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Soft Matter and Biological Physics

Question Sheet

Michaelmas 2011

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Question 0: Sedimentation

Initially consider identical small particles uniformly suspended in a vessel filled with solvent. The average concentration of particles is c_0. Consider gravitational force on these particles with $F = mg$, where m is the particle mass corrected for buoyancy.
Write down the equation for the diffusion current for this situation and solve the equation to obtain the equilibrium distribution of particles $c(z)$. Calculate the proportionality constants. Discuss why you could have guessed the answer to this.
Suppose that the suspended particles are in fact droplets of fat in water (e.g. milk) with diameters of around 1 micron. Assume a density for butterfat of 0.91 g/cm^3. Calculate the ratio $c(h)/c(0)$ for a container with height $h = 25$ cm . What do you conclude from this value?

Question 1 Optical tweezers calibration

Consider a dielectric, spherical particle with radius R (of order of 1 micron), mass m and friction coefficient γ immersed in water, which is held in an optical trap. Which are the main forces in an optical trap? The trapping potential can be approximated as harmonic. The potential is characterised by a trap stiffness κ and corresponding frequency f_c. Write down the Langevin equation in one dimension for this particle taking into account the thermal random force $\xi(t)$. Under which conditions can one neglect the inertial acceleration term in the Langevin equation?

With the the constant power spectrum of an ideal white noise source $S_\xi = |\xi(f)|^2 = 4\gamma k_B T$ calculate the power spectrum of the particle motion in the optical trap $S_x(f) = |x(f)|^2$. Briefly, describe two techniques to register the motion of the particle in the trap.
Sketch $S_x(f)$ for several values of κ and label all axis and relevant points?
What happens for frequencies $f > f_c$ with the power spectrum when the laser power is increased? Remember that part of the laser power is absorbed in the solution.

Question 2: Polymer chains

(a) Consider a freely jointed chain (FJC) polymer consisting of two different types of monomers with length a and b with $a \neq b$. The polymer has a sequence $babababa$... with $N/2$ monomers of each type. Calculate the room-mean-square end-to-end distance for the absence of any applied stretching force. For very low forces, this is a harmonic spring with $F = \kappa\langle z\rangle$. Calculate the value for the spring constant κ of this chain.

(b) Now consider an almost ideal FJC with monomers a only. In this chain of length N the maximum bending angle of the bonds between adjacent monomers is unconstrained between 0 and $\pi/2$ and restricted from exceeding $pi/2$. Introduce $\vec{a_n}$ representing the unit vector indicating the direction of monomer n. Calculate $\langle \vec{a_n} \cdot \vec{a_{n+1}} \rangle$ where $\langle .. \rangle$ represents the average over all possible configurations.

Question 3: Stretching in Electric Fields

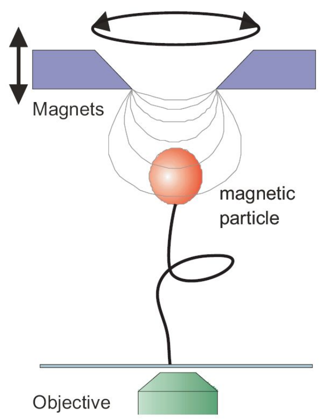
Consider an ideal chain with $N = 1000$ segments of length $a = 0.5$ nm held at one end. Assume that in aqueous solution the chain carries $2e$ charges at the free end. What will be the average end-to-end distance $\langle z \rangle$ in a field $E = 30,000$ V/cm?
At which field would $\langle z \rangle \approx 0.5(Na)$.

Question 4: Twisting DNA

A double-stranded DNA molecule is stretched by magnetic tweezers as shown in the figure below. A constant force F is applied and the magnets can be rotated leading to a torque on the DNA molecule. Upon twisting, elastic energy is stored in the DNA according to

$$E = \frac{k_B T C \vartheta^2}{2L}$$

where ϑ is the twist angle and $C \approx 100$ nm is the torsional persistence length of the DNA. After a certain number of turns n, with a total twist angle of $\vartheta = n2\pi$, the DNA molecule buckles and forms a small loop as shown below.



(i) Write down a general expression for the energy of such a loop considering the bending energy and the fact that DNA is stretched by a force F. Remember from the lecture that the energy to form a bend of $\pi/2$ is given by

$$E(R) = \frac{k_B T l_p}{2} \frac{\pi}{2R}$$

where R is the bending radius and l_p the persistence length.

(ii) What is the minimum energy cost required to form this loop? Start by taking the derivative of the expression derived in (i) with respect to the loop radius R. Compute the associated loop size for $F = 1$ pN. Assume a bending persistence length of $l_p = 50$ nm for DNA.

(iii) Calculate the energy increase associated with increasing the number of turns from n to $n + 1$.

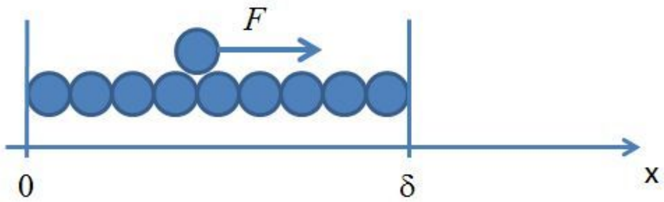
(iv) The torque Γ on a DNA molecule is

$$\Gamma(n) = \frac{k_B T C}{L} 2\pi n$$

Assume that $n \gg 1$ and thus rewrite the expression derived in (iii) for the torsional energy in terms of torque. Use the new expression to obtain the buckling torque for DNA with $F = 1$ pN and a DNA contour length of 10,000 basepairs.

Question 5: First Passage Time

Calculate how long it takes a linear polymer to polymerize to a length δ. Consider two separate cases, first without force ($F = 0$) acting on the diffusing monomer and then with a driving force ($F > 0$) acting on the monomer in steady state.



In order to approach this problem, first calculate the first passage time τ_1 it takes a monomer to diffuse a distance $0 \to \delta$ for $F = 0$. You can assume that the particle reappears at the origin, when it reaches position δ and thus ensuring that probability p of finding the particle in the interval $(0, \delta)$ is $p = 1$. With this boundary condition you get the steady-state diffusion current $j = -D\partial p/\partial x$ with D as diffusion constant.
Solve the steady-state diffusion equation $\partial^2 p/\partial x^2 = 0$ extracting j and the first passage time $\tau_1 = \delta^2/2D$. Now add a driving force F which acts on the monomer with friction coefficient γ and solve the inhomogeneous equation

$$j = -D\frac{\partial c}{\partial x} - \frac{F}{\gamma} p$$

Discuss your result for τ_1 in the case $F\delta \gg k_B T$.

Question 6: Protein Unfolding[1]

[1]This question is based on the paper *Unfolding pathways of individual bacteriorhodopsins* by Oesterhelt *et al.*, Science **288**, 143 (2000).
You can download this paper from the course homepage or directly from the Science webpage through a library computer (or computer with Cambridge IP address).

In some naturally occurring membranes, bacteriorhodopsin proteins order in a near-perfect periodic lattice as shown in the paper by Oesterheldt *et al.*. Yet Fig. 1C from that paper shows a defect in this lattice. Explain why the defect is present and its significance.
By analyzing the data in Fig. 2, estimate the length per amino acid of an unfolded protein. Assume that the freely-jointed chain model provides a good description of this polymer.
The authors are using the lever arm of an atomic force microscope in their experiments. The lever arm extracting the protein can be seen as a harmonic spring with spring constant k_c. Estimate the spring constant from the data in Fig. 1B.

Question 7: Electro-osmotic flow
Assume that the surface of a cylindrical capillary of radius r is charged and has a fixed surface potential $\zeta < 0$. Under the assumption that $r \gg \lambda$ show that the fluid velocity v of the electro-osmotic flow in the centre of the capillary can be written as

$$v = -\frac{\epsilon_0 \epsilon_r \zeta E}{\eta}$$

where η is the fluid viscosity and E the applied electric field along the capillary. Explain why this velocity does not depend on r.

Question 8: Electrophoresis in AC fields [2]
Consider a spherical particle with radius r in water held in an optical trap far from any surface. The particle has charge q and is moving due to an homogeneous electric field alternating with angular frequency ω giving rise to an electrophoretic force F_e. Assume that the optical trap forms a harmonic potential with linear force distance relation $F = -\kappa \Delta x$ where $\kappa = \gamma \omega_c$. Estimate the maximum force on a particle with $q = 20,000e$ in an electric field of 50 V/m. Assuming that the trap has $\omega_c = 1000$ s^{-1} and the particle $r = 1$ μm compare the maximum Δx with the thermal fluctuations of the particle in the trap. How is it still possible to measure the motion in the electric field? Now, write down the 1D-equation of motion for the particle in the field. In the overdamped regime, some terms can be safely neglected, which?
In case the colloid is held close to a charged surface and the AC-field is parallel to it, the equation of motion has to be adapted. How is the particle affected and which other forces become relevant?

Question 9: Gel Electrophoresis [3]
A flexible polymer with N Kuhn segments of length b is moving inside a gel. The gel fibers are spaced far enough apart to only marginally affect the conformation of the polymer chain.

(i) Assume that the polymer has a drag coefficient of $\gamma = \eta N b$ in the gel, with η the viscosity

[2] The solution to this problem is e.g. discussed in Semenov, et al., "Single colloid electrophoresis" J. Coll. Interface Sci. (2009), which can be downloaded from the course webpage.

[3] Part of this question is based on Zimm and Levene, "Problems and prospects in the theory of gel electrophoresis of DNA" Quart. Rev. Biophys (1992). Can be downloaded from the course webpage.

of water. Find an expression for the time τ it takes for the polymer to diffuse a distance equal to its contour length $L = Nb$. Using this expression, estimate τ for double-stranded DNA ($b = 100$ nm) with a length of 30,000 basepairs.

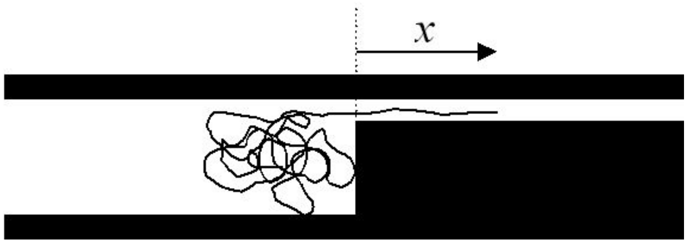
(ii) Now we apply an uniform electric field E in the gel which leads to a total force $F = fN$ on the polymer. Assuming a purely reptation motion, show that the drift velocity in the gel is

$$v_d = \frac{f}{\eta b N}.$$

Estimate the electric field E that you need to drive DNA molecules with 30,000 basepairs through a gel of 10 cm length in 1 hour. Calculate the distance DNA molecules with 25,000 basepairs would have traveled in the same amount of time. In both cases you may assume that the DNA has a charge of $600e$ per 100 nm segment.

Question 10: Polymers in Confinement

Consider an experiment in which a long piece of a charged polymer, with charge per unit length ρ, is situated in front of a narrow constriction, as illustrated in the sketch below. The polymer can only enter the narrow channel by adopting a straight configuration. An electric field E in the narrow part of the channel tries to pull the polymer inside the channel. The difference in entropy gives rise to an average waiting time in front of the narrow channel of the form $t = t_0 \exp(\Delta G^*/k_B T)$, where t_0 is a constant and ΔG^* is the height of the free energy barrier.



(i) Calculate the change in electrostatic potential energy $\Delta U(x)$ of the polymer when it enters the channel.

(ii) The corresponding increase of entropy is $\Delta S(x) = -\gamma x$, where γ is an experimentally determined constant. Give an argument why this is the correct sign and dependence on x. Basic thermodynamics will do the job.

(iii) Using the results obtained in (i) and (ii) calculate ΔG^* as a function of T, ρ, E and γ.

(iv) Discuss the temperature dependence of ΔG^*.

Question 11: Nanopores

(i) Consider a capillary tube with radius r, much larger than the Debye-Huckel screening length λ, containing monovalent dissociated salt ions of concentration $c_0 = c_0^+ = c_0^-$. The solution has a resistivity ρ. The capillary has length l and connects two semi-infinite reservoirs. Calculate the total resistance of the capillary taking into account the access resistance given by $\rho/4r$. Calculate the resistance of a nanopore in 0.1M KCl as a function of radius for a membrane of 20 nm thickness. Plot the resistance between 0 and 100 nm pore diameter.

(ii) Assume that electrodes for the ionic current measurements have to be placed in a microfluidic channel on either side of the nanopore with length 1 mm and cross section 10 by 10 μm^2. How small does the nanopore has to be so that its resistance is 10 times larger than the resistances of the channels connecting the nanopore with the electrodes? The resistivity of 0.1M KCl at 20°C is $\sim 0.856\ \Omega$m.

(iii)Derive the total resistance for a conical capillary with different radii at both its ends r_1 and r_2, where $r_1 > r_2$. Sketch the electric field and potential for the cylindrical case.

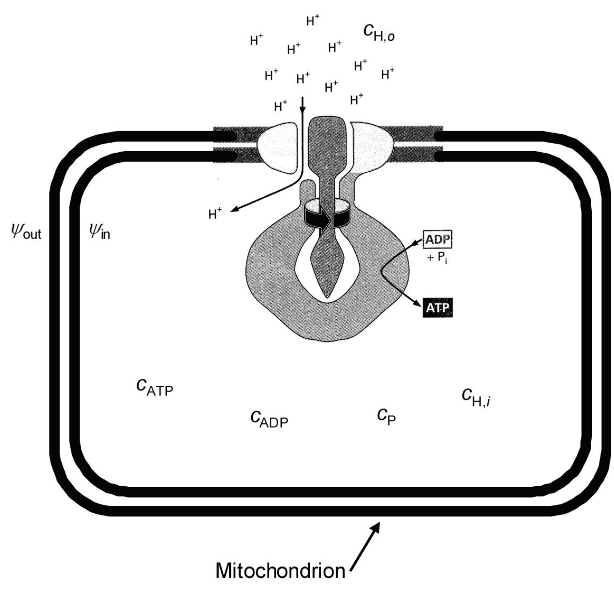
(iv) In a realistic nanopore, its surface will be charged in solution. Consider the resistance of the nanopore upon changing the salt concentration in the reservoirs. Sketch the resistance of the nanopore as a function of salt concentration from 1M to 0M KCl.

Question 12: Polymer Translocation

Compare the translocation time for the freely-jointed and the worm-like polymer chain models. Both molecules have constant charge per segment and are pulled through a nanopore by electrophoretic forces. The chains are very long compared to the nanopore length. Calculate the drag experienced by the polymer coil shrinking in front of the nanopore by assuming that the translocation time is much shorter than all relaxation times of the polymer. How does the translocation time depend on polymer length for the two chain models?

Question 13: Thermodynamics of the ATP synthase molecular motor

The F_0F_1 ATP synthase rotary motor is a protein complex found in the inner membrane of mitochondria. It converts one ADP molecule into one ATP molecule and water. The necessary free energy is obtained from a flow of protons across the membrane:



(i) Suppose that N protons must cross the membrane to convert one ADP molecule and one phosphate into ATP. For a process with no entropy change $\Delta S = 0$, derive an expression for the standard free energy ΔG^0 stored per ATP molecule. The relevant quantities for this are N, the membrane potential $\psi_m = \psi_{in} - \psi_{out}$ and the following concentrations: protons inside $c_{H,i}$ and outside $c_{H,o}$ the mitochondria, ATP and ADP inside the mitochondria c_{ATP} and c_{ADP} and phosphate inside c_p.

(ii) In (i) we assumed $\Delta S = 0$ for the process. If this is not true anymore, is your answer to (i) a lower or an upper bound for ΔG^0? Justify your answer.

Question 14: Linearized Poisson-Boltzmannn Equation

Consider a charged surface in aqueous solution with surface potential ϕ_0. The surface is immersed in a solvent containing monovalent dissociated salt ions of concentration $c_0 = c_0^+ = c_0^-$. Solve the Poisson-Boltzmann equation for the electrostatic potential $\phi(x)$ in this geometry and thus derive the formula for the Debye-Huckel screening length λ in the limit of small surface potential $e\phi_0 \ll k_B T$. Discuss the dependence of the screening length on c_0. Sketch and discuss the distribution of the positive and negative ions close to the surface.

A second, identical surface is now held in close proximity to the first surface at a distance D. Find a solution for the Poisson-Boltzmann equation again in the limit of $e\phi_0 \ll k_B T$. The calculation is simplified if you place the origin in the centre between the two surfaces. Make a sketch of the potential between the surfaces.

What happens if $D \to \infty$ and $D \to 0$ with $\phi(x = 0)$.

By calculating the total electrostatic energy per unit area of this ionic solution between the surfaces, $E(D)$, find the added pressure between them.