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EXAM I COURSE
TFY4310 MOLECULAR BIOPHYSICS

Thursday, 17 December 2015
Time: kl. 09.00 - 13.00

Exercise 1.

Justify **eight** (8) of the following sentences:

1. The C–C single bonds are shorter and stronger in $H_2C=CH–CH=CH_2$ than in $H_2C=CH–CH_2–CH=CH_2$.

2. Mean-field theories based on the Poisson-Boltzmann equation, do not account for the attractive forces that may arise between surfaces with equal charge sign (for example, DNA condensation in the presence of trivalent ions).

3. The hydrogen bond is best described as a Coulombic interaction, than as a (point) dipole-dipole interaction.

4. The formation of surfactant micelles is entropically driven.

5. When applying the freely-rotating statistical polymer chain model, a suitable value for the θ angle is 109.4°.

6. Brownian dynamic techniques are more suitable to follow the folding of a protein than Monte Carlo simulations.

7. Spin-spin (T_2) relaxation does not involve the flipping of spins between levels.

8. COSY and NOESY are complementary techniques in the study of biomacromolecular conformation.

9. Infra-red and Raman spectroscopies are complementary techniques.

10. The Maxwell model is useful in predicting the response of a polymer during stress relaxation where a constant strain is imposed $\gamma = \gamma_0$.

11. In dilute macromolecule solutions, shear thinning occurs when the shear rate (rate of deformation) is faster than rate of orientation of the macromolecules.

Exercise 2.

Chromatin is the complex of DNA and eight proteins (histone octamer) found in all eukaryotic cells. The fundamental repeating unit of chromatin is the nucleosome particle. The properties of DNA and protein in nucleosomes, in water, were determined using a range of techniques.

Data obtained from dynamic light scattering, and plotted on a graph of the $\ln(g^{(1)}(q, \tau))$ versus τ, was found to be linear with a slope: -1.381×10^4 s^{-1}. The scattering angle was $90°$ and the wavelength of the light through the medium was 500 nm. The temperature was 20 °C.

In the same solution velocity sedimentation performed at 18,100 revolutions per minute, obtained the following data:

Time (minutes)	Boundary position r (cm)
0	4.460
80	4.593
160	4.713
240	4.844

Gel electrophoresis showed that the DNA molecule associated with a single nucleosome protein complex is 200 base pairs in length. The average molecular weight of a DNA base pair is 600 g mol^{-1}.

1. Calculate the translational diffusion coefficient of the nucleosomes.

2. What is the molecular weight of the nucleosome particle? Assume that the specific partial volume of the nucleosome particle is 0.66 cm^3/g.

3. Assuming the nucleosome particle to be spherical, calculate its Stokes (hydrodynamic) radius.

4. Each base pair in DNA is separated from the adjacent base pairs by about 3.4×10^{-10} m. Calculate the length of the DNA in the nucleosome and comment this result in view of the result obtained in question 2.3.

5. The rotational coefficient of the DNA molecules can be studied using transient electrically-induced birefringence (TEB). Describe briefly the main modules of the TEB instrumentation and the experimental procedure. What is the observable and how is the rotational friction coefficient calculated from the obtained data?

6. How are the proteins and DNA packed in the nucleosome? To answer this question, assume that the histone octamer forms a unhydrated spherical complex with specific volume 0.74 cm^3/g.

   i Calculate the radius of this hypothetical protein sphere.

   ii Contrast matching experiments performed with a small-angle neutron scattering equipment allow to determine that the DNA in the nucleosome was organized as a toroid (donut) with an inner radius of around 3.5 nm and an outer radius of roughly 4.9 nm. Discuss the overall structure of the nucleosome. Discuss qualitatively what is meant with contrast matching and how this is done experimentally.

Exercise 3.

Consider a solution of spherical and negatively charged hydrogel particles.

1. Discuss the (three) different terms that contribute to the swelling behavior of the hydrogel particles. Name, for each of the three terms, a solution property and a property of the particle that are expected to influence the swelling behavior.

2. Explain the concepts of Stern layer and diffuse electric double-layer.

3. What is the influence of ionic strength on the (i) swelling behavior of the gel particles and (ii) the stability of the particles in solution? Justify.

4. Let us imagine that the particles have collapse into a rigid and (overall) neutral spherical structure. Under these circumstances the excluded volume is defined by surface contact between solute molecules and the reduced osmotic pressure, Π/c, can be written according to:
$$\frac{\Pi}{c} = RT \ \left(\frac{1}{M_\mathrm{w}} + B\,c \right),$$
where the second virial coefficient B is defined in terms of the excluded volume u as
$$B = \frac{1}{2}\frac{N_\mathrm{Av}u}{M_\mathrm{w}^2}.$$

A plot of Π/c versus c for an aqueous solution of these particles at 25 °C shows a linear behavior, where the intercept and the slope of the line are 35.5 N m kg^{-1} and 0.182 N m^4 kg^{-2}, respectively.

  i. Evaluate the molecular weight and the excluded volume of the particles.

  ii. How do you expect the osmotic pressure to change when the particles are charged?

The following formulas and data may or may not be of use in answering the preceding questions. You do not need to derive any of the formulas but all parameters must be defined, if used.

Electron charge: $\qquad e = 1.602 \times 10^{-19}$ C

Avogadro constant: $\qquad N_\mathrm{Av} = 6.022 \times 10^{23}$ mol^{-1}

Boltzmann constant: $\qquad k_\mathrm{B} = 1.380 \times 10^{-23}$ m^2 kg s^{-2} K^{-1}

Properties of water at 20 °C:
$$\varepsilon = 78.4; \quad \eta = 0.01 \text{ g cm}^{-1}\text{s}^{-1}; \quad \rho = 1.02 \text{ g/cm}^3$$

Temperature: $\qquad$ [K] = [°C] + 273.15

Atomic orbitals: H: $1s^1$; C: $1s^2 2s^2 2p_x^1 2p_y^1$; O: $1s^2 2s^2 2p_x^2 2p_y^1 2p_z^1$

Atomic weights: $A_r(H) = 1.0$; $A_r(C) = 12.0$

Thermodynamics
$$G = H - TS \qquad A = U - TS \qquad \vec{F} = -\vec{\nabla}A$$
$$S = k_B \ln W$$

Statistical chain molecules
$$\left\langle R_{ee}^2 \right\rangle = Q^2 n$$

$$\left\langle R_{ee}^2 \right\rangle = Q^2 n \left(\frac{1 - \cos\theta}{1 + \cos\theta} \right)$$

$$\left\langle R_{ee}^2 \right\rangle = Q^2 n \left(\frac{1 - \cos\theta}{1 + \cos\theta} \right) \left(\frac{1 + \langle \cos\phi \rangle}{1 - \langle \cos\phi \rangle} \right)$$

Coulomb potential
$$V(r) = \frac{z_1 z_2\, e^2}{4\pi\epsilon_0 \epsilon r}$$

Screened Coulomb potential
$$V(r) = \frac{z_1 z_2\, e^2}{4\pi\epsilon_0 \epsilon r} \exp\left(-\frac{r}{\lambda_D} \right)$$

Debye screening length
$$\lambda_D^2 = \frac{\epsilon k_B T}{\sum_i (e Z_i)^2\, n_{i\infty}}$$

Friction coefficients
$$\vec{F} = -f\vec{v}, \qquad \vec{M} = -\xi\vec{\omega}$$

Stokes formula
$$f = 6\pi\eta R_h, \qquad \xi = 8\pi\eta R_h^3$$

For long chains and the random walk model
$$\left\langle R_{ee}^2 \right\rangle = 6 \left\langle R_G^2 \right\rangle$$

Hydrodynamic volume
$$v_{h,1} = \left(\overline{V}_1^{(S)} + \delta\overline{V}_0^{(S)} \right) \frac{M_1}{N_{Av}}$$

Specific volume (per mass)
$$V_1^{(S)} = v_1 \left(\frac{N_{Av}}{M_1} \right)$$

Fick's laws
$$\frac{\partial c}{\partial t} = -\vec{\nabla} \cdot \vec{J}, \qquad \vec{J} = -D_T \vec{\nabla}c, \qquad \frac{\partial c}{\partial t} = D_T \frac{\partial^2 c}{\partial x^2}$$

Nernst-Einstein relations
$$f D_T = k_B T, \qquad \xi D_R = k_B T$$

Lamm-equation
$$\frac{\partial c(r,t)}{\partial t} = D_T \left(\frac{\partial^2 c(r,t)}{\partial r^2} + \frac{1}{r} \frac{\partial c(r,t)}{\partial r} \right) - s\omega^2 \left(r \frac{\partial c(r,t)}{\partial r} + 2c(r,t) \right)$$

Sedimentation centrifugation:
$$s = \frac{\ln(c_0/c_p(t))}{2\omega^2 t}; \quad s = \frac{\ln(r_2/r_1)}{\omega^2(t_2 - t_1)}$$

Svedberg equation
$$s = \left(1 - \overline{V}_1^{(S)}\rho\right)\frac{M_1}{N_{\text{Av}}f}$$

Equilibrium centrifugation:
$$m_1(r) = m_1(r_{\text{m}})\exp\left\{\frac{M_1(1 - \overline{V}_1^{(S)}\rho)\omega^2(r^2 - r_{\text{m}}^2)}{2RT}\right\}$$

Electrically-induce birefringence:
$$I(t) = \frac{I_0}{4}\delta_0^2\exp(-12D_R t)$$

Nuclear spin
$$\vec{m} = \gamma\vec{L}, \qquad (\vec{m})^2 = \gamma^2\hbar^2\ell(\ell+1), \qquad m_z = m_\ell\,\gamma\,\hbar$$

Gyromagnetic ratio

Nucleus	^{1}H	^{2}H	^{13}C	^{14}N	^{19}F	^{31}P
$\gamma\left(10^7\frac{\text{rad/s}}{\text{T}}\right)$	26.753	4.107	6.728	1.934	25.179	10.840

Small-angle scattering:
$$q = \frac{4\pi}{\lambda}\sin\left(\frac{\theta}{2}\right)$$

Guinier approximation:
$$I_s(q) = I_0\exp\left(-\frac{1}{3}q^2R_G^2\right)$$

Discrete identical homogeneous particles:
$$\langle I_s(q)\rangle = Nb^2(0)P(q)S(q)$$

Static light scattering: RGD regime
$$\frac{\langle I_S(q)\rangle}{I_0} = cM\kappa\frac{1}{R^2},$$

Large systems
$$\frac{\kappa c}{R_\theta} = \frac{1}{M}\left[1 + \frac{16\pi^2}{3\lambda^2}R_G^2\sin^2\frac{\theta}{2}\right]\cdot[1 + 2B_2 c],$$

Dynamic light scattering: Siegert relation:
$$g^{(2)}(q,\tau) = 1 + [g^{(1)}(q,\tau)]^2$$
$$g^{(1)}(q,\tau) = \exp(-q^2 D_T\tau)$$

Constitutive equation of the Maxwell model:
$$\tau + \frac{\eta}{K}\dot{\tau} = \eta\dot{\gamma} \Rightarrow \tau + \lambda\dot{\tau} = \eta\dot{\gamma}$$