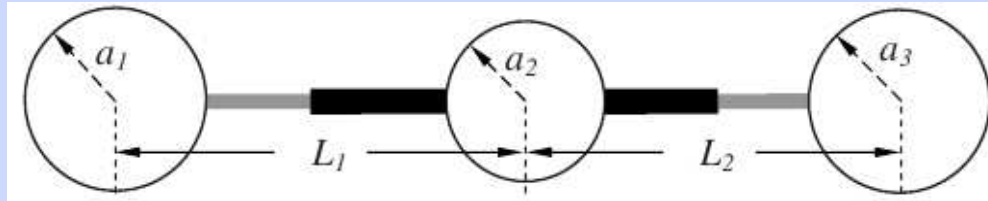
The velocity of the swimmer is

$$U = \frac{1}{2}(U_1 + U_2) = \frac{a_1 - a_2}{2(a_1 + a_2)}\dot{l} + \frac{a_1^2}{l^2}\dot{a}_1. \quad (7)$$

The power consumption $P(t)$ of the swimmer is given by

$$P = 6\pi\mu\left(\frac{1}{a_1} + \frac{1}{a_2}\right)^{-1}\dot{l}^2 + 16\pi\mu(a_1\dot{a}_1^2 + a_2\dot{a}_2^2). \quad (8)$$

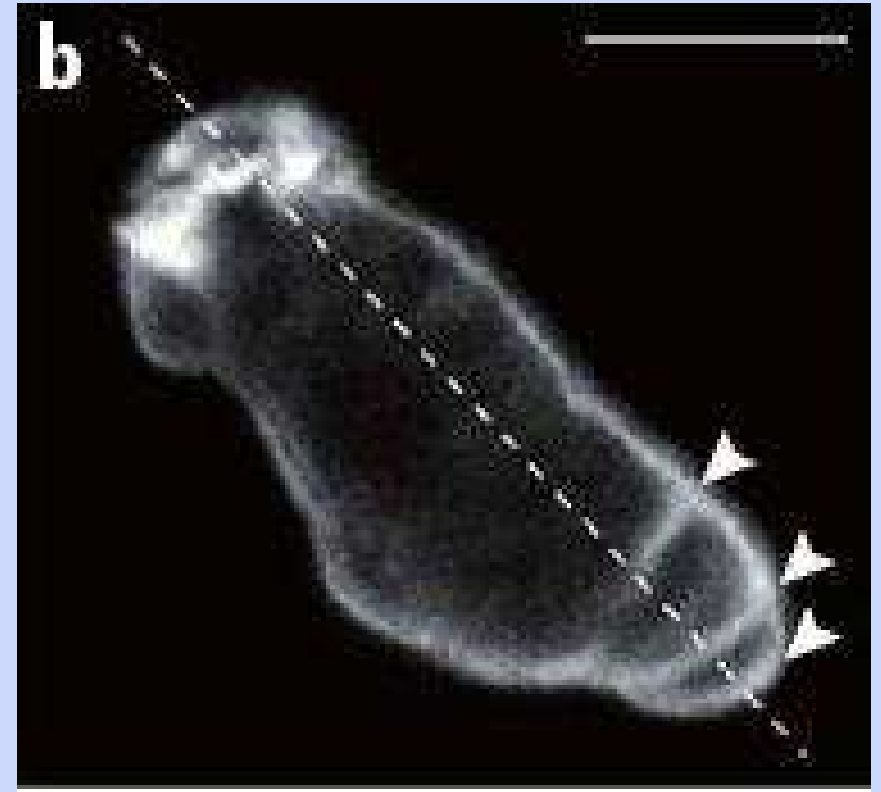
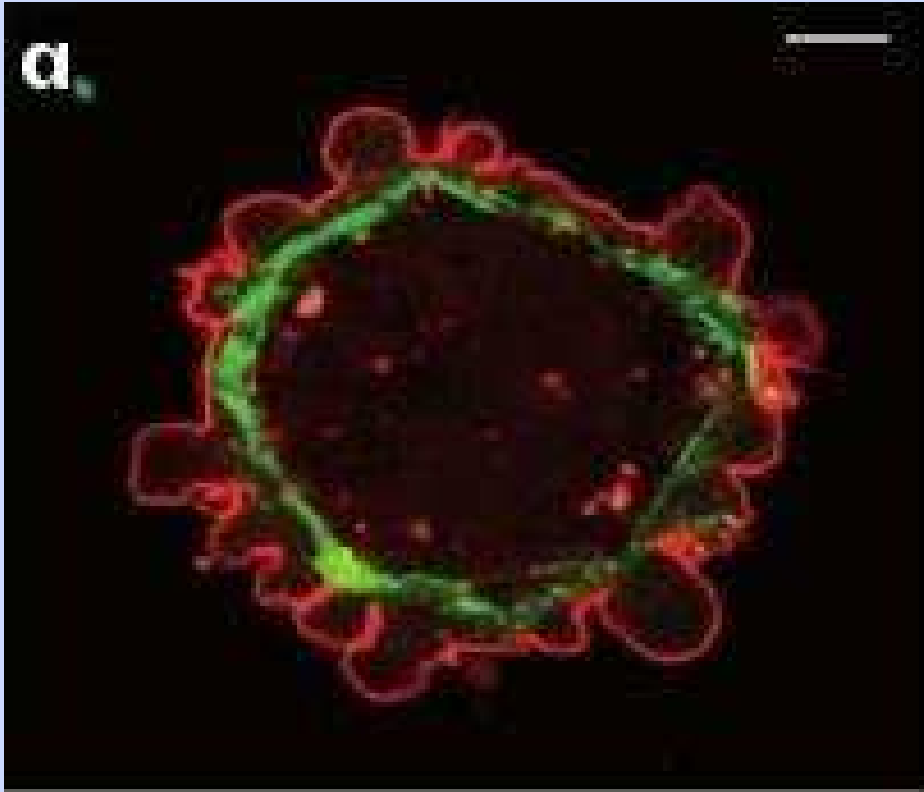
The three-sphere volume-exchange model



- (1) $\delta a_1 = -\delta a_2 = \delta_1 > 0$ while $\delta a_3 \equiv 0$;
- (2) $\delta a_3 = -\delta a_2 = \delta_3 > 0$ while $\delta a_1 \equiv 0$;
- (3) $\delta a_1 = -\delta a_2 = -\delta_1 > 0$ while $\delta a_3 \equiv 0$;
- (4) $\delta a_3 = -\delta a_2 = -\delta_3 > 0$ while $\delta a_1 \equiv 0$.

Models of low Reynolds number swimmers inspired by cell blebbing, Q. Wang, J. Hu and H. G. Othmer, in Natural Locomotion in Fluids and on Surfaces, Springer (2012).

The rationale for the VE model



Analytical results

$$\mathbf{u}(\mathbf{r}; a, \mathbf{f}, \dot{v}) = \frac{1}{24\pi\mu} \left[\left(3 + \xi^2\right) \frac{\mathbf{f}}{r} + 3(1 - \xi^2) \frac{(\mathbf{f} \cdot \mathbf{r})\mathbf{r}}{r^2} \right] + \frac{\dot{v}}{4\pi r^2} \mathbf{r}$$

$$U_1 \sim \frac{f_1}{6\pi\mu a_1} - \frac{\dot{v}_2}{4l^2} - \frac{\dot{v}_3}{16l^2} \quad U_2 \sim \frac{f_2}{6\pi\mu a_2} + \frac{\dot{v}_1}{4l^2} - \frac{\dot{v}_3}{4l^2} \quad U_3 \sim \frac{f_3}{6\pi\mu a_3} + \frac{\dot{v}_1}{16l^2} + \frac{\dot{v}_2}{4l^2}$$

Power needed for a given \dot{v}_i

$$P = \frac{\mu}{\pi} \left[\left(\frac{1}{a_1^3} + \frac{1}{a_2^3} \right) \dot{v}_1^2 + \frac{2}{a_2^3} \dot{v}_1 \dot{v}_3 + \left(\frac{1}{a_2^3} + \frac{1}{a_3^3} \right) \dot{v}_3^2 \right]$$

Efficiency of a stroke γ :

$$e(\gamma) := \frac{6\pi\mu X^2(\gamma)}{\tau \int_0^\tau P dt}.$$

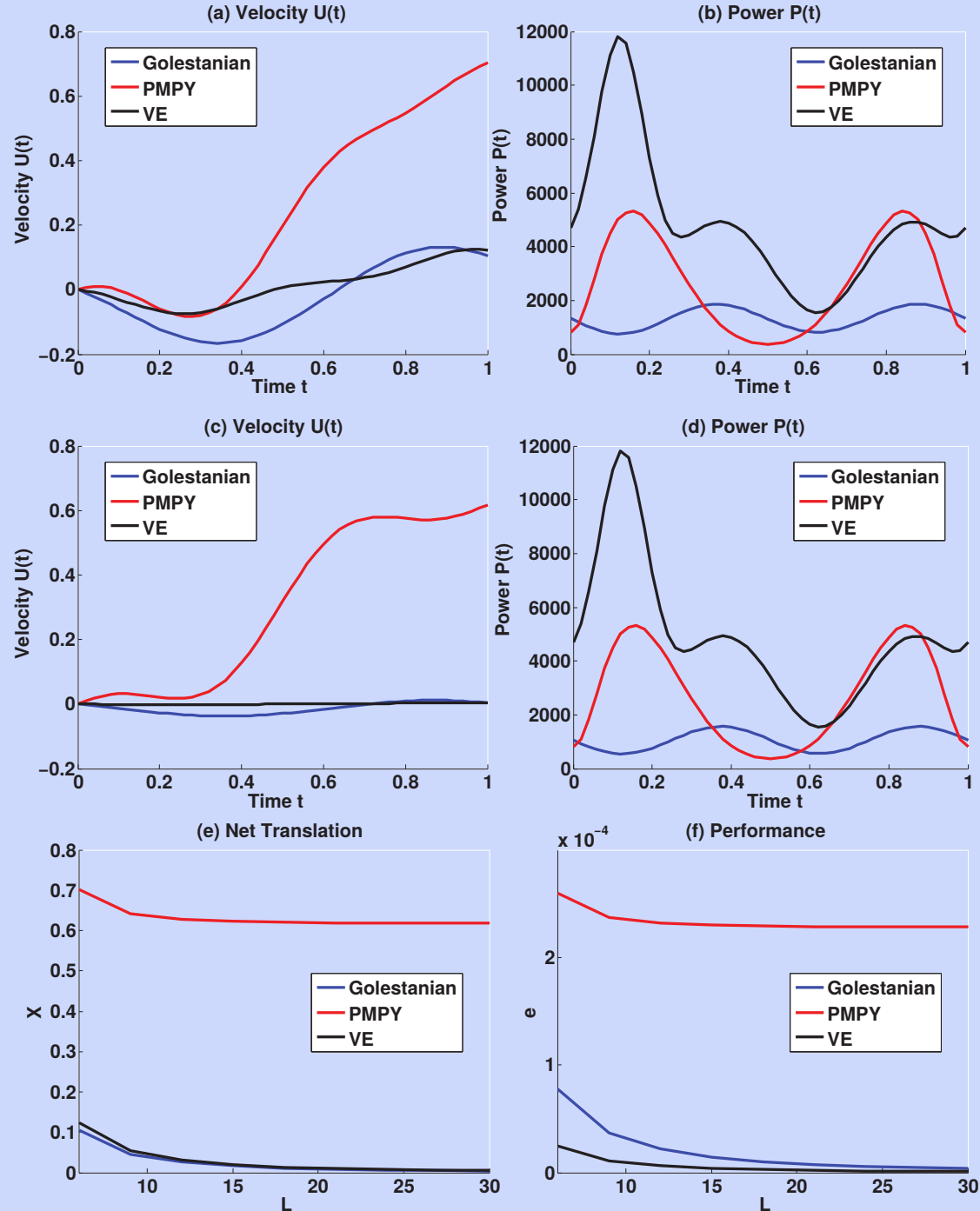
$$\delta X = \frac{7\pi}{4l^2} \left[a_1^2 \partial_{a_3} \frac{a_3}{a_1 + a_2 + a_3} + a_3^2 \partial_{a_1} \frac{a_1}{a_1 + a_2 + a_3} \right] da_1 \wedge da_3,$$

where $da_1 \wedge da_3$ denotes the signed area enclosed by the loop.

Implications ..

- When only one da_i is non-zero, the direction of movement is always from the expanding sphere to the contracting one, provided that the center sphere is large enough.
- For any stroke γ homotopic to S^1 in the (a_1, a_2) plane, an increase of the stroke amplitude will increase the net translation per stroke, while an increase in the initial radius a_{20} of the central sphere (with a_{10} and a_{30} fixed) will decrease the net translation per stroke.
- Increasing the initial radius a_{20} of the central sphere (with a_{10} and a_{30} fixed) decreases the efficiency. Also, for infinitesimal strokes, increasing the stroke amplitude $|da_1 \wedge da_3|$ symmetrically by a factor r (i.e., $\widetilde{da_1} = rda_1$ and $\widetilde{da_3} = rda_3$) will increase the efficiency by r^2 .

A comparison of the three



The next simplest problem is 2D ...

In 2D the Stokes equations

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

are equivalent to

$$\Delta \omega = 0 \quad \Delta p = 0,$$

and these can be solved by introducing a stream function. Define Λ such that

$$u(x, y) = \nabla \times \Lambda = \frac{\partial \Lambda}{\partial y} - i \frac{\partial \Lambda}{\partial x}$$

where now $u = u_x + iu_y$. Then Λ solves the biharmonic equation

$$\Delta^2 \Lambda = 0$$

The general solution to the biharmonic equation in 2D is

$$\Lambda(z, \bar{z}) = -\Im[\bar{z}\phi(z) + \chi(z)]$$

The physical variables ...

Once we know Λ we recover the physical variables as follows.

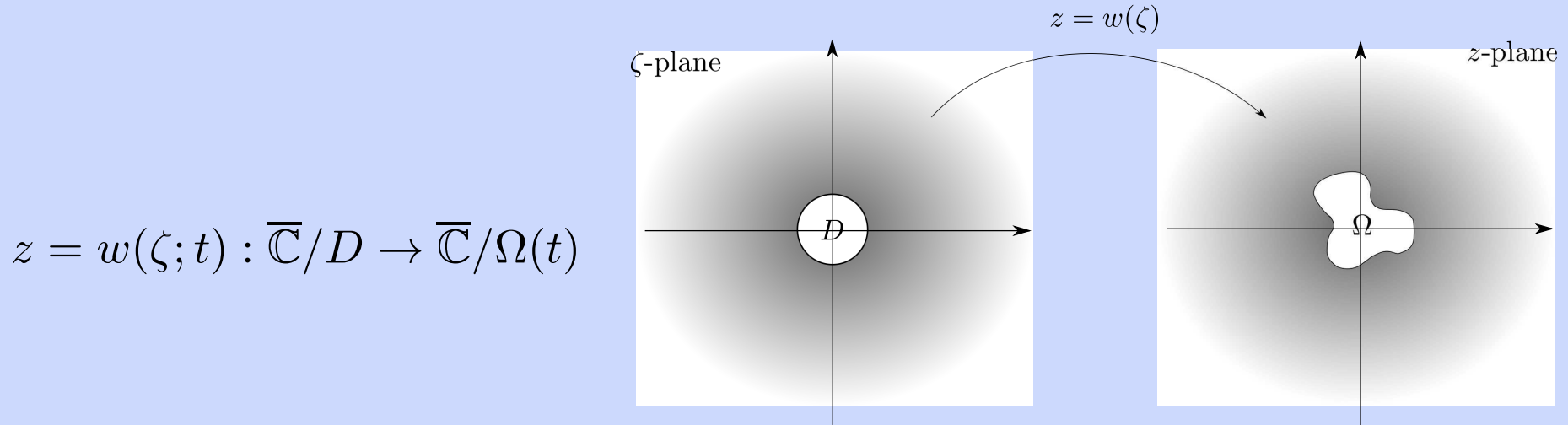
- Velocity: $v = \phi(z) - z\overline{\phi'(z)} - \overline{\chi'(z)}$
- Pressure: $p = -4\mu\Re\{\phi'(z)\}$
- Vorticity: $\omega \left(:= \frac{\partial}{\partial y}\Re v - \frac{\partial}{\partial x}\Im v \right) = -4\Im\{\phi'(z)\}$
- Force: $f(:= \sigma \cdot \mathbf{n}) = 4\mu\Re(\phi')n - 2\mu(z\overline{\phi''} + \overline{\chi''})\overline{n}$

$$\implies f ds = -2i\mu \left[(\phi' + \overline{\phi'})dz + (z\overline{\phi''} + \overline{\chi''})d\overline{z} \right] = -2i\mu d(\phi + z\overline{\phi'} + \overline{\chi'})$$

Some basic problems of the mathematical theory of elasticity. N.I. Muskhelishvili and JMR Radok, 1953, Cambridge Univ Press

Pull-back of the fluid domain and boundary data

Suppose the cell occupies $\Omega(t) \subset \mathbb{C}$, and that the velocity on $\partial\Omega(t)$ is $V(z, \bar{z}; t)$.



- In the z -plane we have to find functions $\phi(z; t)$ and $\psi(z; t)$, analytic on $\overline{\mathbb{C}}/\overline{\Omega(t)}$ and continuous on $\overline{\mathbb{C}}/\Omega(t)$, such that

$$\phi(z; t) - z\overline{\phi'(z; t)} - \overline{\psi(z; t)} = V(z, \bar{z}; t) \quad (z \in \partial\Omega(t))$$

- In the ζ -plane we have to find $\Phi(\zeta; t) = \phi(w(\zeta; t); t)$ and $\Psi(\zeta; t) = \psi(w(\zeta; t); t)$, analytic on $\overline{\mathbb{C}}/\overline{D}$ and continuous on $\overline{\mathbb{C}}/D$ at any time t , such that

$$\Phi(\sigma) - \frac{w(\sigma)}{w'(\sigma)}\overline{\Phi'(\sigma)} - \overline{\Psi(\sigma)} = V(\sigma, t) \quad (\sigma \in S^1)$$

Reduction to an integral equation

- Decompose the boundary condition V by the Plemelj formula:
 $V(\sigma) = V^-(\sigma) - V^+(\sigma)$ on S^1 . $V^-(\zeta)$ is analytic for $|\zeta| < 1$ and $V^+(\zeta)$ is analytic for $|\zeta| > 1$ and $V^+(\infty) = 0$.

- If $V(\sigma; t) = \sum_{k=-\infty}^{\infty} \lambda_k(t) \sigma^k$, then

$$\begin{aligned} V^-(\zeta) &= \lambda_0 + \lambda_1 \zeta + \lambda_2 \zeta^2 + \dots & \text{for } |\zeta| \leq 1; \\ -V^+(\zeta) &= \frac{\lambda_{-1}}{\zeta} + \frac{\lambda_{-2}}{\zeta^2} + \frac{\lambda_{-3}}{\zeta^3} + \dots & \text{for } |\zeta| \geq 1 \end{aligned}$$

- Apply the operator $\frac{1}{2\pi i} \int_{S^1} \frac{d\sigma}{\sigma - \zeta}$ for $|\zeta| > 1$ to the velocity boundary condition

$$\Phi(\sigma) - \frac{w(\sigma)}{w'(\sigma)} \overline{\Phi'(\sigma)} - \overline{\Psi(\sigma)} = V(\sigma) \quad (\sigma \in S^1)$$

Fredholm integral equation

Then $\Phi(\zeta)$ satisfies

$$\Phi(\zeta) + \frac{1}{2\pi i} \int_{S^1} \frac{w(\sigma)}{w'(\sigma)} \frac{\overline{\Phi'(\sigma)}}{\sigma - \zeta} d\sigma = -V^+(\zeta) \quad (|\zeta| \geq 1)$$

If the conformal mapping $z = w(\zeta)$ has only finitely many terms then there exists a function $f_N(\zeta)$ that is analytic on $|\zeta| < 1$, continuous on $|\zeta| \leq 1$, and $f_N(\sigma) = \sigma^N \frac{w(\sigma)}{w'(\sigma)}$ for $\sigma \in S^1$, and the integral equation can be reduced to a finite system of complex linear equations for the coefficients

1. For $n \geq N - 1$, $A_{-n} = \lambda_{-n}$;
2. $(\mathbf{I}_{N-2} + \mathbf{K})(\Re A_{-1}, \dots, \Re A_{-(N-2)})^T = (\Re \lambda_{-1}, \dots, \Re \lambda_{-(N-2)})^T$ $(\mathbf{I}_{N-2} - \mathbf{K})(\Im A_{-1}, \dots, \Im A_{-(N-2)})^T = (\Im \lambda_{-1}, \dots, \Im \lambda_{-(N-2)})^T$

A_n, λ_n of Φ and $-V^+$, resp

$$\begin{aligned} \Phi(\zeta) &= \frac{A_{-1}}{\zeta} + \frac{A_{-2}}{\zeta^2} + \dots + \frac{A_{-n}}{\zeta^n} + \dots \\ -V^+(\zeta) &= \frac{\lambda_{-1}}{\zeta} + \frac{\lambda_{-2}}{\zeta^2} + \dots + \frac{\lambda_{-n}}{\zeta^n} + \dots \end{aligned}$$

Symmetric cyclic shape deformations

Consider a map of the form

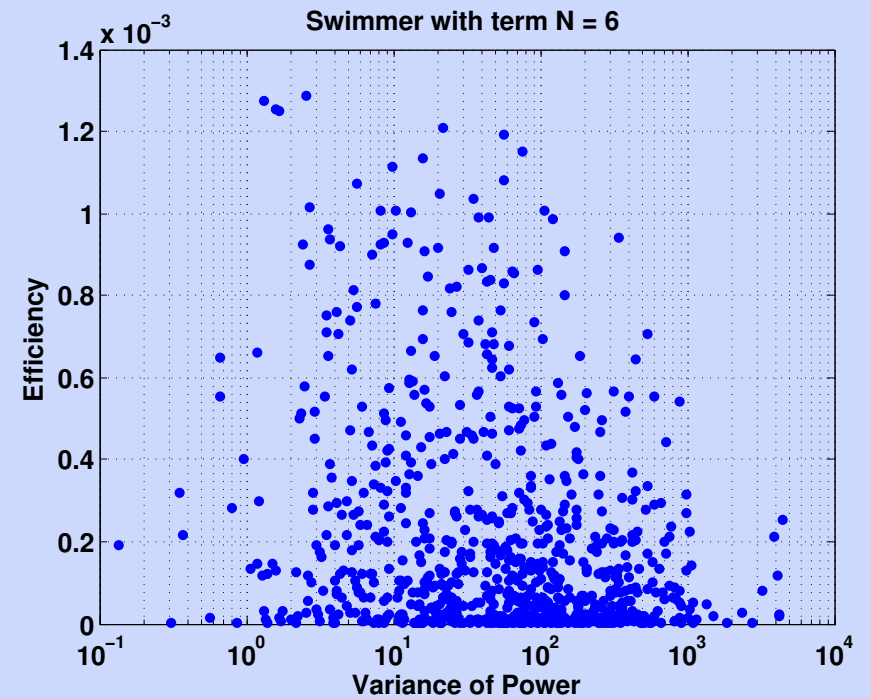
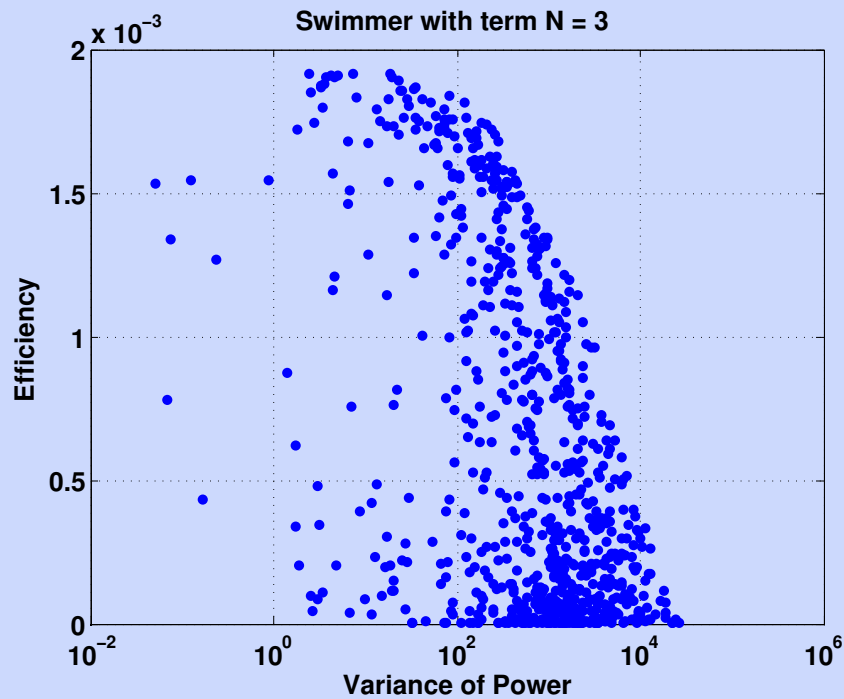
$$w(\zeta; t) = C(t)\zeta + \frac{1}{M} \left[a_1 \frac{\sin(t)}{\zeta} + a_2 \frac{\sin(t + \varphi)}{2\zeta^2} + \cdots + a_N \frac{\sin(t + (N-1)\varphi)}{N\zeta^N} \right]$$

Characteristics of rigid motions

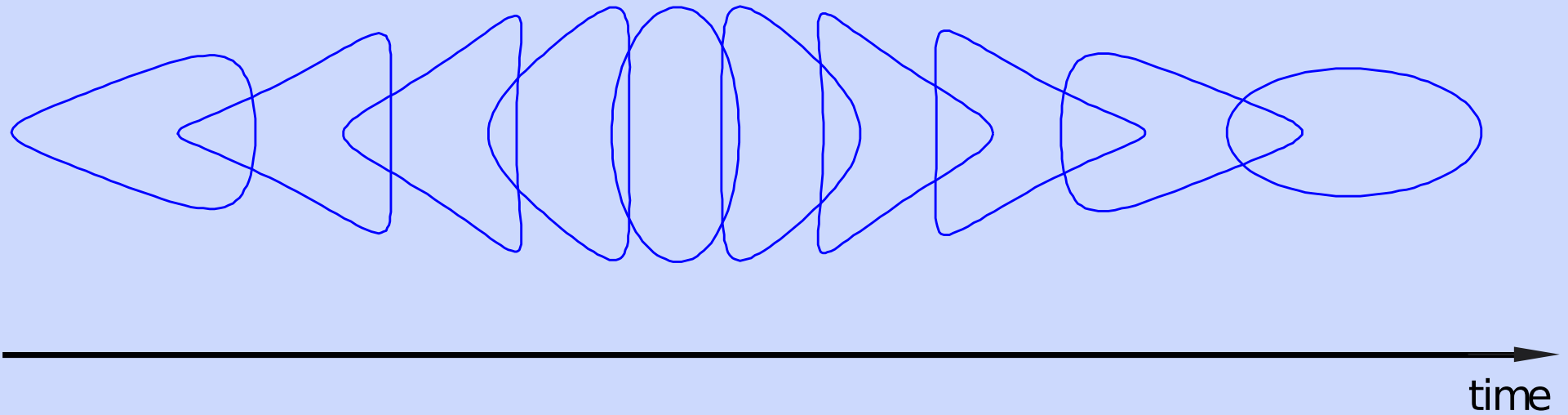
- Rotation: symmetric \Rightarrow Rot \equiv 0.
- Translation: $\text{Tr}(t) = \int_0^t [\Phi(0; s) - \overline{\Psi(0; s)}] ds$.
- Mean velocity within a period: $\overline{U} := \text{Tr}(T)/T$.
- Force distribution: $f(\sigma) = 2\mu\sigma[2\Phi'(\sigma) - V'(\sigma)]/|w'(\sigma)|$.
- Power: $\mathcal{P}(t) = - \oint_{\partial\Omega} \overline{v} f ds$
 - Mean power within a period: $\overline{\mathcal{P}} := T^{-1} \int_0^T \mathcal{P}(t) dt$.
 - Variance of power within a period: $\text{Var}(\mathcal{P}) := T^{-1} \int_0^T [\mathcal{P} - \overline{\mathcal{P}}]^2 dt$.
- Efficiency: $E := \overline{U}^2 / \overline{\mathcal{P}}$.

A computational experiment

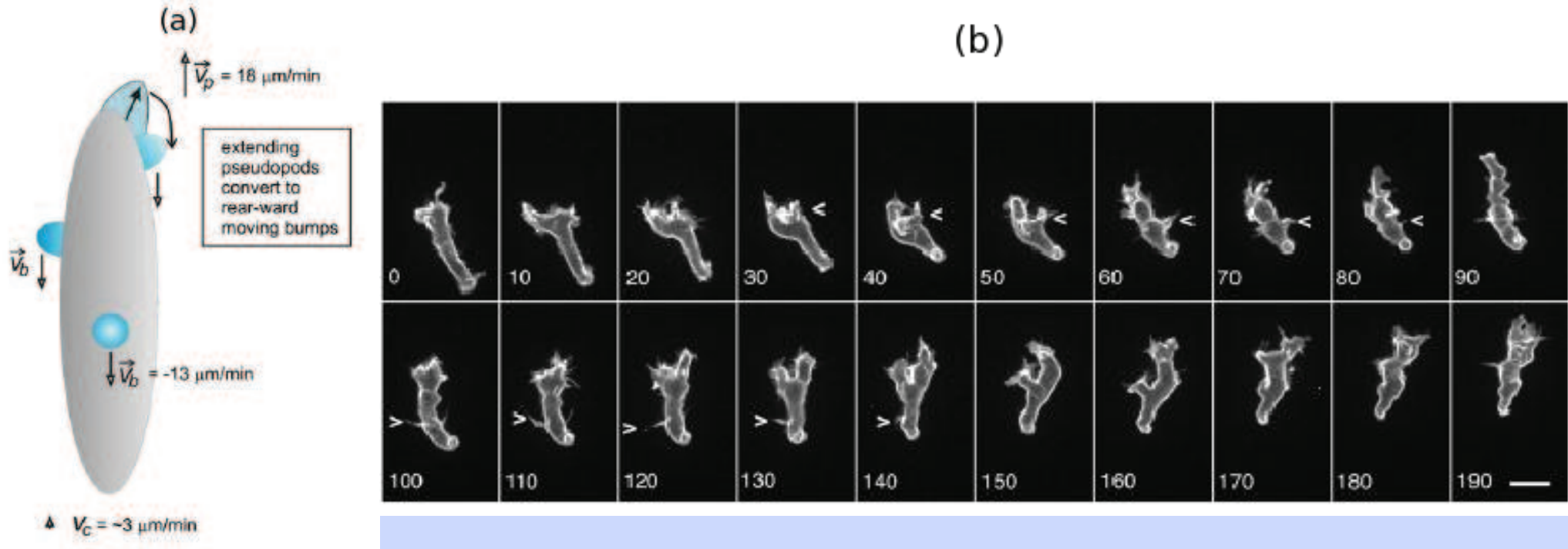
Fix φ , test randomly generated $\mathbf{a}(\sim \mathcal{N}(0, 5)^N)$ where $M = \sum_{k=1}^N |a_k|$, $C(t)$ is determined by area conservation and φ .



A sequence of shape changes for $N=2$



But it's difficult to generate realistic shapes



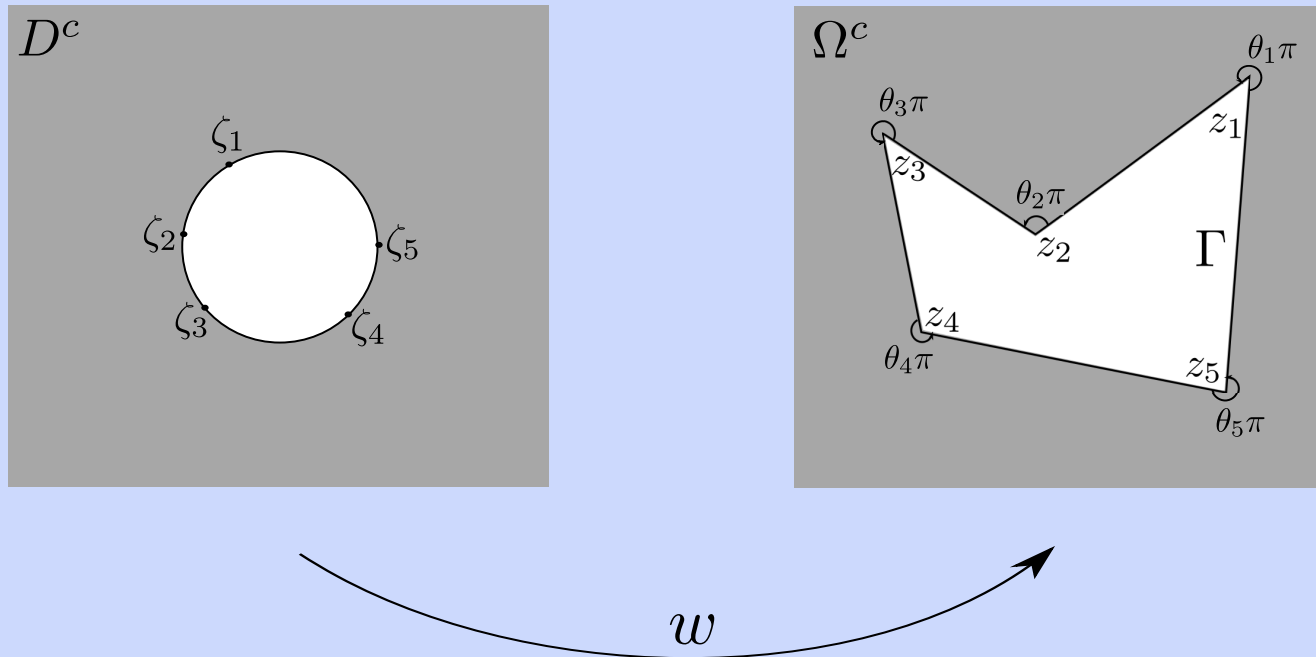
so we need another approach

Schwarz-Christoffel transformations and shape approximations for Dictyostelium

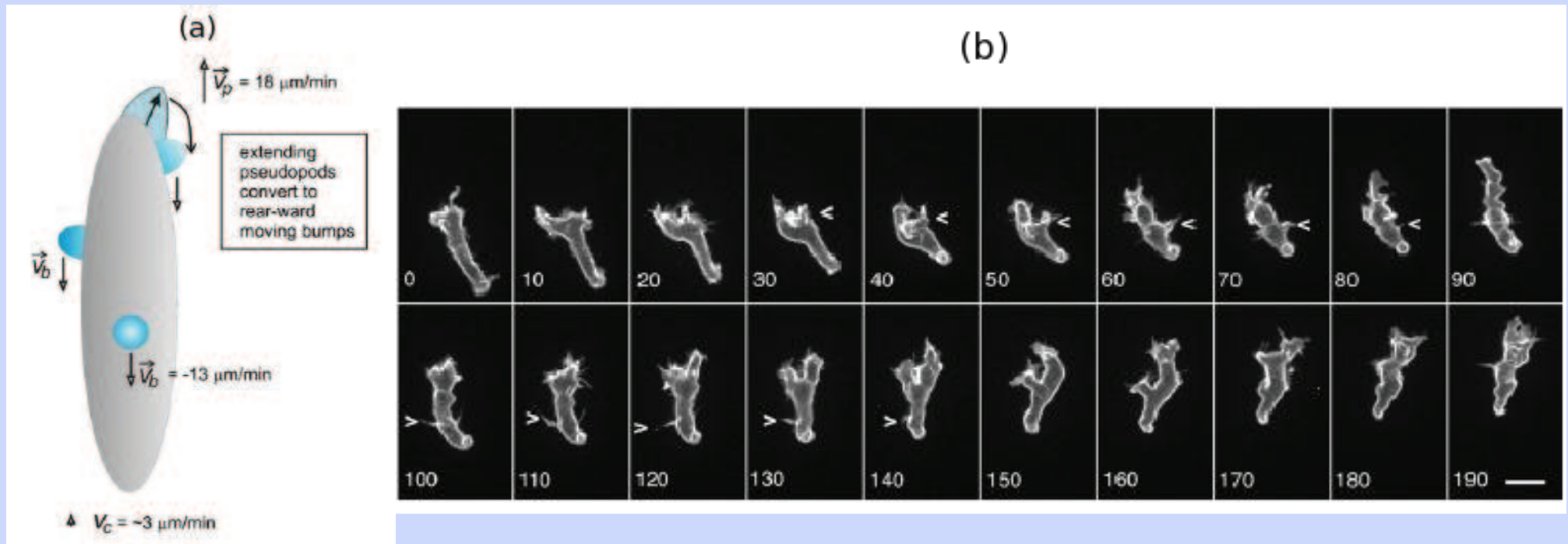
Suppose that we have an n -polygon Γ in the z -plane with vertices z_1, \dots, z_n , and the corresponding exterior angles are $\theta_1, \dots, \theta_n$. Let Ω be the interior region bounded by Γ . The conformal mapping from the exterior of the unit disk D in the ζ -plane to Ω^c is given by

$$z = w(\zeta) = A + C \int^{\zeta} \frac{1}{\xi^2} \prod_{k=1}^n (\xi - \zeta_k)^{\theta_k - 1} d\xi \quad (9)$$

where $z_k = w(\zeta_k)$ and ζ_k is the *prevertex* to the vertex z_k under w .



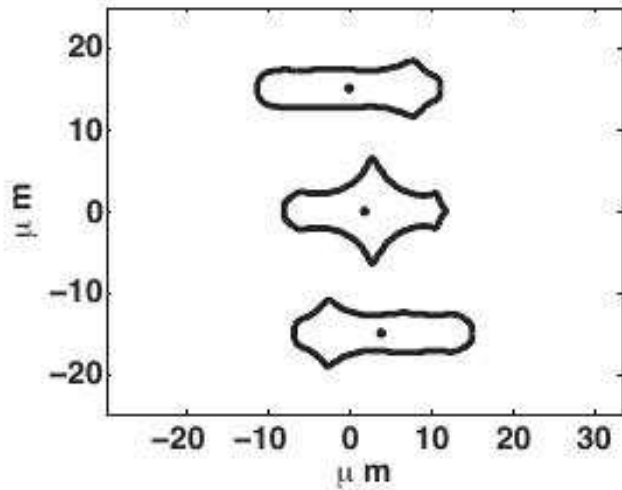
What can we say about Dicty's swimming ?



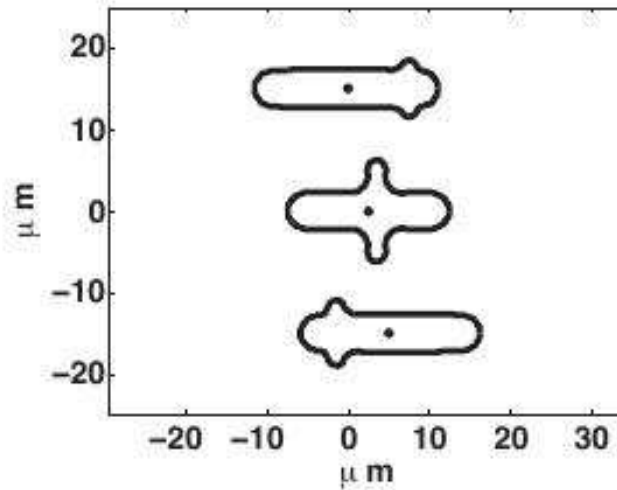
	Haastert	Barry
Maximum cell body length	$\sim 25\mu$	$\sim 22\mu$
Average cell body width	$\sim 6\mu$	$\sim 4\mu$
Maximum protrusion height	$\sim 2\mu$	$\sim 4\mu$
Average protrusion width	$\sim 2\mu$	$\sim 2\mu$
Period of a stroke	$\sim 1 \text{ min}$	$\sim 1.5 \text{ min}$

A comparison of shapes for the two types of Dd

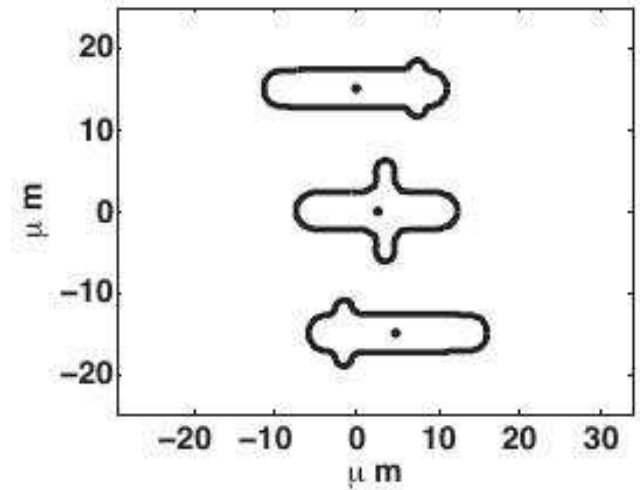
(a) Barry, N=10



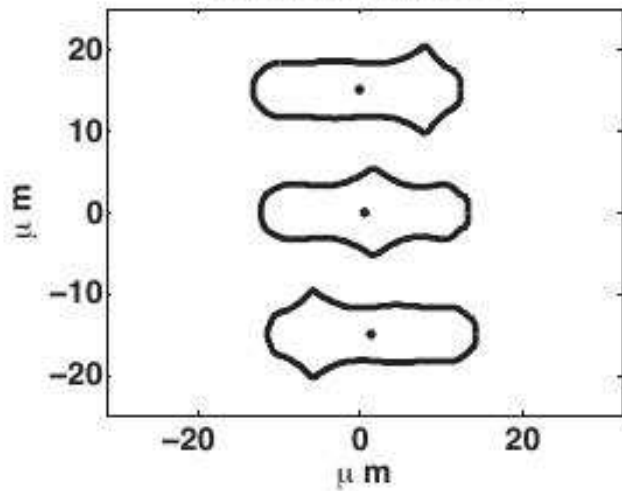
(b) Barry, N=50



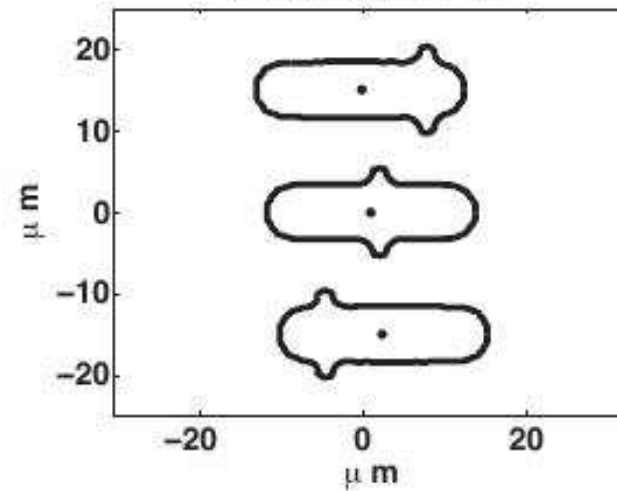
(c) Barry, N=80



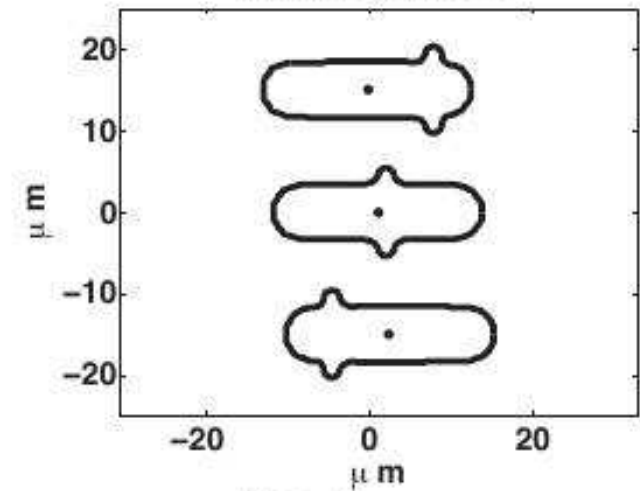
(d) Haastert, N=10



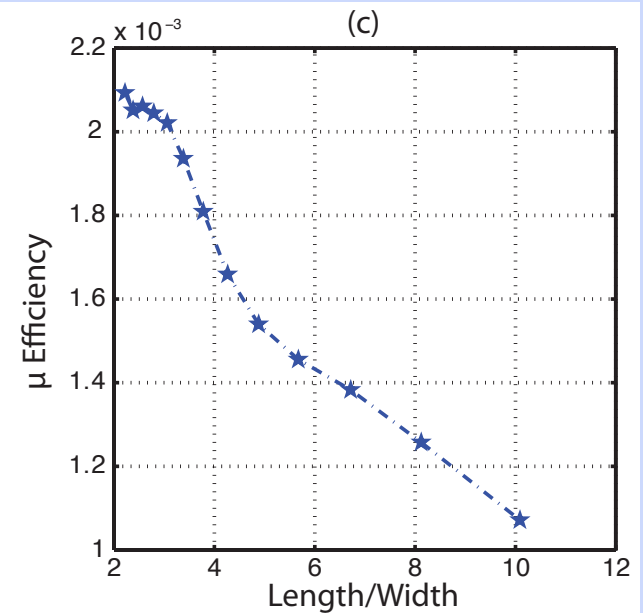
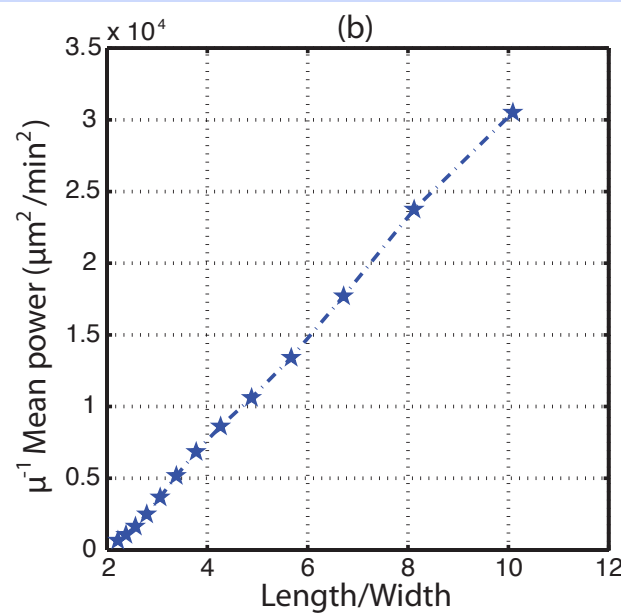
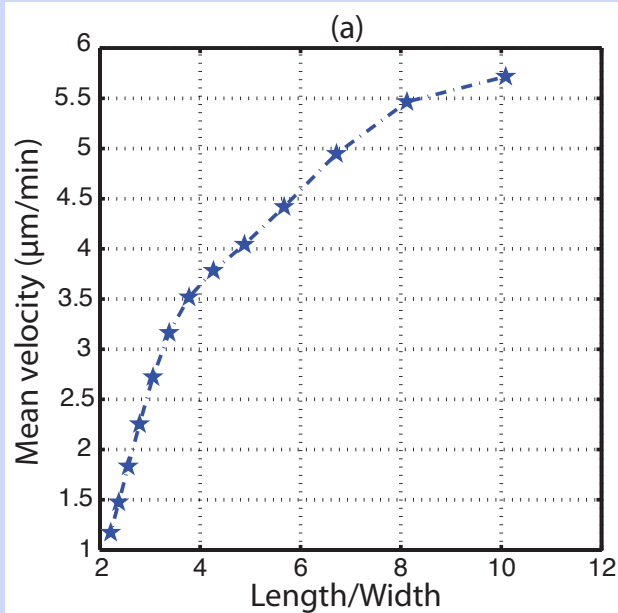
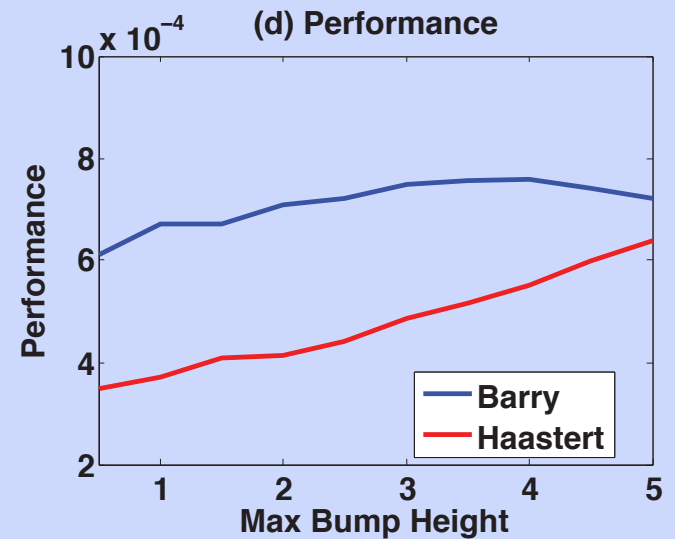
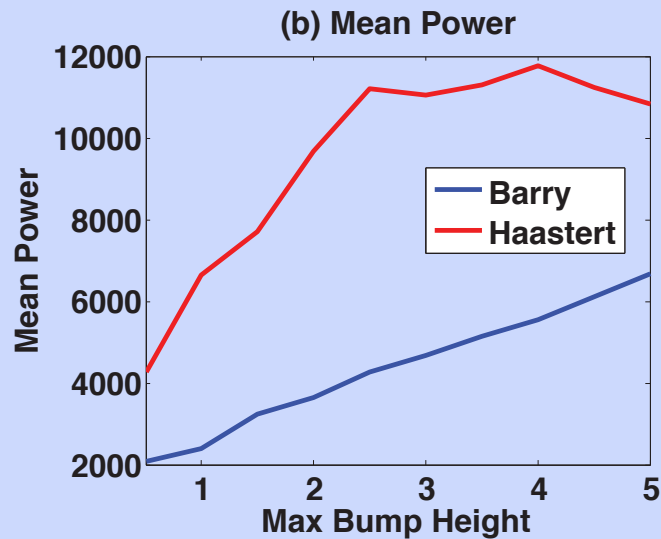
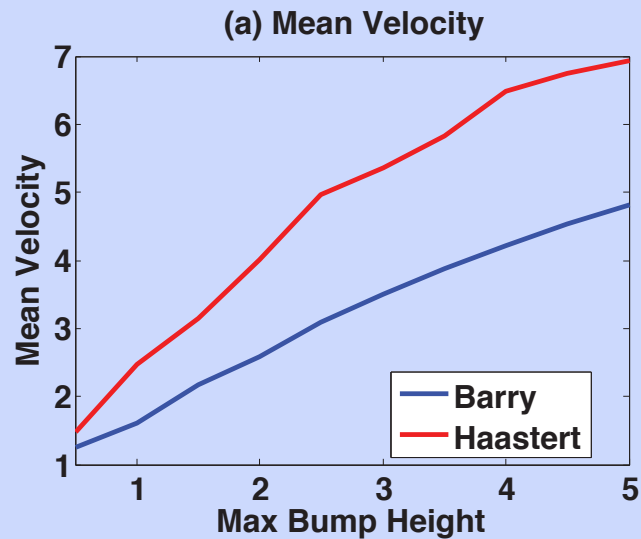
(e) Haastert, N=50



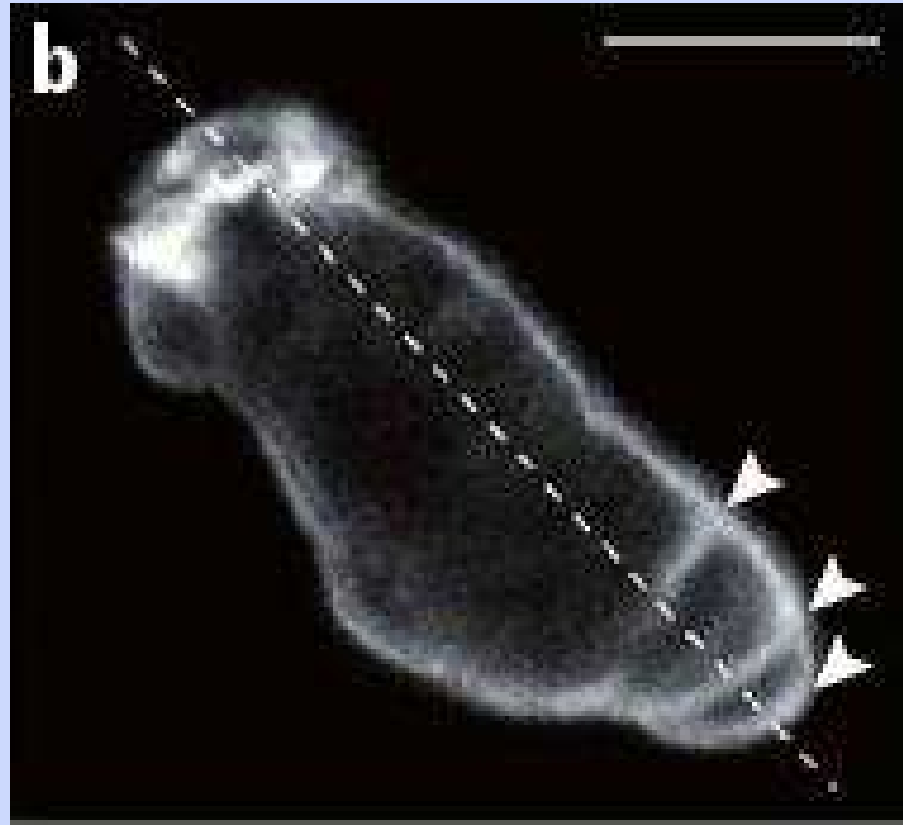
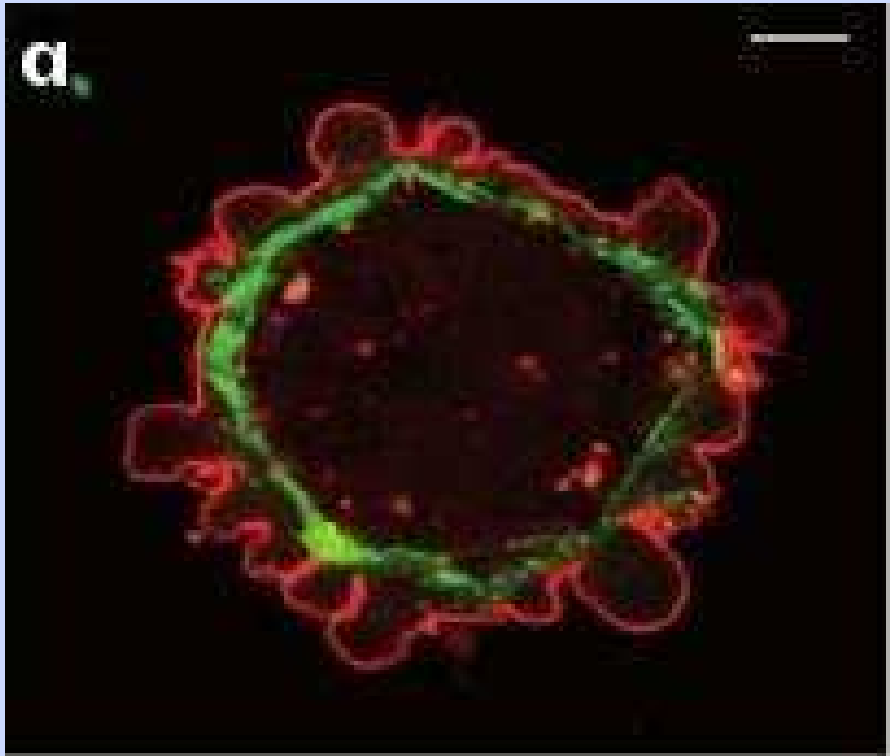
(f) Haastert, N=80



How various factors affect the results ..



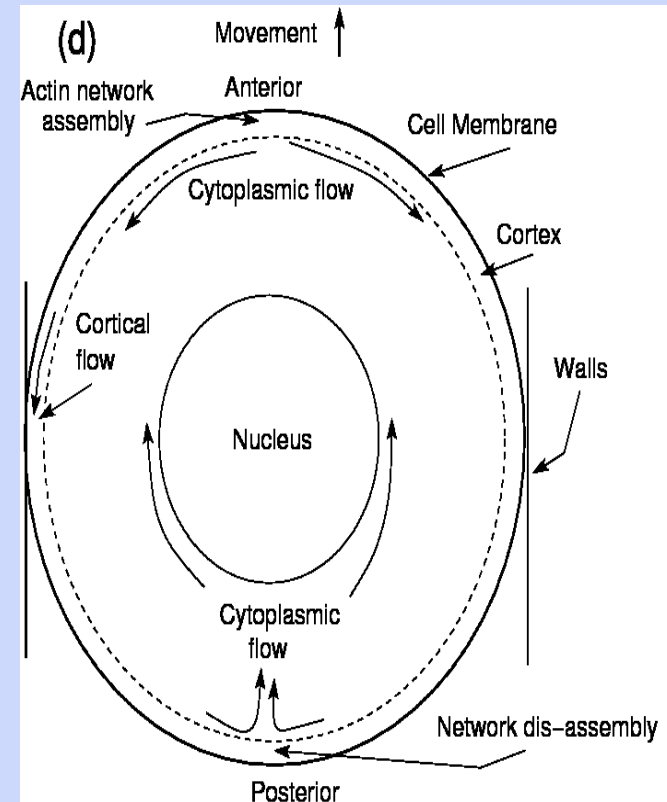
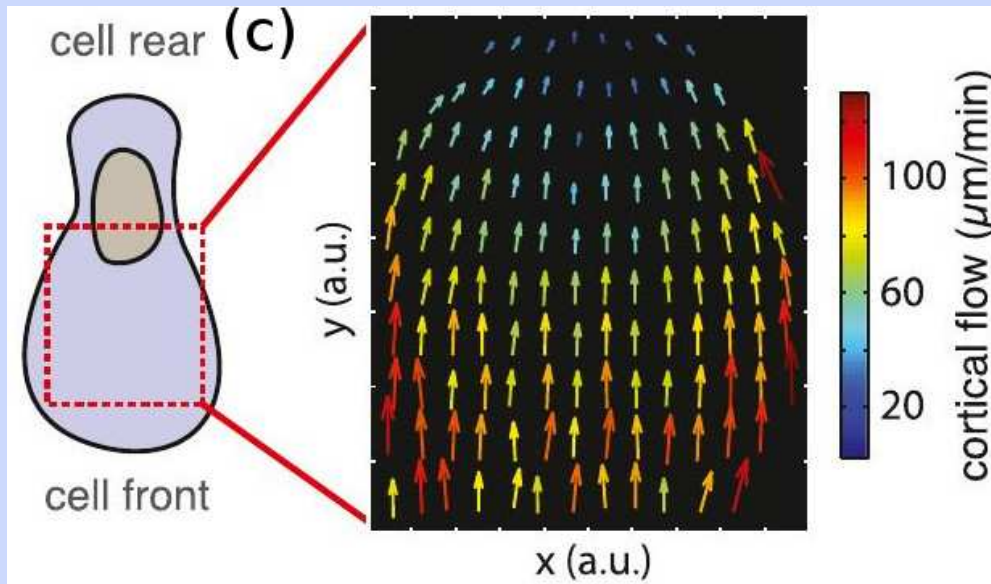
Other modes of cell motility



Charras 1 Liu 1 Liu2 Paluch 1

How do we begin to understand these different modes of movement?

A conceptual model



Hypothesis: The myosin accumulates at the rear and this creates a tension gradient with higher tension at the rear. Assuming that the membrane does not flow, this creates a reverse tension gradient in the membrane, and mechanical balance implies a tension gradient in the exterior fluid.

The mathematical problem

The free energy associated with bending under the constraints of constant surface area A_0 and volume V_0 of the cell

$$\mathcal{F}_B = \int_{\mathcal{S}} 2k_c(H - C_0)^2 dS + \int_{\mathcal{S}} k_G K dS + \int_D \Lambda[\sqrt{g} - \sqrt{g_0}] du^1 du^2 + P[\int_{\Omega} dV - V_0].$$

$H = (\kappa_1 + \kappa_2)/2$ is the mean curvature, $K = \kappa_1 \kappa_2$ is the Gaussian curvature.

A stable equilibrium shape of a cell is a minimizer of \mathcal{F} , and thus a solution of $\delta^{(1)}\mathcal{F}/\delta\mathbf{x} = 0$ for any infinitesimal deformation

$$\mathbf{x} = \mathbf{x}_0 + \phi^i \mathbf{e}_i + \psi \mathbf{n}$$

of \mathcal{S} . This leads to the following shape equations for the normal and tangential components of the membrane force when $C_0 = 0$ and the moduli are constant

$$F^n = -\frac{\delta\mathcal{F}}{\delta\psi} = -2k_B\Delta_s H - 2k_B H (H^2 - K) + 2\Lambda H - P$$

$$F_i^t = \nabla_i \Lambda \quad i = 1, 2.$$

Here Δ_s and ∇_s are the surface Laplacian and gradient, resp. In the first equation one sees that Λ enters the normal component via the term $2\Lambda H$, which couples areal distension to the curvature in the normal component of the force.

The mathematical problem, contd.

When written in (u^1, u^2) coordinates, the first term in F_n defines a fourth-order operator, and given an initial shape Ω_0 , we find a stable minimal surface by solving the following evolution equations, which are predicated on the assumption that the membrane has no mass.

$$\begin{aligned}\mu \frac{d\psi(u^1, u^2)}{dt} &= F^n(H, K, C_0, P, \Lambda, k_B, k_G, u^1, u^2) \\ \gamma_0 \mu \frac{d\phi^i(u^1, u^2)}{dt} &= F_i^t(H, K, C_0, P, \Lambda, k_B, k_G, u^1, u^2) \quad i = 1, 2\end{aligned}$$

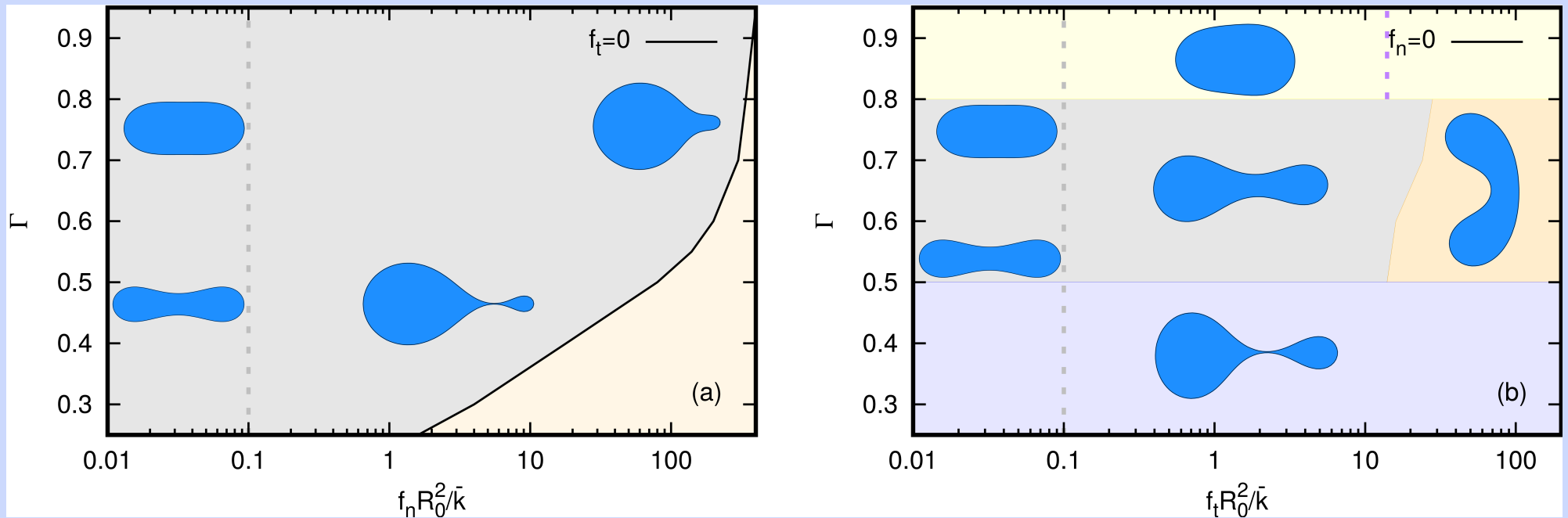
where μ can be thought of as a viscosity.

In the presence of non-conservative cortical forces we must add these to the forces above.

$$\begin{aligned}\frac{d\psi(u^1, u^2)}{dt} &= F_n(H, K, C_0, P, \Lambda, k_B, k_G, u^1, u^2) + f_n \\ \frac{d\phi^i(u^1, u^2)}{dt} &= F_t^i(H, K, C_0, P, \Lambda, k_B, k_G, u^1, u^2) + f_t^i \quad i = 1, 2.\end{aligned}$$

When the cortical forces are incorporated the resulting evolution is no longer a gradient flow, and one simply looks for steady states of these equations.

Shapes of cells under cortical forces ..



(a) A phase diagram showing cell shapes as a function of the dimensionless normal force f_n^* and the reduced area Γ . (b) A similar diagram for the dimensionless tangential force f_t^* and the reduced area Γ .

The fluid-cell interactions at low Re

$$\begin{aligned}\mathbf{v}(\mathbf{x}) = & -\frac{1}{4\pi\mu(1+\lambda)} \int_{\partial\Omega(t)} \mathbf{G}(\mathbf{x}, \bar{\xi}) \cdot \mathbf{F}_m(\bar{\xi}) dS(\bar{\xi}) \\ & + \frac{1-\lambda}{4\pi(1+\lambda)} \int_{\partial\Omega(t)} \mathbf{v}(\bar{\xi}) \cdot \mathbf{T}(\mathbf{x}, \bar{\xi}) \cdot dS(\bar{\xi})\end{aligned}$$

where \mathbf{G} is the Green's function

$$\mathbf{G}(\mathbf{x}, \bar{\xi}) = \frac{1}{r} \left[\boldsymbol{\delta} + \frac{\mathbf{r}\mathbf{r}}{r^2} \right]$$

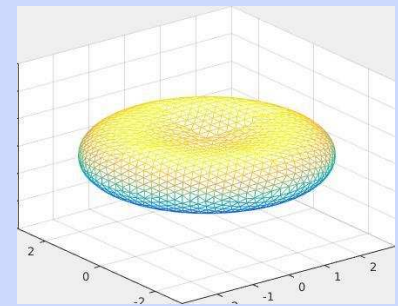
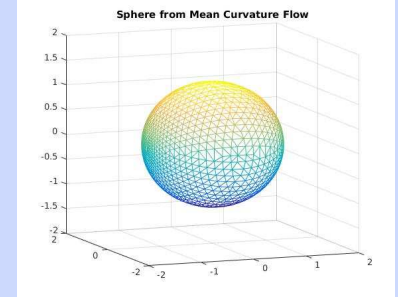
$\mathbf{r} = \mathbf{x} - \bar{\xi}$ and $r = |\mathbf{r}|$. \mathbf{F}_m is the force exerted by the membrane on the fluid, \mathbf{T} is the third-rank stress tensor or stresslet, and λ is the ratio of the interior to exterior viscosities. We assume continuity of the interior, exterior and membrane velocities, and mechanical equilibrium at the membrane, and therefore the force balance reads

$$\mathbf{F}_m \equiv \left[(\boldsymbol{\sigma}_{in} - \boldsymbol{\sigma}_{ext}) \cdot \mathbf{n} \right]_m = \mathbf{f}_m.$$

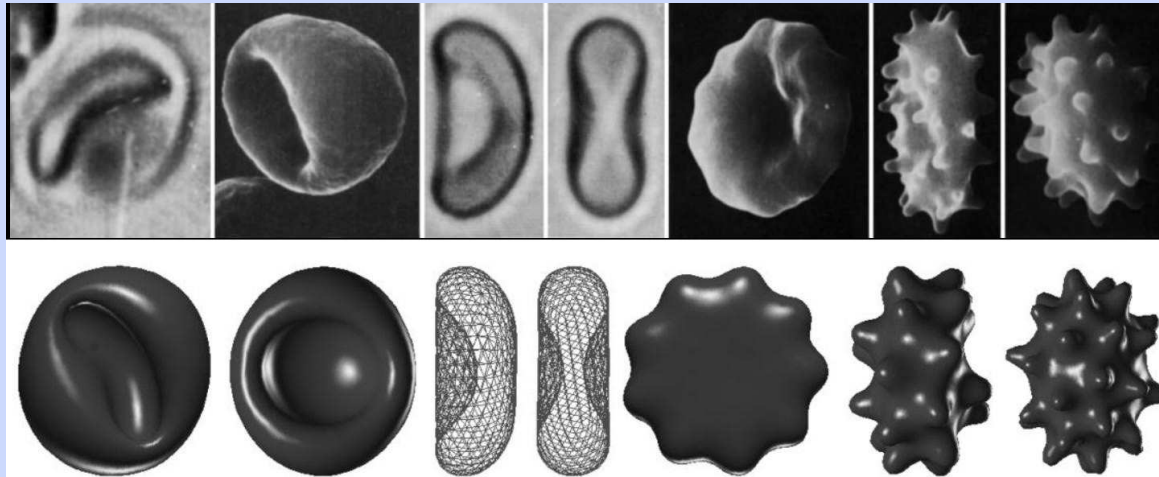
The computational algorithm

Algorithm:

- (1) Solve the evolution equation for fixed Λ and Δp .
- (2) Test how well the area and volume constraints are satisfied.
- (3) Adjust the Lagrange multipliers as needed.
- (4) Return to (1) and iterate.

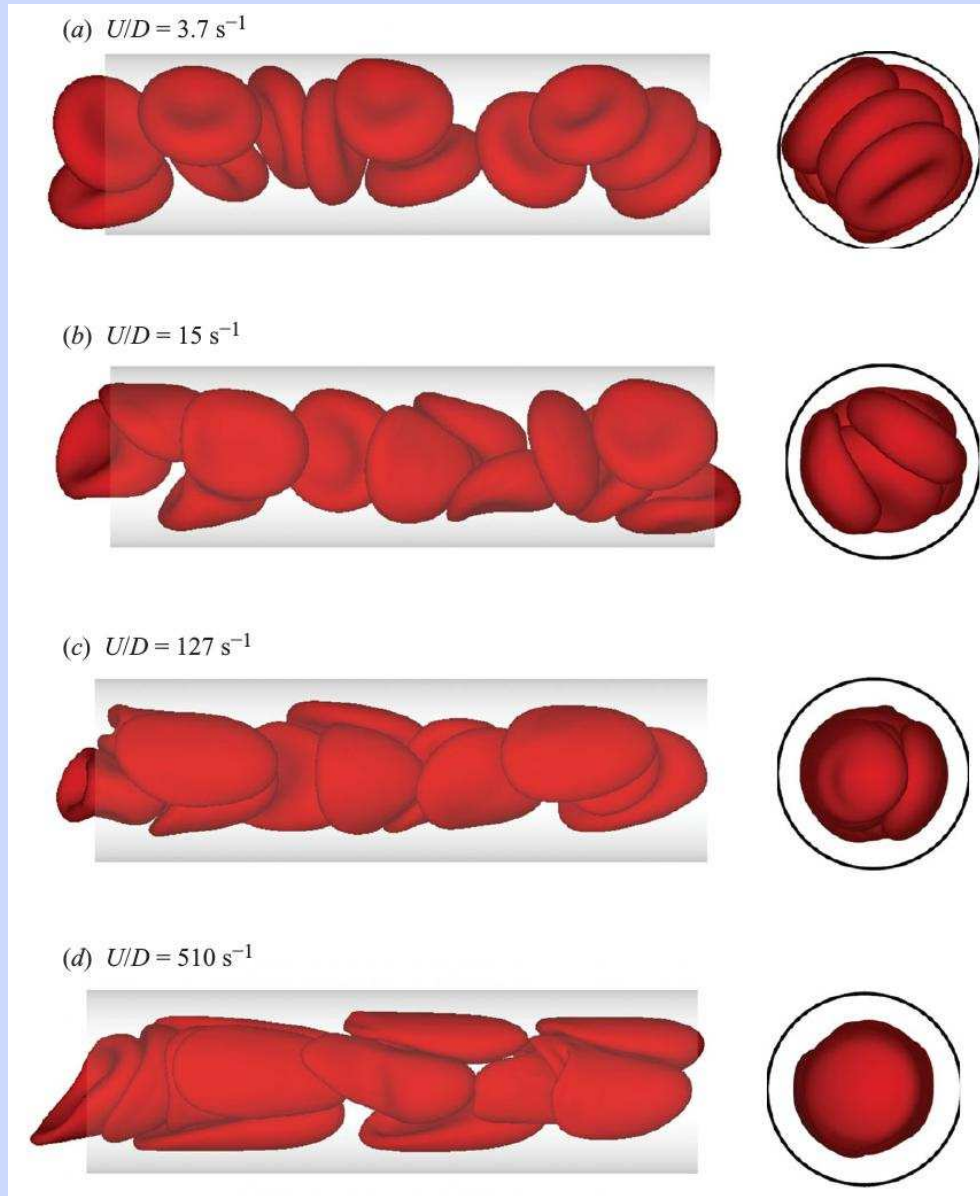


Red blood cells



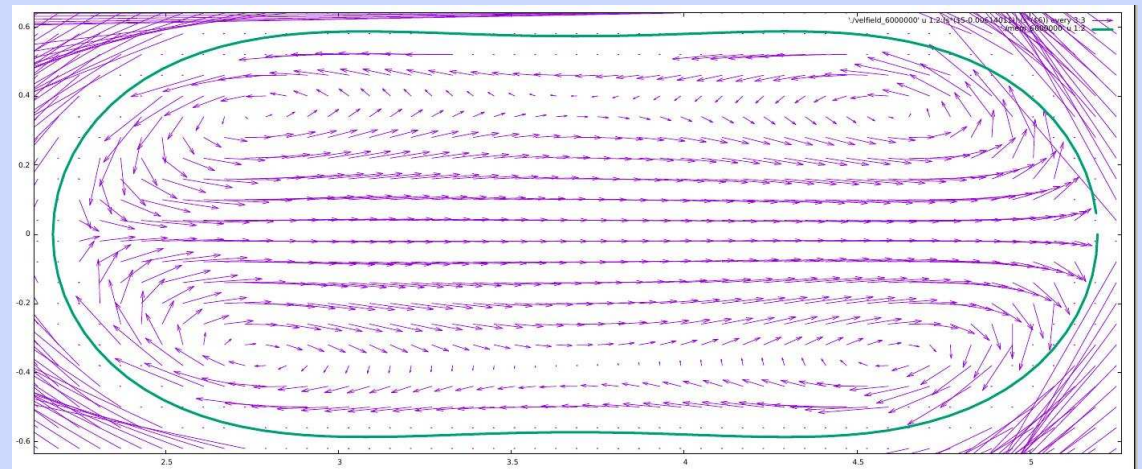
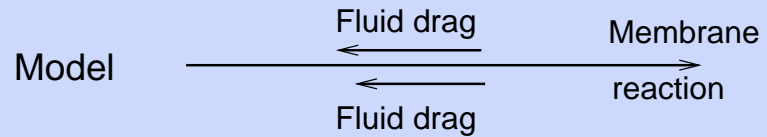
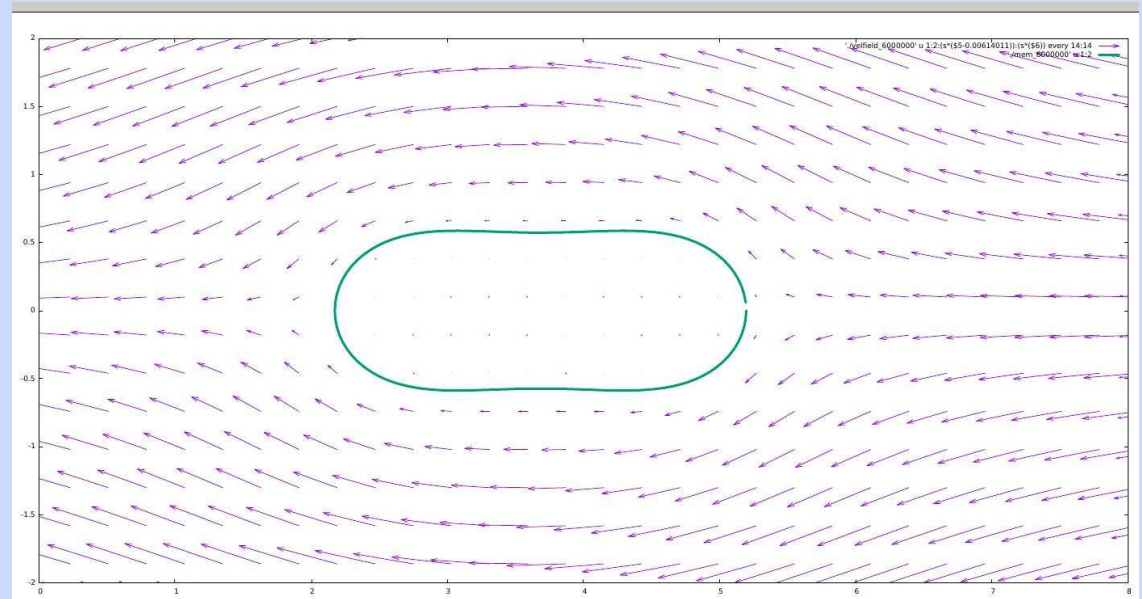
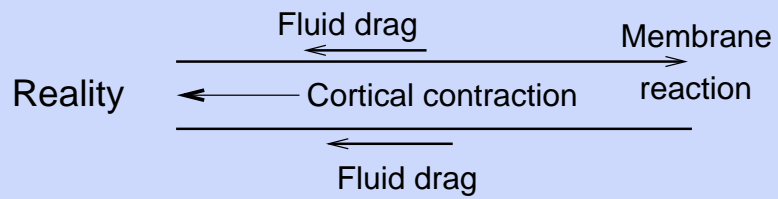
H.W. et al., Stomatocyte-discocyte-echinocyte sequence of the human red blood cell: Evidence for the bilayer-couple hypothesis from membrane mechanics, PNAS, (2002).

Shapes of red blood cells in a fluid flow

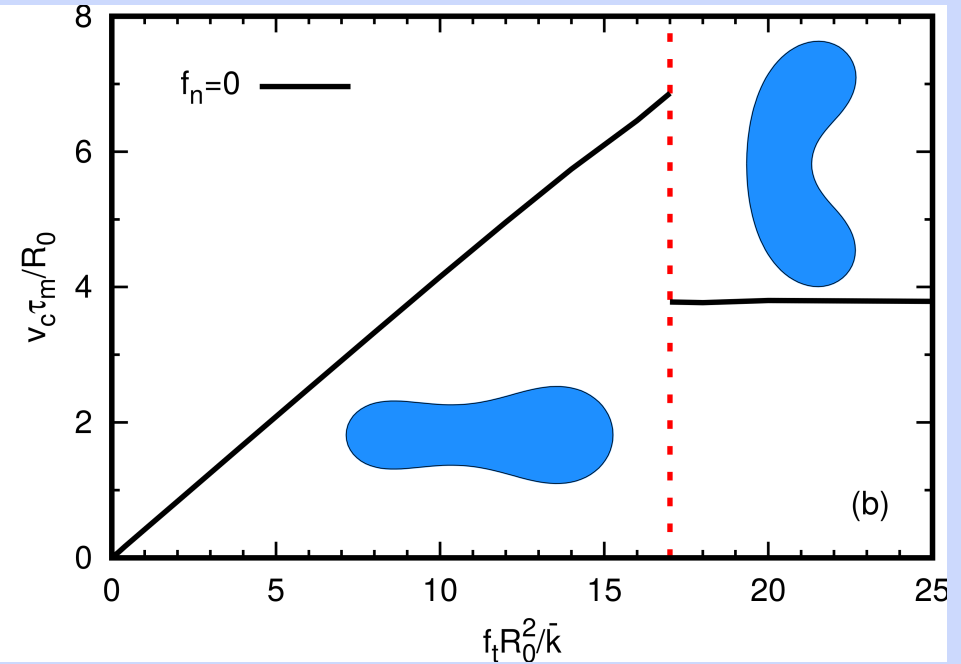
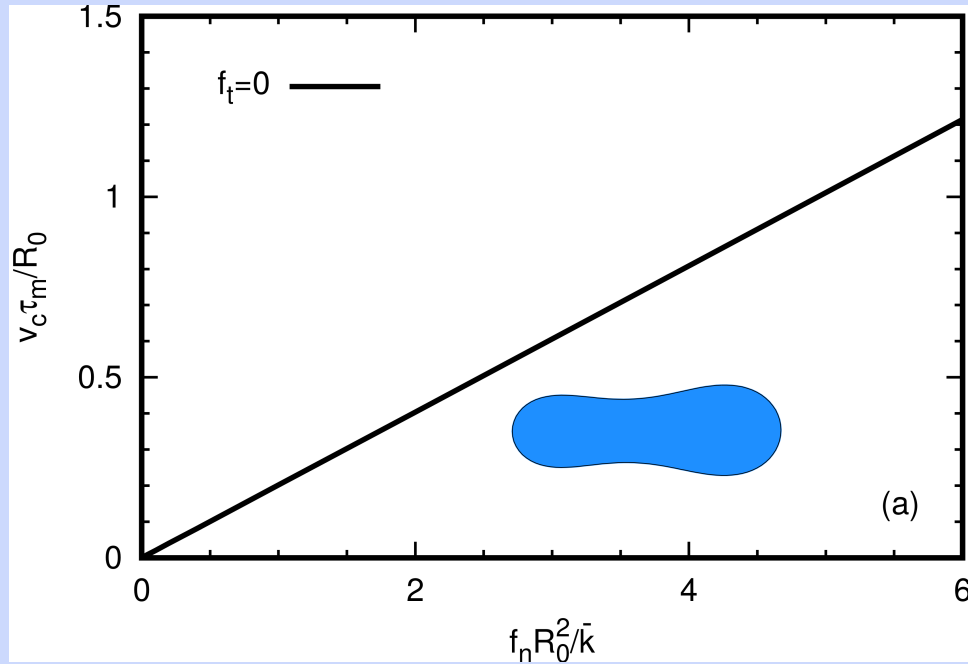


Freund & Zhao, A boundary-integral high-resolution fast method for multiple interacting blood cells, in Computational Hydrodynamics of Capsules and Biological Cells, (2010).

The exterior and interior flows

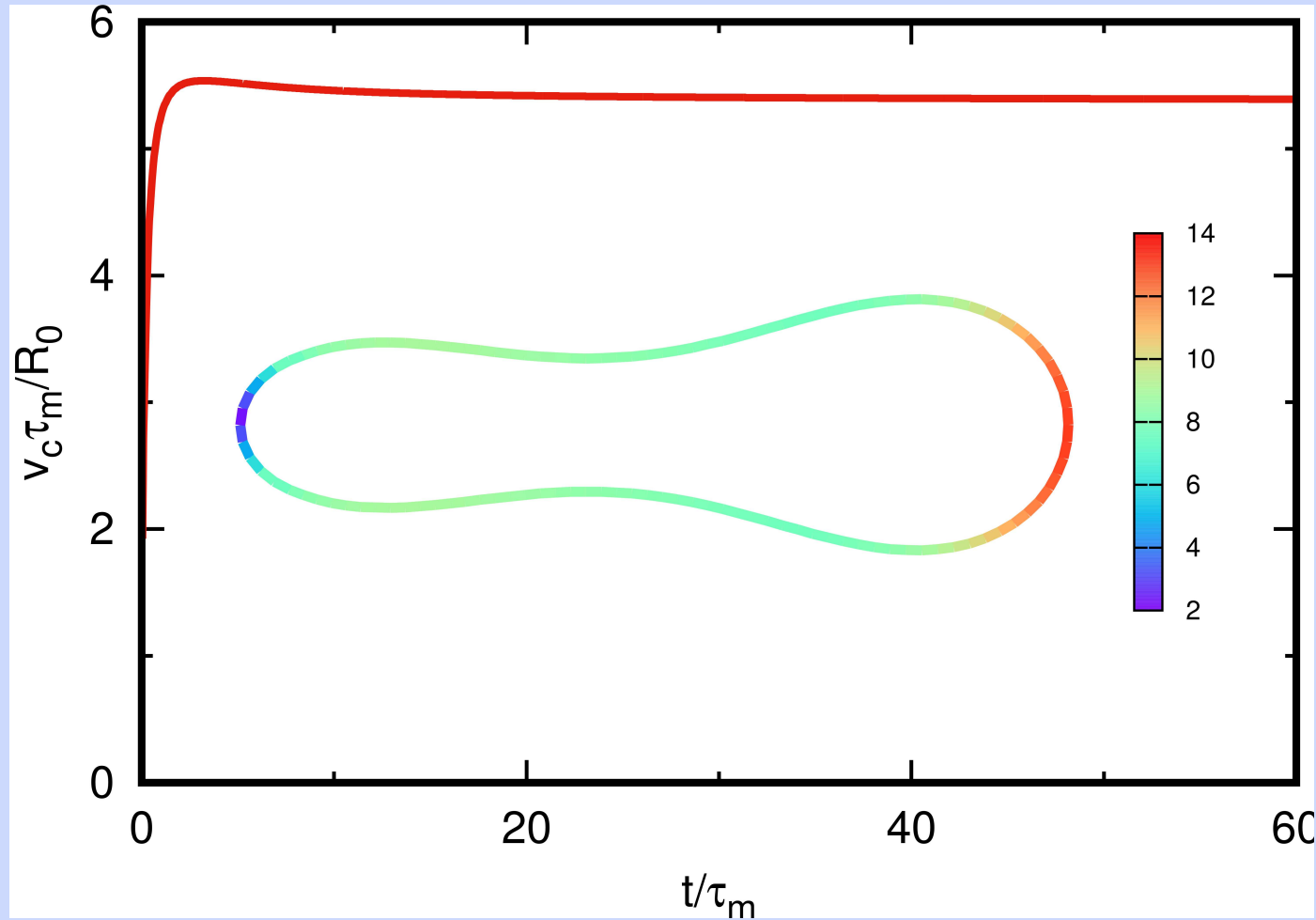


The velocity as a function of the cortical forces



The swimming velocity as a function of the applied forces. The gradient of the forces is reversed from earlier figures, and the cells move to the right. In the both diagrams the cell has a reduced area $\Gamma = 0.6$.

The force distribution on a cell



The velocity, shape and surface force distribution on the cell. The cell shape has a reduced area $\Gamma = 0.5$ with $f_t = 0.0$, $f_n = 0.0$, and $\Delta k_B = 6.0$. The cell moves in the direction of the large lobe