Physics of active and passive motion in biology

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Make sure to read chapters 3 and 4 in Nelson!

1 Exercise: Observation of Brownian motion

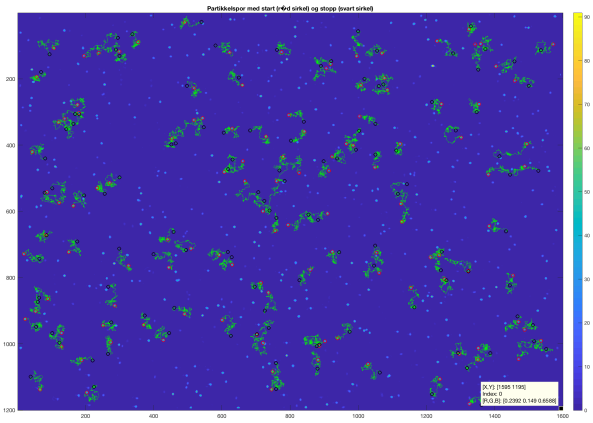


Figure 1: 0.51 μm beads, 40X magnification, 0.1837 μm/pix, framerate 15 fps, 300 images, that is 20 s. Zoom in on the picture and you will see the particles and the tracks.

This is a lab exercise where everything is explained on the blackboard and in the lab. This is a Norwegian lab text that explains the whole lab and how to analyse the data with Matlab. Nowadays we use Trackpy instead. You can start testing this analysis using a short image sequence from an experiment done during this lab. (To see all the images: remove the filename `brownian0000.png` from the address in your browser and you will see the list of files.) Follow the Trackpy Walkthrough. There is also a small Jupyter notebook that shows how you may show a small part of your image and adjust pixelsize (diameter) and the `minmass` to follow only real particles and not all kinds of stuff in the image.

In the end you want to

- use your own complete movie or image sequence
- plot the mean square displacement (MSD) as function of time.

Plot the MSD with linear axis, not logarithmic as in the Walkthrough. The reason is that you want to fit a straight line to the data to get the slope in $\mu m^2/s$. As you continue through this document you will understand why that is the main quantity you want from the experiment.

2 Exercise: Random walk simulation

A random walk is a model of a fundamental physical process in which a random walker — a particle, an atom, a measurement, an individual — moves in random

steps. A typical example is the Browian motion of small particles due to the thermal motion of atoms. Another example is the spreading of an atom throughout a fluid.

A random walker in 1D moves N steps back and forth and has random probability of moving left or right. None of the steps are correlated, the step length is d and the i -th step is thus $u_i = \pm d$. The position after n steps is thus

$$x_n = x_0 + \sum_{i=1}^{n} u_i \tag{1}$$

The ensemble average over a large number of the displacement of walkers is

$$\langle x_n - x_0 \rangle = \langle \sum_{i=1}^{n} u_i \rangle = \sum_{i=1}^{n} \langle u_i \rangle = 0. \tag{2}$$

The mean square displacement (MSD) is

$$\langle (x_n - x_0)^2 \rangle = \langle (\sum_{i=1}^{n} u_i)^2 \rangle = \langle \sum_{i=1}^{n} u_i \sum_{j=1}^{n} u_j \rangle = \sum_{i=1}^{n} \langle u_i^2 \rangle + \sum_{i=1}^{n} \sum_{j=1}^{n} \langle u_i u_j \rangle = nd^2. \tag{3}$$

The last sum equals zero because the steps are uncorrelated. This equation says that the mean square displacement increases linearly with number of steps n and that the slope of this linear relation is d^2.

The Python script `randomwalk_1D.py` is a 1D random walk simulation showing the position distribution and cumulative position distribution at the final time step and the mean square displacement of the walkers.

The Python script `randomwalk_exercise.py` is a very simple realization of a random walk where a number of random walkers are placed randomly in a part of the xy-plane and then moved in a random direction with a normally distributed step length (the width of the distribution is stepsize) over a given number of time steps. The step length is chosen so that the visualization of the simulation resembles what you would see in the microscope during the laboratory exercise. The mean squared displacement shown at the end is calculated based on approximately 4 times as many particles as those shown in the box. The positions of the particles shown in the box are also stored. This list of positions at different time steps has the same structure as the list of particle positions you will create from the experiment in the laboratory exercise.

Run the scripts and analyse theoretically what the slope of the plots should be. Change parameters like number of particles and duration to get similar statistics as in your experiment

3 Diffusion

Diffusion is the mixing of a substance that is unevenly distributed in a medium (gas, liquid or solid). The diffusion equation (here in one dimension) states that

the flux J of the substance is proposrtional to the gradient of the local density, or concentration $\rho = n/V$ of the substance:

$$J = -D\frac{\partial \rho}{\partial x}, \tag{4}$$

where the diffusion coefficient D is the proportionality constant. The conservation of matter (matter cannot appear or disappear) can be formulated by the divergence theorem, also known as the continuity equation:

$$\frac{\partial \rho}{\partial t} + \nabla J = 0 \tag{5}$$

Combine the two to get the partial differential equation for diffusion:

$$\frac{\partial \rho}{\partial t} + D\frac{\partial^2 \rho}{\partial x^2} = 0 \tag{6}$$

Starting with particles in $y = 0$ at time $t = 0$: $\rho(t = 0, x) = \delta(x)$, where δ is the Kroeneker delta function the diffusion equation has solution (you may easily verify this):

$$\rho(t, x) = \frac{1}{\sqrt{4\pi Dt}} \exp(-\frac{x^2}{4Dt}) \tag{7}$$

This is a Gaussian distribution with mean $y = 0$ and standard deviation $\sqrt{4Dt}$. Thus the width of the distribution is proportional to the square root of the diffusion coefficient. When data is sparse and noisy one always obtains a more precise estimate of the width by integrating over all the data. The second moment of the distribution is:

$$\langle x^2 \rangle = \int_{-\infty}^{\infty} x^2 \rho(t, y) dt = 2Dt \tag{8}$$

where I have used that

$$\int_{-\infty}^{\infty} x^2 e^{-x^2/a} dt = \frac{\sqrt{\pi}}{2} a^{3/2} \tag{9}$$

This result, that the mean square displacement (MSD) $= \langle x^2 \rangle = 2Dt$ shows how the random walk and Brownian motion are linked to diffusion.

4 Viscous drag

4.1 Dimensions

All physical quantities have dimensions. In addition we have measurement units like the SI units for all these quantities.

Størrelser	dimensjoner	SI-enheter
Lengde	L	m
Tid	T	s
Masse	M	kg
Areal	L^2	m^2
Volum	L^3	m^3
Hastighet	LT^{-1}	m/s
Akselleresjon	LT^{-2}	m/s^2
Kraft	MLT^{-2}	newton
Tetthet	ML^{-3}	kg/m^3
Arbeid	ML^2T^{-2}	joule
Effekt	ML^2T^{-3}	watt
Trykk, Stress	$ML^{-1}T^{-2}$	pascal
Viskositet (kinematisk)	L^2T^{-1}	m^2/s
Viskositet (dynamisk)	$ML^{-1}T^{-1}$	pascal s

Figure 2: Physical quantities, dimensions and SI units.

4.2 Drag

Drag is the force from the fluid F_d on a body moving with velocity v. You can also think of F_d as the force you need to pull on the particle to keep it a a constant velocity v. When biking on a flat road, the force you put into your pedals to keep at a constant speed is almost equal to the drag force of the air on your body.

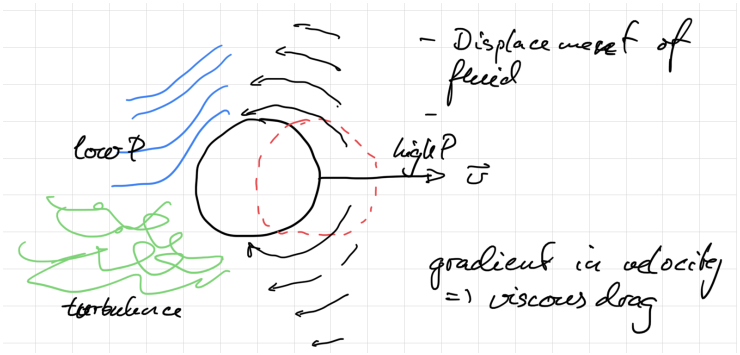


Figure 3: Drag.

What physical quantities are important?

- The drag force: F_d, $[F_d] = MLT^{-2}$
- The velocity with respct to the fluid far away: v, $[v] = LT^{-1}$

- The size of the body: r, $[r] = L$
- The fluid density: ρ, $[\rho] = ML^{-3}$
- The fluid viscosity: η, $[\mu] = ML^{-1}T^{-1}$

4.3 Viscosity

What is viscosity?

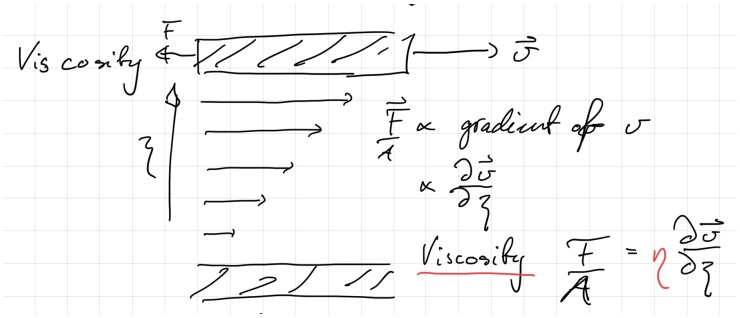


Figure 4: Viscosity.

4.4 Dimensional analysis

Buckingham's Π-theorem:

The number of independent dimensionless parameters necessary to describe a system is the number of physical quantities minus the number of independent dimensions.

In our case this gives: 5-3=2 dimensionless quantities that govern the behaviour of the system.

Let's try use the other quantities to make a dimensionless parameter with F_d and start with ρ: $[F_d/\rho] = T^{-2}L^4$. Then let's remove the dimension T: $[F_d/\rho v^2] = L^2$ and then L:

$$C_R = \frac{F_d}{\rho v^2 r^2}. \tag{10}$$

C_R is a dimensionless number that we will call the R drag coefficient

But we may also use η to remove the mass dimension from F_d: $[F_d/\eta] = L^2T^{-1}$, then we use v to remove the time: $[F_d/\eta v] = L$ and then the length:

$$C_S = \frac{F_d}{\eta v r}. \tag{11}$$

C_S is a dimensionless number that we will call the S drag coefficient. The two drag coefficients are pure numbers that depend on the shape of the body. According to Buckingham's Pi-theorem we have now found the two dimensionless numbers that are needed to describe the system.

4.5 Stokes and Reynolds drag

But these two dimensionless numbers correspond to two very different drag forces. How can they both be a description of the same physical phenomenon? Well, they describe two different ways the fluid can react to the moving body, either flowing smoothly as a *laminar flow* around the body or by whirling *turbulently* in the wake of the body. Let's have a look at the ratio between the two drag forces:

$$\frac{F_{dR}}{F_{dS}} = \frac{C_R \rho v^2 r^2}{C_S \eta v r} = \frac{C_R \rho v r}{C_S \eta} \approx \frac{\rho v r}{\eta} = Re \tag{12}$$

The ratio $\frac{F_{dR}}{F_{dS}}$ is the ratio between the inertial and viscous drag forces. This is called the **Reynolds number** Re. This tells us that when $Re >> 1$ the inertial, Rayleigh, drag force F_{dR} dominates. This is the case when the fluid accelerates a lot and becomes turbulent. When $Re << 1$ the viscous, Stokes, drag force F_{dS} dominates. This is true when the flow is laminar. Stokes drag for a sphere is $F_{dS} = C_s \eta v r = 6\pi\eta v r$.

What is the Reynolds number of the Brownian particles in our experiment? $Re = \frac{\rho v r}{\eta} \approx \frac{10^3 10^{-6} 10^{-6}}{10^{-3}} = 10^{-6}$, clearly they are in the Stokes, low Reynolds number regime.

Sometimes we also use the viscous friction coefficient ξ that is defined as the ratio between the drag force and the velocity.

$$\xi = \frac{F_d}{v} \tag{13}$$

The viscous friction coefficient in the Stokes regime ($Re << 1$) for a sphere is $\xi = 6\pi\eta r$.

5 Theory of Brownian motion

5.1 The childhood of statistical physics

In the beginning of the 1900s, it became increasingly clear to physicists that the "molecular-kinetic theory" (which described a statistical microscopic basis for thermodynamics) had to prevail. One of the final nails in the coffin for those who opposed it was one of Einstein's 1905 articles: Investigations on the theory of the Brownian movement. Einstein had been made aware of microscopic observations by biologist Brown where small pollen particles in a liquid moved around randomly. Einstein used this as a basis and created a quantitative model where measurable quantities could be compared. It did not take many years before experimentalists were able to measure the different

quantities independently and thus confirm Einstein's model and thereby the microscopic theory of heat that we take for granted today.

5.2 The Langevin equation: fluctuating forces and fluid friction

In 1908 Langevin published a simpler and more elegant derivation of the model of Brownian motion: Sur la theorie du mouvement brownien. Molecular motion and the equipartition principle are fundamental to the microscopic theory of heat:

The equipartition principle.
The kinetic energy of every quadratic degree of freedom of motion is $kT/2$

where k is the Boltzmann constant and T the temperature. For the translational velocity $v_x = dx/dt$ of a molecule in the x-direction the kinetic energy is

$$\frac{1}{2}m < v_x^2 >= \frac{1}{2}kT, \tag{14}$$

where $< ... >$ means the the "ensemble average" or the average over many molecules.

Viscous damping. For particles that are much larger than the average distance between the liquid molecules, the liquid can be treated as a continuum and the hydrodynamic damping of the particle motion can be studied. Fluid resistance for a sphere in a viscous liquid at low Reynolds numbers is, as shown above:

$$F_d = 6\pi\eta v_x r, \tag{15}$$

where η is the shear viscosity of the fluid and r is the radius of the sphere

The Langevin equation. The macroscopic particles are subject to a *rapidly varying random force* F_r due to the thermal motion of the liquid molecules and a *slowly varying damping force* F_d due to the viscosity of the liquid. Langevin combined these forces into an equation of motion for the particles:

$$m\frac{d^2x}{dt^2} = F_r - F_d = F_r - 6\pi\eta r\frac{dx}{dt}. \tag{16}$$

This type of equation of motion for systems that can be divided into a fast varying and a slow varying force is called a Langevin equation. By multiplying both sides with x and using the chain rule in differentiation, (16) can be written as

$$\frac{1}{2}m\left(\frac{d^2x^2}{dt^2} - 2v_x^2\right) = xF_r - 3\pi\eta r\frac{dx^2}{dt}. \tag{17}$$

Take the ensemble average and solve the equation. If one takes the ensemble average of (17) the direct contribution from F_r disappears because $< xF_r >= 0$ because the force F_r is not correlated with itself in time or space. Equation (17) can now be written as:

$$\frac{1}{2}m\frac{d^2 < x^2 >}{dt^2} - kT = -3\pi\eta r\frac{d < x^2 >}{dt}. \tag{18}$$

This equation can be solved:

$$\frac{d < x^2 >}{dt} = \frac{kT}{3\pi\eta r} + Ce^{6\pi\eta rt/m}, \tag{19}$$

where the last term disappears when $t >> m/6\pi\eta r \sim 10^{-8}$ s. That means that if we can track the positions of many particles and calculate the mean square displacement per unit of time, and we know the viscosity and radius of the particle, we can determine Boltzmann's constant, k. Such a determination of k and comparison with other methods of determining k was the first test of Einstein's model for Brownian motion.

Eistein relation. Since $2D = \frac{d\langle x^2\rangle}{dt}$ and $\xi = 6\pi\eta r$, then according to equation (19) $\frac{d\langle x^2\rangle}{dt} = \frac{kT}{\xi/2}$ then we get the

Einstein relation.

$$\xi D = kT \tag{20}$$

6 Life at low Reynolds number

We will read the beautiful paper Life at low Reynolds number by E. M. Purcell.

7 Biological relevance of diffusion

7.1 Permeation through a membrane

Flux (flow rate per unit area): $J_i = \frac{1}{A}\frac{\Delta N_i}{\Delta t}$

How does c_i change with time? (c_0 is const.)

$$\frac{\partial c_i}{\partial t} = -\frac{\partial \Delta c}{\partial t} = \frac{1}{V}\frac{\partial N_i}{\partial t} = \frac{3}{r}J_i \tag{21}$$

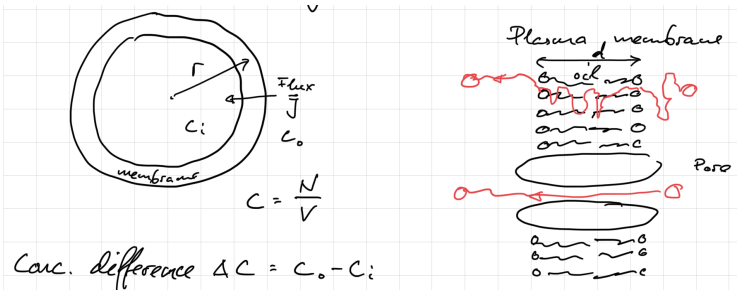


Figure 5: Permeation through a membrane.

because $A = 4\pi r^2$, $V = \frac{4}{3}\pi r^3$, $V/A = r/3$. The permeability P is defined $J = P\Delta c$. We can enter this into the above equation and solve:

$$-\frac{\partial \Delta c}{t} = \frac{3}{r} P \Delta c \tag{22}$$

$$\int_{\Delta c_0}^{\Delta c} \frac{\Delta c}{\Delta c} = -\frac{3P}{r} \int_0^t \partial t \tag{23}$$

$$\ln \Delta c - \ln \Delta c_0 = -\frac{3P}{t} \tag{24}$$

$$\frac{\Delta c}{\Delta c_0} = e^{-t/\tau}, \qquad \tau = \frac{r}{3P}. \tag{25}$$

The permeation is diffusion through the membrane and resistance to entry/exit. The partition coefficient B is

$$B = \frac{\text{solubility in oil}}{\text{solubility in water}} \tag{26}$$

Diffusion in membrane is

$$J = -D\frac{dc}{dt} = -\frac{DB\Delta c}{L} = P\Delta c \quad \Rightarrow \qquad P = \frac{DB}{L} \tag{27}$$

Some numbers:

- Partition coefficient of water in lipid bilayer membrane: $B = 4.2 \cdot 10^{-5}$ (A Finkelstein, J. Gen. Phys. **68**, 127 (1976))
- Thickness of cell membrane: $L = 7.5 - 10$ nm. (B10NUMB3R5)
- This gives a permeability of $P = 10^{-9} 4 \cdot 10^{-5}/10^{-8}$ m/s≈ 4 μm/s.
- And a time constant of permeation of water into a cell with radius 10 μm: $\tau = r/(3P) \approx 1$ s. That's pretty fast!
- Partition coefficient of monovalent ions: $B \approx 10^{-60}$. That's why cells need ion channels.

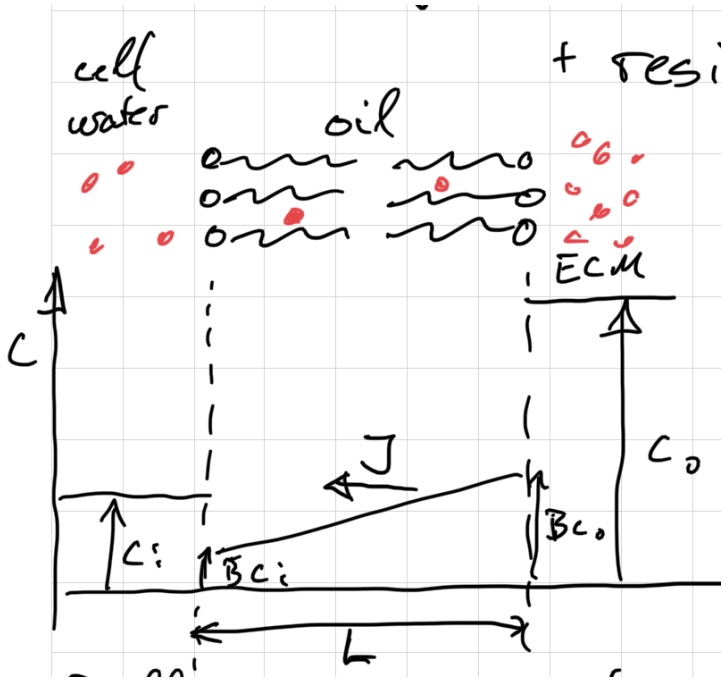


Figure 6: Diffusion through membrane with low partition coefficient.

7.2 Oxygen diffusion limit on microbial metabolism

See Nelson 4.6.2 p.138.

- Oxygen is consumed by microbe
- Transport of oxygen from outside
  - Lakes, ocean: turbulent flow
  - ECM, ponds: diffusion
- Assume instant uptake at microbial surface

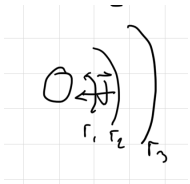


Figure 7: The same current flows through spheres of all radii.

$$J(r) = \frac{I}{4\pi r^2} = -D\frac{dc}{dr} \tag{28}$$

$$-\frac{I}{4\pi r^2}\frac{dr}{r} = dc \tag{29}$$

$$-\frac{I}{4\pi r^2}\left.\frac{1}{r}\right|_{r_0}^{\infty} = c|_0^{c\infty} \tag{30}$$

$$-\frac{I}{4\pi r^2}\left(-\frac{1}{r_0}\right) = c_\infty \tag{31}$$

$$I = 4\pi D c_\infty r_0 \tag{32}$$

This is the maximum rate at which O_2 can be consumed by any bacterium whatsoever.

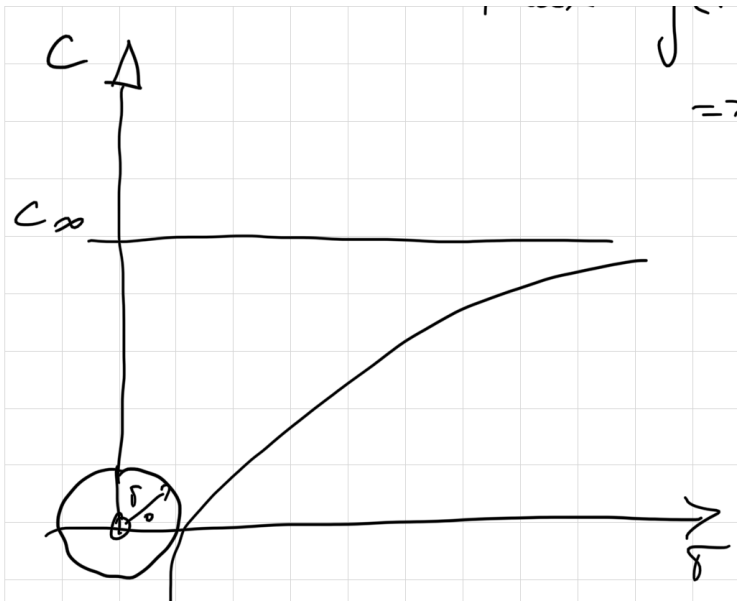


Figure 8: Concentration distribution around a consuming bacteria.

So the maximum O_2 diffusion rate scales linearly with radius r of the microbe. How does the consumption rate scale with size of the organism? A first guess would be $I \propto r^3$, but it turns out there is an empirical relationship called Kleiber's law that has been shown to be valid all the way down to microbe size: $I \propto M^{0.75}$, where M is the mass of the organism. So since $M \propto r^3$ the scaling is $I \propto r^{9/4} = r^{2.25}$. (T.E. Riedel, W.M. Berelson, K.H. Nealson, S.E. Finkel, Applied and Environ. Microbiol. **79**, 4921 (2013))

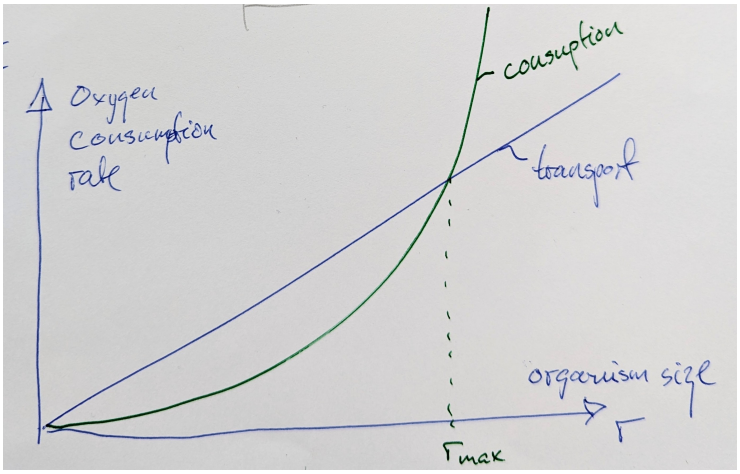


Figure 9: Scaling of consumption and transport rate with bacteria size.

Plotting the scaling of consumption and transport rate with microbe size one finds that there must be an upper limit to the size $r_{\max}$ of a microbe that does noot swim or lives in a turbulent world.

7.3 Ions at membranes, a first look

7.4 Size of eukaryotes and prokaryotes

Here is another nice and simple paper to analyse

8 Active matter

Follow this link: Active matter