Mathematical Mechanical Biology

Module 3: 3D Mathematical Mechanical Biology

Lecture Notes for C5.9
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Contents

HEALTH WARNING:

The following lecture notes are meant as a rough guide to the lectures. They are not meant to replace the lectures. You should expect that some material in these notes will not be covered in class and that extra material will be covered during the lectures (especially longer proofs, examples, and applications). Nevertheless, I will try to follow the notation and the overall structure of the notes as much as possible.

■ Scope and coverage

In 2019, we will only consider sections 1,2.

1 Introduction

Previously we have considered mechanical biology for filaments and membranes, ie. mechanics in one and two dimensions Here, we proceed to three dimensional mechanics where we must be highly selective in scope. In section 2, we will first initially consider aspects of biofluid mechanics at the level of cell, and focus on fluid actuation by the movement of slender cellular appendages, in particular cilia and flagella.

In later sections, we briefly touch upon models of tissue and engineered artificial tissue, which have both solid elements, in particular, collagen meshes, and interstitial fluid, with a classical example from cartilage modelling, though such models and their generalisations are more recently finding application in the mechanics of tissue engineering and also brain tissue.

2 Biofluids

■ **Overview**

Here, we summarise the Navier Stokes equations for fluid dynamics, before motivating their reduction to Stokes equation for the scale of a cell. We proceed to see how individual cells can actuate their surrounding fluid. In generality this is either for transporting the surrounding fluid, as with ciliary pumping which drives fluids in our lungs and the cerebrospinal system for example, or for moving the cell itself, as with cell motility. This required actuation is often achieved by the beating of a slender filament, in particular either a cilium or a flagellum and we will focus on such examples.

2.1 The equations of Newtonian fluid dynamics

We deal only with an incompressible Newtonian fluid, which is a very good model for water and water with physiological salts and buffers. Thus we require the relationship between stress and rate of strain to be isotropic, homogeneous and linear.

2.1.1 Conservation of mass and incompressibility

Let $\mathbf{x}$ be an Eulerian coordinates, that is fixed relative to an inertial frame. With $\rho(\mathbf{x},t)$ the fluid density and $\mathbf{u}(\mathbf{x},t)$ the velocity vector field of the fluid, mass balance for a material element $V(t)$ gives

$$0 = \underbrace{\frac{d}{dt}\int_{V(t)} dV\,\rho(\mathbf{x},t)}_{\substack{\text{Rate of change of}\\ \text{mass in volume } V(t)}} = \int_{V(t)} dV \left\{ \frac{\partial \rho}{\partial t}(\mathbf{x},t) + \nabla\cdot[\mathbf{u}(\mathbf{x},t)\rho(\mathbf{x},t)] \right\},$$

via use of Reynolds' transport theorem. Noting that $V(t)$ is arbitrary, we have

$$\frac{\partial \rho}{\partial t}(\mathbf{x},t) + \nabla\cdot[\mathbf{u}(\mathbf{x},t)\rho(\mathbf{x},t)] = 0. \tag{1}$$

Incompressibility gives

$$0 = \underbrace{\lim_{\delta t \to 0} \left(\frac{\rho(\mathbf{x} + \mathbf{u}\delta t, t + \delta t) - \rho(\mathbf{x}, t)}{\delta t} \right)}_{\text{The rate of change of } \rho \text{ following the flow}} = \frac{\partial \rho}{\partial t}(\mathbf{x}, t) + \mathbf{u}(\mathbf{x}, t) \cdot \nabla \rho(\mathbf{x}, t).$$

Combining these enforces

$$\nabla \cdot \mathbf{u} = 0. \tag{2}$$

Note also that if ρ is initially constant, then ρ is constant for all time thereafter and we assume this throughout below.

2.1.2 Conservation of momentum

With $\boldsymbol{\sigma}$ the stress tensor and assuming no body force (which is valid for cells and their cilia or flagella moving in water as these are all neutrally buoyant) the conservation of momentum gives

$$\rho \frac{D\mathbf{u}}{Dt} = \nabla \cdot \boldsymbol{\sigma},$$

where $D/Dt = \partial/\partial t + \mathbf{u} \cdot \nabla$ is the advective derivative. Further the assumptions of incompressibility and a Newtonian fluid give

$$\boldsymbol{\sigma} = -p\boldsymbol{I} + \mu \left(\nabla \mathbf{u} + (\mathbf{u})^T \right),$$

where μ is a positive constant, denoted viscosity, and the i, j Cartesian component of $\nabla \mathbf{u}$ is $\partial u_i / \partial x_j$, with transpose $\partial u_j / \partial x_i$. Hence

$$\frac{D\mathbf{u}}{Dt} = -\nabla p + \mu \nabla^2 \mathbf{u}, \tag{3}$$

and equations (2,3) form the Navier Stokes equations.

2.1.3 Characteristic Scales of Incompressible Newtonian Fluid Mechanics and The Stokes Equations

Assuming the characteristic velocity scale is U, the characteristic lengthscale of spatial variation of the velocity vector field is L, the characteristic timescale of temporal variation of the velocity vector field is T, we can non-dimensionalise via

$$t = Tt', \quad \mathbf{u} = U\mathbf{u}', \quad \mathbf{x} = L\mathbf{x}', \quad p = \frac{\mu U}{L} p'$$

to find

$$\beta \frac{\partial \mathbf{u}'}{\partial t'} + \mathrm{Re}\ \mathbf{u}' \cdot \nabla' \mathbf{u}' = -\nabla p + \nabla^2 \mathbf{u},$$

with

$$\beta = \frac{\rho L^2}{\mu T}, \quad \mathrm{Re} = \frac{\rho U L}{\mu},$$

where Re denotes the Reynolds number.

For a eukaryotic cell, typical scales are $L \sim 10\mu$m, the size of the cell, $T \sim 0.1$s as the frequency of a beating cilium or flagellum is very roughly 10Hz and $U \sim 100\mu\text{ms}^{-1}$ as cell swimming speeds (or ciliary fluid propulsion speeds) are about 100μms¹; also $\rho/\mu \sim 10^6$ SI units for water. Hence

$$\beta \sim 10^{-3}, \quad \text{Re} \sim 10^{-3}$$

and one can safely neglect the inertial terms

$$\beta \frac{\partial \mathbf{u}'}{\partial t'}, \quad \text{Re}\ \mathbf{u}' \cdot \nabla' \mathbf{u}'.$$

Thus, for cellular fluid dynamics, the Navier Stokes equations reduce to Stokes' equations

$$\nabla \cdot \mathbf{u} = 0, \qquad 0 = -\nabla p + \mu \nabla^2 \mathbf{u} \tag{4}$$

to excellent accuracy.

Force and torque free swimming

Consider a neutrally buoyant swimmer, so that gravity and buoyancy cancel. The equation of motion for its centre of mass $\mathbf{X}$ is given by

$$M\ddot{\mathbf{X}} = \int_{Swimmer} \boldsymbol{\sigma} \cdot \mathbf{n} \mathrm{d}S,$$

where $\boldsymbol{\sigma} \sim \mu U/L$ is the stress tensor associated with the fluid movement, so that

$$\int_{Swimmer} \boldsymbol{\sigma} \cdot \mathbf{n} \mathrm{d}S,$$

is the total force exerted on the swimmer by the fluid. The lengthscale L is also the lengthscale of the swimmer and the swimmer's density is that of the fluid as it is neutrally buoyant. Hence the ratio of the scale of the inertial term $M\ddot{\mathbf{X}}$ to the fluid force, R_S, and referred to as the Stokes number, is given by

$$\text{R}_S \sim \frac{\rho L^3 \cdot T^2}{\mu \frac{U}{L} L^2} \sim \frac{\rho}{\mu} \frac{L^3}{T^2 U}.$$

Generally the velocity scale U is the order of L/T for swimming, as the flow is driven by a boundary of size L moving at a frequency of $1/T$. Hence

$$\text{R}_S \sim \frac{\rho U L}{\mu} = \text{Re}.$$

Hence, to an excellent approximation, there is not net force on a neutrally buoyant swimmer in Stokes flow. A similar argument shows there is no net torque.

2.1.4 Boundary conditions for Stokes equations

Conditions at infinity If the modelling approximation includes an infinite domain, one must specify the velocity at infinity as part of the boundary conditions:

$$\mathbf{u}(\mathbf{x}, t) \to \mathbf{u}_\infty(\theta, \varphi, t) \qquad \text{as } |\mathbf{x}| \to \infty, \tag{5}$$

where $\theta,\ \varphi$ are spherical polar angles. Often, but not always, $\mathbf{u}_\infty = 0$.

Solid surface boundary condition (No-slip BCs) The boundary conditions depend on the physical nature of the boundary. At a solid, non-permeable, surface Λ moving at speed $\mathbf{U}_\Lambda$, which is typically but necessarily zero, one imposes *the no-slip condition*

$$\mathbf{u}(\mathbf{x}, t) = \mathbf{u}_\Lambda, \quad \mathbf{x} \in \Lambda. \tag{6}$$

One should note that the non-slip boundary condition is empirically based, rather than derived from underlying physical principles though it is typically observed to hold; exceptions are typically either the modelling of rarefied media or moving contact lines, where fluid wets or dewets a surface. The need to consider the breakdown of this boundary condition is rare in physiologically inspired modelling (though an exception is tear film break-up on the surface of the eye, which is of interest in the context of the impact of dry-eye).

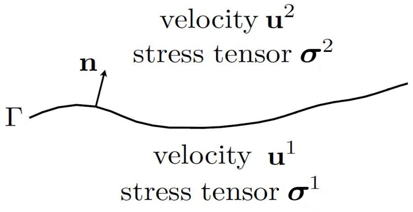


Figure 1: An interface between two fluids.

Interfacial boundary conditions At an interface between two fluids, Γ, with normal $\boldsymbol{n}$ with velocity fields $\mathbf{u}_1$, $\mathbf{u}_2$ and stress tensors $\boldsymbol{\sigma}^1$, $\boldsymbol{\sigma}^2$ either side of the interface, one has the continuity of normal velocity

$$\boldsymbol{n} \cdot \mathbf{u}^1 = \boldsymbol{n} \cdot \mathbf{u}^2, \quad \mathbf{x} \in \Gamma. \tag{7}$$

and stress balance

$$\boldsymbol{\sigma}^1 \cdot \boldsymbol{n} - \boldsymbol{\sigma}^2 \boldsymbol{n} = \gamma \kappa \boldsymbol{n}, \quad \mathbf{x} \in \Gamma. \tag{8}$$

where γ is the *constant* surface tension between the two fluids and $\kappa = 2H = -\nabla \cdot \boldsymbol{n}$. These conditions generalise with some very interesting dynamics when the surface tension is not constant (for example "wine tears".)

Initial conditions The neglect of inertial terms entails that no initial conditions are required to solve Stokes' equations. The time dependence in cellular dynamics typically arises because the boundary conditions are imposed on a moving surface, such as a beating cilium or flagellum.

2.2 Purcell's Scallop theorem

Purcell's Scallop Theorem. In Stokes flow, a swimmer exhibiting reciprocal motion has no net movement.

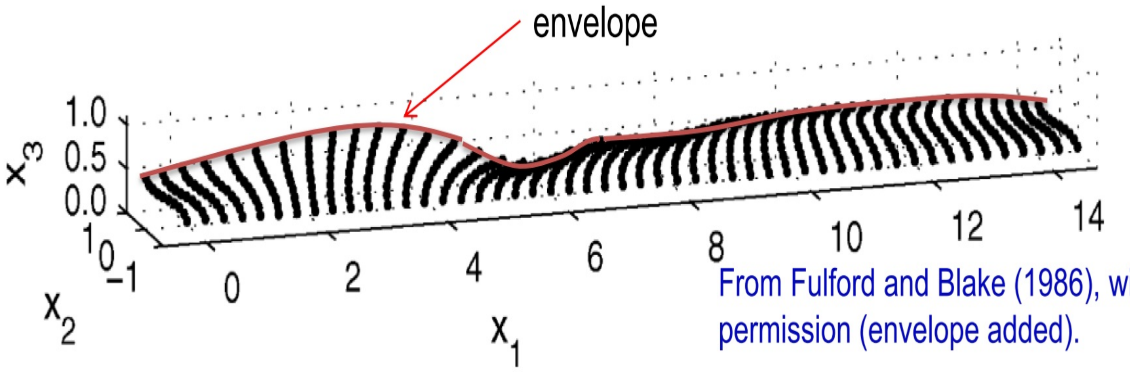
In the original paper, the summary of a semi-popular talk, Purcell stated "I change my body into a certain shape and then I go back to the original shape by going through the sequence in reverse ... So, if the animal tries to swim by [such] a reciprocal motion, it cannot go anywhere."

It is called the scallop theorem because a scallop, with its single hinge, thus cannot swim in the Stokes flow regime. A scallop of course can swim as it is sufficiently large for inertial effects to be important.

■ Proof of Purcell's Scallop Theorem

Note also that time is simply a parameter within the boundary conditions; hence speeding up or slowing down the movement makes no difference. This adds a significant complication to the means by which cells, or artificial microdevices, can move (or, by an immediate generalisation, pump fluid).

2.3 Ciliary Pumping



From Fulford and Blake (1986), without permission (envelope added).

Figure 2: Ciliary beating on the surface of the lung forms a wave, denoted the metachronal wave. In the simplest model, the envelope of this wave is considered as an undulating, impermeable sheet. A fundamental question is: what speed is the fluid above the cilia pumped at, given the time-dependent geometry of the deforming sheet.

As detailed further in this section's supplementary information, cilia line the surface of the lung, where

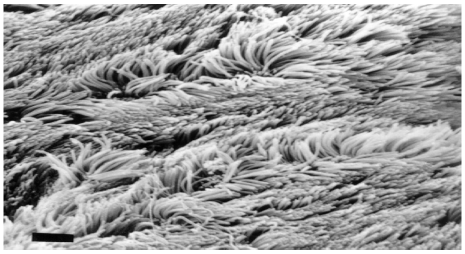


Figure 3: An image of cilia from rabbit trachea. Note how close the cilia are spaced; to give an idea of scale the length of a cilium is about 6 microns.

they beat in a coordinated manner. The beating of an individual cilium relative to its nearest neighbour is slightly out of phase, and hence a long wavelength metachronal wave is formed. Given how close respiratory tract cilia are placed, a common assumption is model the envelope of cilia tips as an impermeable surface, generating the envelope model. The fundamental question we address is, given the metachronal wave movement, how fast is the fluid pumped by the cilia? This was originally addressed by Blake [1].

From the start, we non-dimensionalise length with respect to the inverse wavenumber of the metachronal wave, k^{-1}, time with respect to the inverse frequency, ω^{-1} and velocity with respect to the scale ωk^{-1}. The non-dimensional equations for the fluid are

$$\nabla \cdot \mathbf{u} = 0, \qquad 0 = -\nabla p + \nabla^2 \mathbf{u}. \tag{9}$$

We further simplify. The envelope wave amplitudes are taken to be small relative to k^{-1}, single frequency, and $\pi/2$ out of phase, with x along the lung surface assumed flat, y perpendicular to the lung surface and homogeneity in the third direction. With the y coordinate such that the plane $y = 0$ coincides with the mid plane of the metachronal wave, and noting the non-dimensionalisation, the envelope of the metachronal wave is then given by

$$x_e = x + \epsilon a \cos(x - t), \qquad y_e = \epsilon b \sin(x - t),$$

with $\epsilon \ll 1$ by the small wave amplitude assumption. Thus with $\mathbf{u} = (u, v)$, we have the boundary condition

$$u(x_e, y_e) = \frac{\partial x_e}{\partial t} = \epsilon a \sin(x - t), \qquad v(x_e, y_e) = \frac{\partial y_e}{\partial t} = -\epsilon b \cos(kx - t),$$

We also have

$$(u, v) \to (U, 0) \ \text{ as } \ y \to \infty,$$

where U is a priori unknown, and the fundamental quantity we seek, but must be found as part of the solution.

Since $\nabla \cdot \mathbf{u} = 0$, we can express $\mathbf{u}$ via the streamfunction

$$u = \frac{\partial \psi}{\partial y}, \qquad v = -\frac{\partial \psi}{\partial x}.$$

Fundamental equations for ψ, U. Taking the curl of the momentum equation we have

$$\nabla^4 \psi = 0$$

with

$$\frac{\partial\psi}{\partial y}(x_e, y_e) = \epsilon a\sin(x-t), \qquad \frac{\partial\psi}{\partial x}(x_e, y_e) = \epsilon b\cos(kx-t),$$

$$x_e = x + \epsilon a\cos(x-t), \qquad y_e = \epsilon b\sin(x-t),$$

and

$$\left(\frac{\partial\psi}{\partial y}, \frac{\partial\psi}{\partial x}\right) \to (U, 0) \quad \text{as} \quad y \to \infty.$$

Solution We seek a perturbative solution. Clearly if $\epsilon = 0$ the solution is $U = \psi = 0$ as nothing is driving the flow. Hence we write

$$\psi = \epsilon\psi_1(x,y) + \epsilon^2\psi_2(x,y) + O(\epsilon^3), \quad U = \epsilon U_1 + \epsilon^2 U_2 + O(\epsilon^3), \; .$$

■ **Finding $\psi_1,\ U_1$**

Hence we find

$$U_1 = 0, \quad \psi_1 = (b + (a+b)y)e^{-y}\sin(x-t).$$

Thus we must go to second order to find the pumping speed. We do not try to find ψ_2 but to seek the solution for U_2 as quickly as possible.

■ **Finding U_2**

Hence we find $U_2 = \frac{1}{2}\left(b^2 + 2ab - a^2\right)$, which gives the (non-dimensional) speed which the cilia are predicted to pump the fluid in the far field.

2.4 Cellular Motility

2.4.1 Some simple observations about, and solutions for, Stokes equations

Before we consider cellular motility in detail, we consider some simple observations about, and solutions for Stokes flow that we will need later.

The Stokeslet. Below, we will need the Stokeslet, which generates the solution of Stokes flow, with a point forcing located at $\mathbf{x}_0$. It can be obtained by considering the Stokes equations for a point force $\mathbf{m}$ located at $\mathbf{x} = \mathbf{x}_0$:

$$-\nabla p + \mu \nabla^2 \mathbf{u} + \mathbf{m}\delta(\mathbf{x} - \mathbf{x}_0) = 0, \quad \nabla \cdot \mathbf{u} = 0. \tag{10}$$

■ Derivation of the Stokeslet

Hence, with $\hat{\mathbf{x}} = \mathbf{x} - \mathbf{x}_0$ and $r = |\mathbf{x} - \mathbf{x}_0|$ we have (with summation convention) that

$$u_i = \frac{1}{8\pi\mu} G_{ij} m_j, \tag{11}$$

where

$$G_{ij} = \frac{\delta_{ij}}{r} + \frac{\hat{x}_i \hat{x}_j}{r^3},$$

which is the Stokeslet (also known as the Oseen-Burgers tensor or the free-space Greens function).

The potential dipole This is very useful as Stokes equation are linear and hence we can build up solutions by the linear superposition of solutions which have point forces outside the domain, in direct analogy to the method of images for the solution of problems in electrostatics, or Laplace's equation for example. Other solutions of Stokes equations are useful this purpose too; the simplest is associated with a constant pressure, and the gradient of a potential

$$u_i = -\frac{\partial}{\partial x_i}\left(\frac{1}{r}\right) = \frac{\hat{\mathbf{x}}}{r^3},$$

where once more $\hat{\mathbf{x}} = \mathbf{x} - \mathbf{x}_0$ and $r = |\mathbf{x} - \mathbf{x}_0|$. Because the only boundary constraint is decay at infinity, one can differentiate such solutions with respect to the location of the singularity, $\mathbf{x_0}$, to find another solution.

■ The point source dipole, also known as the potential dipole

Hence

$$D_{ij} = \frac{\partial}{\partial x_{0,j}}\left(\frac{\hat{\mathbf{x}}}{r^3}\right) = -\frac{\delta_{ij}}{r^3} + 3\frac{\hat{x}_i\hat{x}_j}{r^5}$$

and (with summation)

$$u_i = D_{ij}q_j$$

is a solution of Stokes equations for any constant vector $\mathbf{q}$.

The solution for a translating sphere By linearity, any linear combination of the potential dipole and stokeslet also solves Stokes equations. We can combine them to find the solution to Stokes equations for a neutrally buoyant sphere of radius a translating at constant speed $\mathbf{U}$ in the absence of other boundaries:

$$-\nabla p + \mu\nabla^2\mathbf{u} = \mathbf{0}, \quad \nabla\cdot\mathbf{u} = 0 \quad \text{for} \quad |\mathbf{x}-\mathbf{x}_0| > a \tag{12}$$

with

$$\mathbf{u} = \mathbf{U}, \ \text{ const,} \quad \text{for} \quad |\mathbf{x}-\mathbf{x}_0| = a$$

and $\mathbf{u} \to \mathbf{0}$ at spatial infinity, with the sphere centred at $\mathbf{x}_0$ at any given instant.

To find the flow field at the field point $\mathbf{x}$ external to, or on the sphere, consider

$$u_i = G_{ij}g_j + D_{ij}q_j.$$

By construction it is a solution of the Stokes equation and decays at spatial infinity. Imposing the no-slip condition on the sphere boundary $r = a$ we have

$$U_i = \frac{g_i}{a} - \frac{q_i}{a^3} + \hat{x}_i\hat{x}_j\left[\frac{1}{a^3}g_j + \frac{3}{a^5}q_j\right].$$

Comparing coefficients, we have

$$\mathbf{q} = -\frac{a^2}{3}\mathbf{g} \ \text{ and hence } \ \mathbf{g} = \frac{3}{4}a\mathbf{U} = \frac{1}{8\pi\mu}[6\pi a\mu\mathbf{U}],$$

giving the solution for the flow around a translating sphere.

This readily allows us to calculate the viscous drag exerted by the surrounding fluid on a translating sphere, which is known as Stokes drag. In particular the potential dipole does not contribute to the force (it is the limit of a linear combination of “equal but opposite” solutions, which thus do not exert a force prior to taking the limit, and hence do not exert a force after taking the limit).

■ Stokes Drag

Let $\sigma_{ij}^{Stk} = T_{ijp}^{Stk} m_p$ be the stress associated with Stokeslet solution 11. We thus have

$$\nabla_j \sigma_{ij}^{Stk} = m_p \nabla_j T_{ijp}^{Stk} = -m_i \delta(\mathbf{x} - \mathbf{x}_0).$$

The stress due to the Stokeslet contributions for the sphere solution is thus

$$\sigma_{ij}^{Sphere} = 8\pi\mu T_{ijp}^{Stk} g_p$$

and hence the total drag force, that is the force exerted by the fluid on the sphere, is

$$\begin{aligned} F_i &= \int_{Sphere} \sigma_{ij}^{Sphere} \cdot n_j \mathrm{d}S = \int_{Sphere} \nabla_j \sigma_{ij}^{Sphere} \mathrm{d}V \\ &= 8\pi\mu \int_{Sphere} g_p \nabla_j T_{ijk}^{Sphere} dV = -8\pi\mu \int_{Sphere} g_p \delta(\mathbf{x} - \mathbf{x}_0) dV = -8\pi\mu g_p. \end{aligned}$$

Hence the drag force is given by

$$\mathbf{F} = -6\pi\mu a \mathbf{U}. \tag{13}$$

2.4.2 Resistive force theory

■ Foundation of resistive force theory

Consider a small element of a very slender filament of circular cross section moving in a viscous fluid. To provide the foundation for resistive force theory, our objective is to relate the drag force per unit length, $\mathbf{f}$ to the velocity of the filament, analogous to the relationship between the drag $\mathbf{F}$ and velocity $\mathbf{U}$ of a sphere in equation 13.

By the linearity of Stokes equations and symmetry of the circular cross section, the relation between drag per unit length and velocity must be of the form

$$\mathbf{f} = -C_N(\mathbf{I} - \mathbf{e}_T\mathbf{e}_T)\mathbf{U} - C_T(\mathbf{e}_T \cdot \mathbf{U})\mathbf{e}_T. \tag{14}$$

Thus our task reduces to finding $C_T,\ C_N$.

■ Resistive Force Theory

Definition. Any theory of swimming that considers the mechanics of a beating cilium or flagellum by using only the relationship between velocity and drag for isolated infinitesimal filament elements given by equation (14), is referred to as *resistive force theory.* Such theories neglect possible non-local hydrodynamic interactions between different parts of the filament, eg if it turns back on itself, or hydrodynamic interactions between a cilium/flagellum and the cell to which it is attached

To derive the relationship between drag and velocity for resistive force theory, consider a straight filament of length L and cross section radius a, with $a/L \ll 1$.

Suppose the filament is aligned along the x axis, between $x = 0$ and $x = L$, and is subject to a constant external force, uniformly distributed along its length, with force density per unit length $\mathbf{f}^{ext}$. We split the rod into $N = L/a \gg 1$ elements of equal length, a.

Initially all hydrodynamic interactions of an element with its neighbours is neglected; the force each element exerts on the fluid is then $(L/N)\mathbf{f}^{ext}$.

Invoking linearity of Stokes equations, the speed of the α^{th} element must be of the form

$$u_i^\alpha = \frac{L}{N} A_{ij}^\alpha f_j^{ext},$$

where the tensor $\mathbf{A}_{ij}^\alpha$ has $O(1)$ coefficients and, by the no slip boundary condition, this is also the speed of the fluid on the surface of the rod element. As all elements are equivalent the tensor A_{ij}^α in fact does not depend on α and we drop the superscript in the following.

To consider hydrodynamical interactions, at least approximately, we approximate each rod element by a Stokeslet, of strength $L\mathbf{f}^{ext}/N$, at locations $\mathbf{x}_0^\alpha = (L/[2N], 0, 0) + (L\alpha/N, 0, 0)$, for $\alpha \in \{1, ..., N\}$. This is equivalent to approximating each rod element as a sphere of radius $a = L/[2N]$; the far field of such an object is dominated by the Stokeslet which decays like the inverse of distance; the potential dipole decays like the inverse of the cubed distance. Even at a distance of $2a$, ie. the next element, this approximation induces a relative error of about $2/2^3$, i.e. 25%, with improvements in considering more distant elements. Given the level of accuracy of resistive force theory, this is a tolerable error.

The flow induced by the α^{th} stokeslet is

$$u_i^\alpha(\mathbf{x}) = \frac{1}{8\pi\mu}\frac{L}{N} G_{ij}(\mathbf{x}, \mathbf{x}_0^\alpha) f_j^{ext}.$$

Invoking linearity once more, the velocity at the β^{th} segment is thus the linear superposition of the flow induced by the β^{th} element and the flow induced by (our Stokeslet approximation of) all the other elements.

■ Foundation of resistive force theory

Hence, the flow at a point on the surface of the β^{th} element, $\mathbf{x}^\beta \in \partial\Omega^\beta$, is

$$\begin{aligned} u_i^\beta(\mathbf{x}^\beta) &= A_{ij} f_j^{ext} L/N + \sum_{\alpha;\ \alpha\neq\beta} \frac{L}{N} G_{ij}(\mathbf{x}^\beta, \mathbf{x}_0^\alpha) f_j^{ext} \\ &= A_{ij} f_j^{ext} L/N + \sum_{\alpha;\ \alpha\neq\beta} \frac{L}{8\pi\mu N} \left\{ \frac{\delta_{ij}}{r} + \frac{r_i r_j}{r^3} \right\} f_j^{ext} \end{aligned}$$

where $\mathbf{r} = \mathbf{x}^\beta - \mathbf{x}_0^\alpha$, $r = |\mathbf{r}|$.

■ Foundation of resistive force theory

For $N \gg 1$ we have the velocity at the centre of filament can be derived as follows.

We approximate the sum by an integral, excluding a region around $\mathbf{x}^\beta$. Thus, we have

$$\begin{aligned} u_i^\beta(\mathbf{x}^\beta) &= A_{ij} f_j^{ext} L/N + \frac{1}{8\pi\mu}\int_0^{s^\beta} ds \left\{\frac{\delta_{ij}}{r} + \frac{r_i r_j}{r^3}\right\} f_j^{ext} \\ &+ \frac{1}{8\pi\mu}\int_{s^\beta+2a}^{L} ds \left\{\frac{\delta_{ij}}{r} + \frac{r_i r_j}{r^3}\right\} f_j^{ext} + O(L/N) \end{aligned}$$

where $s^\beta = \beta L/N$ and $\mathbf{x}^\alpha \to s\mathbf{e}_x$ noting that $\mathbf{x}^\beta$ is still a fixed point on $\partial\Omega^\beta$. With the (crude!) approximation

$$\mathbf{r} \sim \left(s^\beta + \frac{L}{2N} - s\right)\mathbf{e}_x,$$

and using $L/[2N] = a$, we have

$$\begin{aligned} u_i^\beta &\sim A_{ij} f_j^{ext} L/N + \frac{1}{8\pi\mu}\left[\delta_{ij} + \delta_{i1}\delta_{j1}\right] f_j^{ext} \left[\int_0^{s^\beta} \frac{ds}{|s^\beta - s + a|} + \int_{2a+s^\beta}^{L} \frac{ds}{|s^\beta - s + a|}\right] \\ &\sim A_{ij} f_j^{ext} L/N \\ &+ \frac{1}{8\pi\mu}\left[\delta_{ij} + \delta_{i1}\delta_{j1}\right] f_j^{ext} \log\left(\frac{s^\beta(L-s^\beta)}{a^2}\right)\left(1 + O\left(\frac{a(L-2s^\beta)}{s^\beta(L-s^\beta)} \frac{1}{\log\left(\frac{s^\beta(L-s^\beta)}{a^2}\right)}\right)\right) \end{aligned}$$

Considering away from the ends of the rod, so that $s^\beta = \gamma L$, with γ not close to zero or unity, so that $|\log(\gamma(1-\gamma))| \sim O(1)$, we have

$$u_i^\beta \sim A_{ij} f_j^{ext} L/N + \frac{1}{4\pi\mu}\left[\delta_{ij} + \delta_{i1}\delta_{j1}\right] f_j^{ext} \log\left(\frac{L}{a}\right)\left(1 + \frac{1}{2}\frac{\log(\gamma(1-\gamma))}{\log\left(\frac{L}{a}\right)} + h.o.t.\right).$$

Hence

$$u_i^\beta \sim \frac{1}{4\pi\mu}\left[\delta_{ij} + \delta_{i1}\delta_{j1}\right] f_j^{ext} \log\left(\frac{L}{a}\right) \quad \text{as } \frac{1}{N}, \frac{a}{L} \to 0,$$

though extensive further work (eg matching into a prolate ellipsoid cap) is required to determine corrections at the ends.

A flagellum. Approximating a flagellum as a collection of slender straight elements, the velocity of the centre of each rod is related to the hydrodynamic force density exerted on the rod, at this level of approximation, by

$$u_i \sim \frac{1}{4\pi\mu}\left[\delta_{ij} + \delta_{i1}\delta_{j1}\right] f_j^{ext} \log\left(\frac{L}{a}\right).$$

Note this gives the velocity of a segment given the force per unit length applied on the fluid by the filament. We require the drag force per unit length, ie the force per unit length exerted on the filament by the fluid; this differs just by a minus sign (by Newton's third law).

Hence, the relationship between the hydrodynamic forces and velocities of elements of a flagellum are related by

$$f_T = -C_T u_T, \quad f_N = -C_N u_N, \quad \text{where} \;\; C_N = 2C_T = \frac{4\pi\mu}{\log\left(\frac{L}{a}\right)},$$

with f_T, u_T, C_T denoting the force density, velocity and resistance coefficient in the tangential direction and f_N, u_N, C_N denoting the analogous quantities in the normal and binormal directions.

The original, more rigorous but harder, analysis can be found in [4], where the flow field adjacent to a sinusoidally moving filament is determined invoking asymptotics in a/L. Differentiating these flow field yields the stress tensor, and hence the resistance coefficient can be explicitly determined, as first noted by [3]. You will immediately note the increase in complexity of the analysis if you read the original papers with further complexity if the careful asymptotics of [5] are explored; therefore a crude technique, rather than a rigorous one, is presented here.

2.4.3 Example. Predicting the speed of a swimming cell.

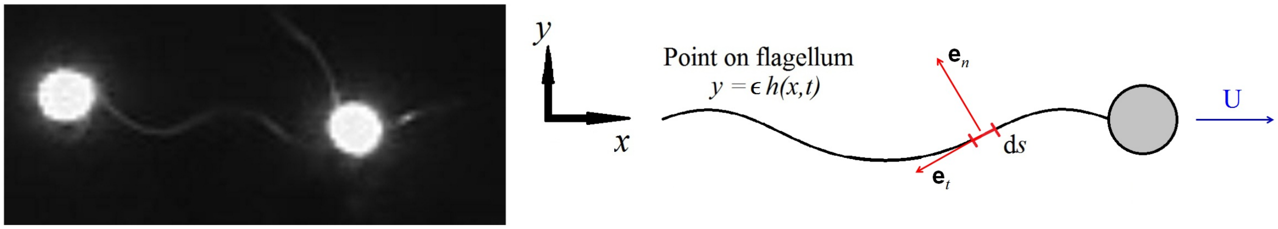


Figure 4: Left. An image of two carp spermatozoa highlighting the spherical cell body, courtesy of Galina Prokopchuk and Jacky Cosson, University of South Bohemia, Faculty of Fisheries and Protection of Waters, Research Institute of Fish Culture and Hydrobiology. The head radius is exaggerated in the image due to an optical effect as the microscopy is fine tuned to make the flagellum visible, which requires phase contrast microscopy, rather than standard microscopy, since the flagellar cross sectional radius is less than a wavelength of light. Right. The model; shallow planar waves of the form $y = \epsilon h(x,t)$ propagate down the flagellum, where the plane $y = 0$ is the mid-plane of the flagellum.

For simplicity, we consider a swimmer with a spherical cell body. These are not that common – instead there is an array of interesting cell shape geometries. Nonetheless, numerous fish spermatozoa, for instance carp and turbot, have spherical bodies.

Let $y = 0$ correspond to the midplane about which the flagellum beats, and let $y = \epsilon h(s,t)$ denote the location of the flagellum at time t and arclength s. We assume a small amplitude beat so that $\epsilon \ll 1$.

Finally, in most expositions, it is assumed that the spermatozoon body has negligible velocity in the y direction, i.e. that the cell body velocity is $(U, 0)$ and that it does not rotate. Below we make this assumption, but it is generally unjustified. See for example page 13 of the supplementary information, where the trajectory a cell head is the magenta curve. We consider when such assumptions are valid in more detail in the problems.

Our objective below is thus to find U, that is the swimming velocity, in terms of $h(x,t)$.

Total force balance on the flagellum

- The spherical cell body moves with speed $\mathbf{U}$. Hence it experiences a drag force of $-6\pi\mu a\mathbf{U}$ from the fluid.
- Considered in isolation there is no net force on the cell as the Stokes number R_S, is essentially zero.
- Thus
$$-6\pi\mu a\mathbf{U} + (\text{Drag force on flagellum}) = \mathbf{0}.$$

Hence

$$6\pi\mu a\mathbf{U} = (\text{Drag force on flagellum}). \tag{15}$$

We now use resistive force theory to determine the drag force on the flagellum in terms of $h(s,t)$. This gives us an equation for $\mathbf{U}$, and we takes its projection onto the x-axis to find U, the swimming speed in the x direction, working to the leading non-trivial order in $\epsilon \ll 1$.

Prediction for U via resistive force theory

We have $\mathbf{e}_t = (-1, \epsilon h_s)$, $\mathbf{e}_n = (\epsilon h_s, 1)$ and the velocity of the flagellum element is given by $\mathbf{U} = (U, \epsilon h_t)$ noting there is no cell body velocity in the y-direction. Hence the drag force per unit length on the element ds is given by

$$\mathbf{f} = -\left[C_N \mathbf{e}_n \cdot \mathbf{U}\mathbf{e}_n + C_T \mathbf{e}_t \cdot \mathbf{U}\mathbf{e}_t\right] = -\left[(C_N - C_T)\mathbf{e}_n \cdot \mathbf{U}\mathbf{e}_n + C_T\mathbf{U}\right]$$

and projecting this onto the x-direction we have

$$\begin{aligned}\mathbf{f}\cdot\mathbf{e}_x &= -\left[(C_N - C_T)\mathbf{e}_n \cdot \mathbf{U}\mathbf{e}_n \cdot \mathbf{e}_x + C_T U\right] \\ &= -\left[(C_N - C_T)(\epsilon^2 h_s^2 U) + (C_N - C_T)(\epsilon^2 h_s h_t) + C_T U\right]\end{aligned}$$

Hence, by equation (15)

$$6\pi a\mu U = -\int_0^L \left[(C_N - C_T)\epsilon^2 h_s^2 U + (C_N - C_T)(\epsilon^2 h_s h_t) + C_T U\right] \mathrm{d}s \tag{16}$$

Rearranging gives

$$\left[6\pi a\mu + (C_N - C_T)\epsilon^2 \int_0^L h_s^2 ds + C_T L\right] U = -(C_N - C_T)\epsilon^2 \int_0^L h_s h_t \mathrm{d}s.$$

Dropping the clearly subleading $O(\epsilon^2)$ term on the left-hand side immediately yields

$$U = \epsilon^2 \frac{C_T - C_N}{6\pi a\mu + C_T L} \int_0^L h_s h_t \mathrm{d}s.$$

We note that Friedrich et. al [2] have recently reported a very good agreement between resistive force theory predictions and spermatozoan trajectories.

3 An introduction to Poroelasticity. To be written.

■ **Overview**

Here, we combine ideas from 3D biological fluid and solid mechanics to consider models of tissue where both the interstitial fluids bathing the tissue and the elastic component of the tissue, typically a collagen mesh, are both mechanically important. The fluid and solid are inter-mixed at the microscale and hence a volume element of a continuum model possess both fluid and solid constituents. To formulate a model, one balances mass and momentum individually for both of these constituent phases, including interaction forces between them in the momentum balance. They are many physiological applications, for instance in the mechanics of cartilage and brain tissue.

3.1 Volume fractions and no voids

3.2 Mass balance

3.3 Momentum balance and fluid-solid drag

3.4 Constitutive Laws

3.4.1 Restrictions on the constitutive laws due to the second law of thermodynamics.

3.5 Summary of equations

3.5.1 Boundary conditions and initial conditions

3.5.2 Further tissue complications: Osmotic pressures

3.6 Application: cartilage models and confined compression experiments

4 Problems

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1) (a) Briefly explain why the moment exerted on the element, V_*, about a point within the volume, and taken to be the origin, is given by

$$\int_{\partial V_*} x_p \epsilon_{ipq} \sigma_{qs} n_s dA.$$

Show that this is equal to

$$\int_{V_*} \epsilon_{isq} \left(\sigma_{qs} + x_p \frac{\partial \sigma_{qm}}{\partial x_m} \right) dV$$

You may assume that the stress tensor has bounded derivatives. By considering moment balance as the volume V_* is taken arbitrarily small, explain why the stress tensor is symmetric, i.e. $\boldsymbol{\sigma} = \boldsymbol{\sigma}^T$.

(b) Show that a neutrally buoyant inertialess swimmer is torque-free, i.e. the total torque exerted by the fluid on the swimmer is zero.

2) **Ciliary Pumping**

Blake [1] considered a more general metachronal wave which, after non-dimensionalisation, takes the form

$$x_e = x + \epsilon \sum_{n=1}^{\infty} (a_n \sin(n[x+t]) - b_n \cos(n[x+t])), \qquad y_e = \epsilon \sum_{n=1}^{\infty} (c_n \sin(n[x+t]) - d_n \cos(n[x+t])).$$

(a) Using the result in the lecture notes, without detailed calculation, show that at leading non-trivial order

$$U = \frac{1}{2} \epsilon^2 \sum_{n=1}^{\infty} n^2 [c_n^2 + d_n^2 - a_n^2 - b_n^2 + 2(a_n d_n - c_n b_n)].$$

(b) Blake also found the non-dimensional power required per unit surface area of envelope at leading non-trivial order:

$$P = \epsilon^2 \sum_{n=1}^{\infty} n^3 [c_n^2 + d_n^2 + a_n^2 + b_n^2].$$

Find the metachronal wave (or waves) that maximises the modulus of U, the velocity of the far field flow for a fixed power per unit area, P, and find the associated non-dimensional value of $|U|$.

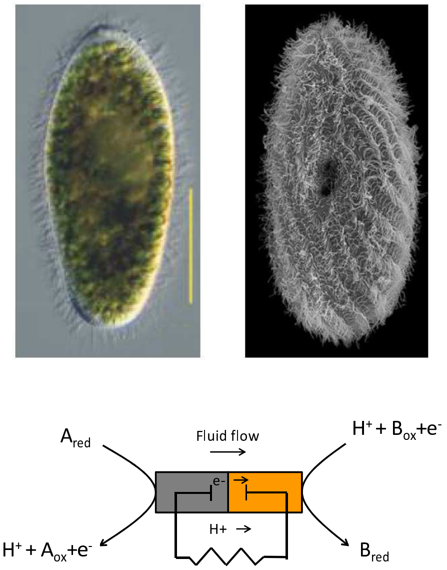

Figure 5: Images of the ciliate, *Paramecium (Viridoparamecium) chlorelligerum.* Upper Left, (a). An image from flash photomicrography of freely motile specimen after disturbance. Scale bar, 50μm. Upper Right, (b). A scanning electron microscope image of the dorsal side, illustrating the density of cilia on the cell surface. Reproduced, without permission, from Kreutz et. al [6]. Lower (c). A schematic of a prospective self-electrophoretic propulsion mechanism for a conducting Janus particle within an acidic environment, whereby a slip-velocity is induced by the ion flows generated by a simultaneous catalytic oxidation of a fuel present in the solute, A, on one side of the particle and a catalytic reduction of a fuel, B, on the other. From Paxton et. al [7], without permission.

3) **Ciliate Motility** Consider a ciliate, that is a cell covered in beating cilia, which induce movement. As a simple model, suppose that the cell is spherical and that the ciliary envelope is such that the cell radius does not deform (at least approximately). Alternatively, this could represent the streaming velocity around a spherical Janus particle; see figure.

   In particular suppose the cell moves its surface in a tangential direction such that, in the non-dimensionalised system, the radius of the cell is $r = 1$ and during the deformation the polar angle θ (such that $z = r\cos\theta$) is mapped to Θ with

$$\Theta = \theta + \epsilon\beta_1(t)V_1(\cos\theta),$$

   where

$$V_n(x) = \frac{2\sqrt{1-x^2}}{n(n+1)}\frac{\mathrm{d}P_n}{\mathrm{d}x}(x)$$

   is the associated Legendre function of the n^{th} Legendre function $P_n(x)$. In particular $P_1(x) = x$.

   By working in a frame comoving with the cell, show that its swimming speed is

$$\frac{2}{3}\epsilon\dot{\beta}_1(t).$$

   *[Difficult] Show the cell moves with the same swimming speed if instead

$$\Theta = \theta + \epsilon\sum_{n=1}^{\infty}\beta_n(t)V_n(\cos\theta).$$

4) **Rotating Sphere in Stokes Flow**

With $\hat{\mathbf{x}} = \mathbf{x} - \mathbf{x}_0$, $r = |\mathbf{x} - \mathbf{x}_0|$ and

$$G_{ij} = \frac{\delta_{ij}}{r} + \frac{\hat{x}_i \hat{x}_j}{r^3},$$

define the rotational dipole $\mathbf{G}^c$ by

$$G^c_{im} := \frac{1}{2}\epsilon_{mlj}\frac{\partial G_{ij}}{\partial x_{0,l}},$$

where

$$\epsilon_{mlj} := \begin{cases} +1 & \text{if} \quad (m,l,j) = (1,2,3) \text{ or } (3,1,2) \text{ or } (2,3,1) \\ -1 & \text{if} \quad (m,l,j) = (1,3,2) \text{ or } (2,1,3) \text{ or } (3,2,1) \\ 0 & \text{if} \quad \text{any of } i,j,k \text{ are equal} \end{cases}$$

$\mathbf{G}^c$ is also known as a rotlet or couplet.

(a) Show that

$$G^c_{im} = \epsilon_{iml}\frac{\hat{x}_l}{r^3}.$$

(b) Show the solution for the Stokes flow associated with a sphere of radius a centred at $\mathbf{x}_0$ and rotating with angular velocity $\boldsymbol{\Omega}$ is given by $a^3 G^C_{im}\Omega_m$.

(c) With an origin at the centre of the sphere, show that the fluid exerts a torque of $-8\pi\mu a^3\boldsymbol{\Omega}$ on the sphere.

5) **Resistive Force theory** Throughout this question, one can work with the leading non-trivial order of the parameter ϵ, where the flagellum location is given by $y = \epsilon h(s,t)$.

In the lecture notes any possible movement of the cell in the y-direction was neglected. With the movement of the cell body given by $\mathbf{U} = (U, V)$ and the velocity of a flagellar element given by $(U, V + \epsilon h_t)$ write down a set of simultaneous equations for U, V. Hence find U and determine conditions on $h(x,t)$ where the neglect of V in the notes is a good approximation.

6) **Resistive Force theory. Possible Msc special topic or DPhil "broadening" problem.** In the lecture notes and the above question, the possibility of cell rotation was neglected. Recollect that the drag torque on the swimmer is zero (e.g. generalise the results in the lecture notes, as in Q1).

- The torque on the swimmer is relative to a fixed point in an inertial frame. Use the the fact that the viscous drag on the swimmer is zero to show that the torque about the centre of the spherical swimmer cell body is also zero.
- Write down the total torque on the cell, including its flagellum, about an origin at the centre of the cell body, in terms of
  - the cell body speed, $\mathbf{U} = U\mathbf{e}_x + V\mathbf{e}_y$,
  - the cell body angular velocity $\boldsymbol{\Omega} = \Omega\mathbf{e}_z$
  - the flagellar amplitude $h(s,t)$ and its derivatives

  N.B. Note at this stage, and in contrast to the lecture notes, do not approximate via $\epsilon \ll 1$.
- Hence write down a set of three simultaneous equations for U, V, Ω.

- With the rescaling $h(s,t) \to \epsilon h(s,t)$, keep only the leading non-trivial terms in the above. Numerically solve these equations for

  $$h(s,t) = \epsilon D s \sin(ks - \omega t)$$

  and

  $$h(s,t) = \epsilon D s (1 - \cos(ks - \omega t)),$$

  with $\omega = 10$Hz, a flagellum length of 50μm, $2\pi/k = 40\mu$m, and various values of the amplitude ϵD. In terms of $h(s,t)$ when will the cell swim, on average, in an approximately straight line and when will it circle? If it circles can you find the radius of the circular trajectory?

7) **Possible Msc special topic or DPhil "broadening" problem.** Compute the axisymmetric deformation on an initially flat sheet under atomic force microscopy. Compute the force necessary to deform the sheet by a distance h_0 both in the Monge representation and in the nonlinear case (Follow the derivation from the paper by Norouzi *et al*, Phys. Rev. E 74, 061914, 2006).

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