NORWEGIAN UNIVERSITY OF
SCIENCE AND TECHNOLOGY,
DEPARTMENT OF PHYSICS

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EXAM I COURSE
TFY4310 MOLECULAR BIOPHYSICS

Saturday, 7 December 2013
Time: kl. 09.00 - 13.00

During the exam the student may use:

Simple calculator in accordance with current NTNU rules and regulations,

Rottmann: Mathematical ematisk formelsamling,

Aylward & Findlay: SI Chemical Data,

O. Øgrim & B.E. Lian: Størrelse og enheter I fysikk og teknikk.

Note: In addition you will find some selected formulas and data at the end of this text.

Exercise 1.

a) Describe the bonding and the molecular orbitals of the ethylene ($H_2C=CH_2$) and make a sketch that shows the electron density distribution.

b) The ethylene is a planar molecule with bond angles of about 120 °. Justify.

c) The melting temperature of a lipid membrane is directly proportional to the entropy of the lipid hydrocarbon chain. How do you expect the melting temperature to change with an increase in the chain length and with the presence of unsaturated bonds? Justify.

d) The denaturation of a charged globular protein can be achieved by (i) an increase in the temperature, (ii) an increase in salt concentration, (iii) the addition of 6 M of urea (H_2-CO-NH_2), and (iv) the addition of alcohol. Discuss in detail the intramolecular interactions involved in the stabilization and destabilization of a globular protein in solution and how these are affected by the variations described above.

Exercise 2.

a) Calculate the molecular weight of a polyethylene polymer (CH_2 repeating unit) assuming that it takes the form of a spherical-like gaussian chain in solution. Dynamic light scattering measurements give an hydrodynamic radius of 275.8 Å and sedimentation velocity measurements yield a sedimentation coefficient of 613.1 S (10^{-13} s). Assume that the solution has a viscosity of 1.0 $\times 10^{-3}$ Ns/m^2 and a density of 1.0 g/cm^3 and that the polymer has a specific partial volume of 0.73 cm^3/g.

b) The relations used in a) assume that the solution is very dilute. Describe the experimental procedure that allows to determine the molecular weight of a macromolecule more accurately.

c) Assuming that the bond length, 1.53 Å corresponds to one CH_2 unit, calculate the R_G of the polyethylene polymer considered above using the freely-jointed, the freely-rotating and the hindered-rotating chain models. Take $\theta = 112°$ and $\langle \cos \phi \rangle = -0.4$. Give a brief description of the selected models and compare the results with the experimental value obtained above (take $R_h \approx R_G$).

Exercise 3.

a) Below is a ^{1}H NMR spectrum of a given molecule, where the chemical shift is given relatively to TMS (not included). The number correspond to the area under each peak. Discuss the structure of the molecule.
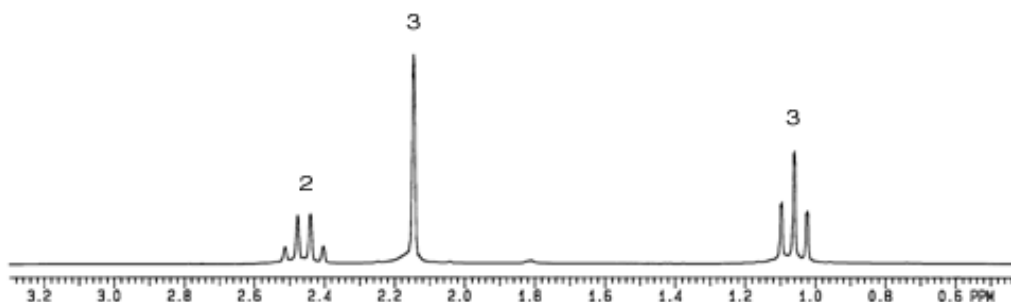
b) We can write, from the Bloch equations:
$$\text{Signal} = \text{const } N \left(\frac{\mu_z^2 B_z^2}{k_B T} \right) \left(\frac{\gamma^2 B_{xy} T_2}{1 + T_2^2 (\omega_0 - \omega)^2 + \gamma^2 B_{xy}^2 T_1 T_2} \right)$$
Define all parameters in this equation. Explain in detail why the NMR signal decreases with an increase in temperature. Explain the difference between T_1 and T_2.

Exercise 4.

a) Large DNA molecules showing a coil (gaussian) conformation can undergo compaction to smaller globular structures by the addition of oppositely charged polymers (polycations). If the concentrations of DNA and polycations is sufficiently large the (neutralized) DNA-polycation complexes precipitate out of solution.

Name three techniques that can be used to study the compaction of DNA in solution and/or precipitation of DNA-polycation complexes. Justify your choice by describing, for each of the three techniques, the molecular properties that are determined, as well as one advantage and disadvantage.

b) Some experimental work has been done on DNA gels, for studying DNA – polycation interaction.

i) Name the advantages and disadvantages of using this methodology.

ii) The swelling equilibrium of ionic networks can be written in a simplified way, according to:

$$\Pi_{\text{tot}} = \Pi_{\text{mixt}} + \Pi_{\text{elas}} + \Pi_{\text{ionic}}$$

Describe qualitatively each of the three terms. Refer, justifying, two properties of the system that may influence each of the terms.

iii) Do you expect the DNA gel to swell or deswell in the presence of the polycations? If the gel was prepared from single-stranded DNA molecules, would you expect the swelling/deswelling to be larger or smaller? Justify.

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

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

Values for dielectric constants
at 25°C $\qquad \epsilon_{\text{r}}(\text{water}) = 78.4; \quad \epsilon_{\text{r}}(\text{ethanol}) = 19.9; \quad \epsilon_{\text{r}}(\text{chloroform}) = 4.81$

Avogadro constant: $\qquad N_{\text{Av}} = 6.022 \times 10^{23}$

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

Atomic weights: $A_r(\text{H}) = 1.0$; $A_r(\text{C}) = 12.0$

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

$\qquad\qquad\qquad\qquad S = k_{\text{B}} \ln W$

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

$$\left\langle R_{\text{ee}}^2 \right\rangle = Q^2 n^2$$

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

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

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

Debye screening length $\qquad \lambda_{\text{D}}^2 = \dfrac{\epsilon k_{\text{B}} T}{\sum_i (e Z_i)^2 \, n_{i\infty}}$

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

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

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

Fluid dynamic volume
$$v_{\text{h},i} = m_i \left(\overline{V}_i^{(S)} + \delta\overline{V}_0^{(S)} \right)$$

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

Nernst-Einstein relations $\quad f D_{\text{T}} = k_{\text{B}}T, \qquad \xi D_{\text{R}} = k_{\text{B}}T$

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

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

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

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

Scattering from molecules $\quad I(\vec{S}) \propto \underbrace{\left|F(\vec{S})\right|^2}_{\text{structure factor}} \cdot \underbrace{\left|P(\vec{S})\right|^2}_{\text{form factor}}$

Static light scattering:
Rayleigh regime
$$\frac{\kappa C}{R_\theta} = \frac{1}{M_w}\left[1 + 2B_2 C \right],$$

Laurenz-Mie regime
$$\frac{\kappa C}{R_\theta} = \frac{1}{M_w}\left[1 + \frac{2\pi}{3}S^2 \cdot R_G^2 \right] \cdot \left[1 + 2B_2 C \right],$$

where :

$$S = 2|\sin\theta|/\lambda$$

Typical values of chemical shifts in proton NMR (Note! The δ given in the table is a simplification and not all possible groups are displayed):

Type of proton		Chemical Shift (ppm)
Primary alkyl	RC$\underline{H}_3$	0.8-1.0
Secondary alkyl	R$_2$C $\underline{H}_2$	1.2-1.4
Tertiary alkyl	R$_3$C $\underline{H}$	1.4-1.7
benzylic	ArC$\underline{H}_3$	2.2-2.5
Alkyl chloride	RC$\underline{H}_2$Cl	3.6-3.8
Alkyl bromide	RC$\underline{H}_2$Br	3.4-3.6
Alkyl iodide	RC$\underline{H}_2$I	3.1-3.3
Alkyl fluoride	RC$\underline{H}_2$F	4.0-4.5
Ether	ROC$\underline{H}_2$R	3.3-3.9
Ester	RCOOC$\underline{H}_2$R	3.3-3.9
Alcohol	HOC$\underline{H}_2$R	3.3-4.0
Ketone	RCC$\underline{H}_3$ ‖ O	2.1-2.6
Ester	RC$\underline{H}_2$COOR	2.1-2.6
Aldehyde	RC$\underline{H}$ ‖ O	9.0-10.0
Vinylic	R$_2$C=C$\underline{H}_2$	4.6-5.0
Aromatic	Ar$\underline{H}$	6.0-9.0
Alcohol Hydroxyl	RO$\underline{H}$	0.5-6.0
Carboxylic	RCOO$\underline{H}$	10-13
Phenolic	ArO$\underline{H}$	4.5-7.7
Amino	RN$\underline{H}_2$	1.0-5.0
Amide	RCN$\underline{H}$R ‖ O	5.0-9.0