NORWEGIAN UNIVERSITY OF SCIENCE AND TECHNOLOGY
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EXAM
TFY4335 BIONANOTECHNOLOGY

Wed 15th of December 2010. 09:00

Examination support materials:

- Formula sheet - see Appendix A
- Simple calculator (according to NTNU exam regulations)
- K. Rottmann: Matematisk formelsamling (eller tilsvarende)
- Carl Angell og Bjørn Ebbe Lian: Fysiske størrelser og enheter, navn og symboler (eller tilsvarende)

Answer must be written in English or Norwegian. Number of points given to each sub-question is given in bold font. The maximum score for the exam is **75p**.

Question 1: Various questions (30p)

1. What is described by $\Re$ (eq. 29). Is it important in design of microflusidic or/and paper based microfluidic devices? Explain why? (**5p**)
   Reinolds number describes balance between viscous friction and inertia in a flowing liquid. $\Re$ (as discussed in the lectures) can not be defined for a paper based microfluidics (as we do not have a liquid flowing in a channel but liquid wetting a porous material; $\Re$ could be defined on the microscopic level, but not directly using equations 28 and 29 on the macroscopic flow level). Wetting kinetics and capillary flow will dominate; diffusion are important for paper based microfluidics.
2. When describing mechanical properties of single polymer molecules, what is defined by a term "cooperativity". What is the relevant model which can be used to describe a polymer chain. Explain how we can use models derived to describe mechanical properties of single polymer molecules to study helix-coil transition in protein. (**5p**)
   This is an extension to FJC model (bassic assumptions for FJC model must be described) which includes `potential energy term between segments`. This allows us to include a "bias" which makes adjucant segments to point in the same direction. This term is included to account for elastic energy involved in bending and not to account for overlaps between chain segments in a simple 1D representation. Less pot. energy is stored in the chain if the segments are pointing in the same direction. Of course thermal motion will try to make segment orientation as random as possible and will balance the potential energy

term (chain configuration will be given by minimizing free energy). Gives more realistic description of force/extension behaviour of single polymer chains, as the force is not only entropic in origin. The same method can be used to describe helix/coil transition where we do not use mechanical force but we sample free energy of the system by changing temperature. The total change in free energy on helix-coil transition will include both energy (for example formation and breaking of different hydrogen bonds) and entropy contributions and balance between the two will change as we change the temperature. In stead of chain direction (as in FJC model) we can describe the segment conformation as helix or not helix and investigate change in the free energy as a function of increasing for example helix content. Cooperativity here is important as a segment will tend to take helix conformation if the neighbours are in a helix conformation (in that way hydrophobic interactions and hydrogen bonds between chain segments can form).

3. Is cooperativity important for basic understanding of rubber elasticity. Explain shortly why or why not. (**5p**)
   On the simplest level, rubber elasticity can be understood as a pure entropic effect (entropic force) and for that cooperativity is not important . Mechanical stretching limits the entropy of individual polymer chains, as this is why the material resists that. FJC model is sufficient to predict behaviour of rubber and produce correct temperature dependence of the elasticity.

4. What connects cell membrane, amphiphilic molecules and term "CMC". Explain. (**5p**) Cell membranes are made from amphiphilic molecules. Those are molecules which typically have a hydrophilic and hydrophobic part. For molecules forming micels and bilayers, the hydropobic part is a long hydrocarbon chain and hudrophilic part is a realtivelly small head group, often charged. CMC is a critical micels concentration. If one dissolves amphiphilic molecules in water, **above** certain concentration they will start forming micels (or other structures) in a cooperative manner. This can be observed by for example monitoring osmotic pressure

5. Equation 23 describes flux of molecules or particles under centrifugal force. Describe physical meaning of the two terms in brackets and define all symbols/constants in the equation. Imagine that you try to centrifuge particles with a diameter of 3nm and 10nm (density = 1gcm^3) not in liquid but in air. What will be different in this experiment? Is the equation still valid? Use viscosity of air $\eta = 2 \times 10^{-5}\text{kgm}^{-1}\text{s}^{-1}$ and air density $\rho = 1.2\text{kgm}^3$ (**5p**)
   Total flux of molecules under centrifugal force will be given by a difference between flux due to diffusion and concentration gradient (first term) which try to oppose the flux due to centrifugation (2nd term). D diffusion constant; c concentration, function of distance; m_{eff} effective mass corrected for buoyancy. For given particle density, the effective mass is zero, so centrifugation in water will not work. If we do the experiment in air, larger particles might spontaneously sediment due to gravity (should be mentioned, could be estimated using difference in potential energy on the lab length scales (few cm)). D will have to be calculated using viscosity of air and it should be mentioned that this is only valid if we are still in the viscous friction dominated regime. Also D effects both fluxes in the same way as it is outside the bracket. The effective mass is now close to the mass of the particles. Also since viscous friction is much less in air the Einstein-Stokkes equation might not be valid (small particles will move at large velocity). Finally if the centrifugation works, and the particles do not sediment due to gravity, after we stop rotating, the time system will need to go back to $\frac{\text{dc}}{\text{d}r} = 0$ will be much shorter then in the case of solution (can be shown by diffusion time).

6. What is the origin of "hydrophobic interactions". (**5p**)
   Ordering of water molecules around hydrophobic groups in solution (in order to maximize

the number of H-bonds) and a consequent increase of the total system entropy if some of those molecules are realised due to hydrophobic groups coming in contact (reduced hydrophobic are in contact with water).

Question 2 Electrostatics (20p)

Protein molecules A has a small positively charged region on it's surface which can be approximated by a circular region with a radius R and charge density $\sigma_A = \sigma$. Protein B is designed to bind to protein A and it has a similar charged region (opposite charge density $\sigma_B = -\sigma$ also radius R). Both molecules are placed in a buffer solution (pH = 7, [NaCl] = 0.9M). For this buffer λ_D (in nm) can be calculated using equation 56.

1. Describe origin of the attractive force between charged surfaces as two protein molecules approach each other. How this interaction will depend on the ion concentration in solution? (**5p**).
   Attractive force involves electrostatics only at small separation distances $\sim \lambda_D$. At separations $> \lambda_D$ the attractive force will be an entripic force resulting from a gain in entropy as some counter ions can be released from the gap between the surfaces as they approach each other. This is relatively long range - the ion concentration is still $\sim 1\%$ larger/smaller then the solution concentration at separation $5\lambda_D$. The interaction will be weaker for higher ion concentration, as relative entropy gain for the whole system will be smaller.
2. Once the two charged areas of the protein molecules get in contact with each other. What holds them together? Will this interaction depend on the composition of the solution around?(**5p**)
   pure electrostatic interactions, this can be very strong; in principle this will only weekly depend on the electrolyte concentration ($\sim \sqrt{c^{-1}}$) as energy needed to break the bond will be reduced as the λ_D goes down. As calculated in part 4; this is still a very strong bond (comparing to k_BT) even in high salt concentration.
3. What is defined by λ_D. Explain. (**3p**)
   Debye screening length, describes at what disstance away from the charged surface the interactions will be screened by the ions in solutiuon. This works for solutions containing not zero amounts of both positive and negative ions.
4. Can you estimate the strength of that interaction (energy needed to break it) in relation to k_BT. Use R = 10nm; $\sigma = 1e\text{nm}^{-2}$ (**7p**)
   Equations 57 and 58 describes electrostatic energy stored in a charged surface. For a sutuation in pure watre eq. 57 is used, otherwise we have to use eq. 58. l_B is caclulated for water where $\varepsilon = 80\varepsilon_0$.

$$\begin{aligned}
\lambda_B &= \frac{e^2}{4\pi\varepsilon k_BT} = \frac{(1.6\times10^{-19})^2}{4\pi 8.9\times10^{-12}\cdot 80\cdot 4.1\times10^{-21}} = 0.7\text{nm}\\
\lambda_D &= 0.31\cdot(0.9)^{-1/2}\\
\frac{E}{k_BT} &= A\left(\frac{\sigma}{e}\right)^2\cdot 2\pi\lambda_B\lambda_D\\
\frac{E}{k_BT} &= \pi 10^2\text{nm}^2\cdot 1\text{nm}^{-4}\cdot 2\pi\cdot 0.7\text{nm}\cdot 0.33\text{nm} = 463
\end{aligned}$$

Total energy gain as two oppositely charged surface come together will be twice calculated value. E = 926 k_BT

Question 3 Molecular Motion and Molecular Motors (25p)

1. Fluorescence correlation spectroscopy (FCS) is an experimental method which allows to estimate diffusion constant of molecules in solution, as well as molecular size.
   (a) Does one need a concentration gradient to be able to measure diffusion constant D? Describe relation between diffusion constant and concentration gradient. (**7p**)
   We do not need a concentration gradient if we can follow motion of individual particles, for example using optical microscope (as done during lab exercises). Concentration gradient will result in mass transport due to diffusion (flux)
   (b) How one can we estimate molecular size if we have measured diffusion constant D. What assumptions are necessary? (**5p**)
   Eisntein-stokkes equation. Assuming particles are spherical are small and are moving slowly (this is only correct if we have $\Re \ll 1$). If those assumption are correct we can calculate size R from

$$D\zeta = k_B T$$
$$\zeta = 6\pi\eta R$$

   In case not-spherical particles, we would need to consider diffusion along different directions relative to object shape and also consider both translational and rotational diffusion. So things very much more complicated.

2. Is diffusion important in description of how molecular motors convert chemical energy to mechanical work? Explain why or why not. (**5p**) In the simpliest description of molecular motors, chemical energy is used to direct motion (constrain Brorwnin motion to one direction along the track on which the motor is moving), as diffusion/Brownian motion is responsible for how fast the motor is moving.

3. What is described by equation 67. What kind of model it describes and what are f, v, L and D. (**8p**)
   Dependence of velocity of applied force (load) for a model molecular motor based ob brownian ratchet concept. f applied load (or resistance form cargo due to viscous friction) v - average velocity at which motor is moving; D - diffusion constant of the moving part in the S-ratchet concept or diffusion constant of a single motor head in kinesin example; L - step size or distance between hinges in the S-ratchet model.

Appendix A: Equation Sheet

$$k_B = 1.38 \times 10^{-23}\text{J K}^{-1} \tag{1}$$

$$e = 1.6 \times 10^{-19}\text{coul.} \tag{2}$$

$$\varepsilon_0 = 8.9 \times 10^{-12}\text{F m}^{-1} \tag{3}$$

$$\eta_{water} = 1 \times 10^{-3}\text{Pa s} \tag{4}$$

$$v_{drift} = \frac{f}{\xi} \tag{5}$$

$$\xi = 6\pi\eta R \tag{6}$$

$$\xi D = k_B T \tag{7}$$

$$\lambda_X = \sqrt{2Dt} \tag{8}$$

$$\lambda_{3D} = \sqrt{6Dt} \tag{9}$$

$$\langle r^2 \rangle = N L_{seg}^2 \tag{10}$$

$$D = \frac{1}{\tau} \int_{-\infty}^{\infty} \frac{\Delta^2}{2} \rho(\Delta) d\Delta \tag{11}$$

$$2D\tau = \langle \Delta^2 \rangle \tag{12}$$

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \tag{13}$$

$$j_s = -D \frac{\partial c}{\partial x} \tag{14}$$

$$\frac{\partial c}{\partial t} = -\frac{\partial j}{\partial x} \tag{15}$$

$$j_s = -P_s \Delta c \tag{16}$$

$$\frac{\partial c}{\partial t} = D \nabla^2 c \tag{17}$$

$$\vec{j} = -D \nabla c \tag{18}$$

$$c(\vec{r}, t) = \frac{N}{(4\pi D t)^{3/2}} e^{-\frac{r^2}{4Dt}} \tag{19}$$

$$j = D\left(-\frac{dc}{dx} + \frac{q}{k_B T}\varepsilon c\right) \tag{20}$$

$$\Delta\left[\ln c\right] = -\frac{q}{k_B T}\Delta V \tag{21}$$

$$c\left(z\right) = C e^{\frac{-m_{eff} g z}{k_B T}} \tag{22}$$

$$j\left(r\right) = D\left(-\frac{dc}{dr} + \frac{r\omega^2 m_{eff}}{k_B T} c(r)\right) \tag{23}$$

$$c(r) = C e^{\frac{m_{net}\omega^2 r^2}{2k_B T}} \tag{24}$$

$$v_{crit} = \frac{\eta}{\rho R} \tag{25}$$

$$f_{crit} = \frac{\eta^2}{\rho_m} \tag{26}$$

$$f_{fric} = \frac{\eta \ell^3 v}{R^2} \tag{27}$$

$$f_{inert} = \frac{\rho_m \ell^3 v^2}{R} \tag{28}$$

$$\Re = \frac{vR\rho}{\eta} \tag{29}$$

$$\frac{f}{A} = -G \frac{\Delta z}{d} \tag{30}$$

$$\frac{f}{A} = -\eta \frac{v}{d} \tag{31}$$

$$Q = \frac{\pi R^4 p}{8L\eta} \tag{32}$$

$$\frac{k_B T}{2} = \alpha \frac{\langle x^2 \rangle}{2} \tag{33}$$

$$S \equiv k_B \ln \Omega \tag{34}$$

$$T^{-1} = \left(\frac{dS}{dE}\right) \tag{35}$$

$$\Delta U = \Delta Q + \Delta W \tag{36}$$

$$\Delta S \geq \frac{\Delta Q}{T} \tag{37}$$

$$F_a \equiv E_a - T S_a \tag{38}$$

$$G_a \equiv E_a + pV_a - T S_a \tag{39}$$

$$\frac{P_1}{P_2} = e^{\frac{\Delta E}{k_B T}} \tag{40}$$

$$P_1 = \frac{1}{1 + e^{-\frac{\Delta E}{k_B T}}} \tag{41}$$

$$P_2 = \frac{1}{1 + e^{\frac{\Delta E}{k_B T}}} \tag{42}$$

$$\tau^{-1} = C e^{\frac{-\Delta E^{\ddagger}}{k_B T}} \left(1 + e^{\frac{-\Delta E}{k_B T}}\right) \tag{43}$$

$$\Delta F = \Delta F_0 - f \Delta z \tag{44}$$

$$Z = \sum_j e^{-E_j / k_B T} \tag{45}$$

$$p_{equil} = c_{osm} k_B T \tag{46}$$

$$c_{osm} = \varphi M c \tag{47}$$

$$\Sigma = Rp/2 \tag{48}$$

$$\ell_B \equiv \frac{e^2}{4\pi\varepsilon k_B T} \tag{49}$$

$$\overline{V}(x) = \frac{eV(x)}{k_B T} \tag{50}$$

$$c_+(x) = \frac{2\pi\ell_B \left(\frac{\sigma_q}{e}\right)^2}{\left(1 + 2\pi\ell_B \frac{\sigma_q}{e} x\right)^2} \tag{51}$$

$$x_0 = \left(\frac{e}{2\pi\ell_B \sigma_q}\right) \tag{52}$$

$$\frac{\mathrm{d}^2 \overline{V}}{\mathrm{d}x^2} = -4\pi\ell_B c_0 e^{-\overline{V}} \tag{53}$$

$$\lambda_D = \left(8\pi\ell_B c_\infty\right)^{-\frac{1}{2}} \tag{54}$$

$$V(x) = -\frac{\sigma_q \lambda_D}{\varepsilon} e^{-\frac{x}{\lambda_D}} \tag{55}$$

$$\lambda_D = 0.31[\text{NaCl}]^{-1/2} \tag{56}$$

$$\frac{E}{A} \approx k_B T \left(\frac{\sigma}{e}\right) \tag{57}$$

$$\frac{E}{A} \approx k_B T \left(\frac{\sigma}{e}\right)^2 2\pi\lambda_D \ell_B \tag{58}$$

$$f = 2k_B T b^2 r \quad b^2 \propto \frac{1}{nl^2} \tag{59}$$

$$\langle z/L_{tot} \rangle = \tanh\left(f L_{seg}^{(1d)} / k_B T\right) \tag{60}$$

$$\langle z/L_{tot} \rangle = \coth\left(f L_{seg}/k_B T\right) - \\ - \left(f L_{seg}/k_B T\right)^{-1} \tag{61}$$

$$\langle z/L_{tot} \rangle = \frac{\sinh\alpha}{\sqrt{\sinh^2\alpha + e^{-4\gamma}}} \tag{62}$$

$$\alpha \equiv \frac{f\ell}{k_B T} \quad \alpha \equiv \frac{\Delta G}{-2k_B T} \tag{63}$$

$$j(x) = c v_{drift} - D \frac{\mathrm{d}c}{\mathrm{d}x} \tag{64}$$

$$j^{(1D)} = -MD\left(\frac{\mathrm{d}P}{\mathrm{d}x} + \frac{1}{k_B T} P \frac{\mathrm{d}U_{tot}}{\mathrm{d}x}\right) \tag{65}$$

$$0 = \frac{\mathrm{d}}{\mathrm{d}x}\left(\frac{\mathrm{d}P}{\mathrm{d}x} + \frac{1}{k_B T} P \frac{\mathrm{d}U_{tot}}{\mathrm{d}x}\right) \tag{66}$$

$$v = \left(\frac{f\,L}{k_B T}\right)^2 \frac{D}{L} \left(e^{fL/k_B T} - 1 - \frac{f\,L}{k_B T}\right)^{-1} \tag{67}$$