

ДЕСЬКИЙ НАЦІОНАЛЬНИЙ УНІВЕРСИТЕТ ІМЕНІ І. І. МЕЧНИКОВА

(повне найменування закладу вищої освіти)

Факультет математики, фізики та інформаційних технологій

(повне найменування факультету)

Кафедра фізики та астрономії

(повна назва кафедри)

Кваліфікаційна робота

на здобуття ступеня вищої освіти « магістр »

«рН as an indicator of phase transitions in water-protein solutions»

«рН як індикатор фазових переходів у водно-протеїнових розчинах»

Виконала: здобувач денної форми навчання спеціальності 104- Фізика та астрономія

(код, назва спеціальності)

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Рекомендовано до захисту:

Протокол засідання кафедри

фізики та астрономії

№ ____ від ____ . ____ . 20 ____ р.

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Захищено на засіданні ЕК № _____

протокол № __ від ____ . ____ . 20 ____ р.

Оцінка _____ / _____ / _____

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Одеса 2024

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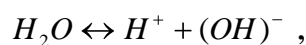
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INTRODUCTION

The main properties of the blood in human and mammal organisms are determined by temperature and so called pH – index. The last is tightly connected with the relative concentration of H^+ ions [1,2]:

$$pH = -\log(n_{H^+} / n_w),$$

where n_{H^+} is the numerical density of H^+ ions and n_w is the same for water molecules in the blood. H^+ ions appear in the blood in the consequence of 1) the self-dissociation of water molecules:



where $(OH)^-$ is so called hydroxyl group, and 2) the dissolution in the blood of smallish quantities of acids of type HCl :



or carbon dioxide CO_2 as well as similar cases. Here H^+ ions arise due to the following successive transformations:



On the first step the carbon acid is formed and on the second step it dissociates with formation of H^+ ion.

Arising H^+ ions can join to the macromolecules of albumin, fibrinogen and other entering to the blood plasma. Inside and outside of these macromolecules form electrical fields which allows them to join many useful molecules and transport them from one place to another.

The change of the density of H^+ ions or the pH – index changes in its turn the electro-physical properties of noted above macromolecules and transport properties of the blood. Some electro-physical properties of these macromolecules are described more adequately with the help of so called dzeta potential ζ [2]. This is local characteristics of electric fields inside and outside of macromolecules. As opposed to it the pH – index is the global characteristics for the distribution of H^+ ions. In this situation the establishment of the interconnection between the ζ –

potential and pH -index is very important question. Its experimental study had been shown that the corresponding equation takes the surprising structure:

$$\zeta / \zeta_0 = \text{tha}(pH - pH_0),$$

characteristic for paramagnets [3], where $\text{th}x$ is the hyperbolic tangent depending on the variable: $x = pH - pH_0$. The Diploma Project is devoted to the consideration of the physical nature of this surprising equation.

1. THE DEFINITION OF H-INDEX. ITS ROLE IN THE FORMATION OF THE BLOOD PROPERTIES

1.1. Determination of the pH-index for pure water

Let us determine the pH-index for pure water. In this case the ions H^+ can appear in water due to the self-dissociation of water molecules:



The most important contribution to the self-dissociation mechanism is caused by binary collisions of water molecules. The corresponding fraction of water molecules, which have the energy, sufficient for the destruction of water molecules at temperature T , is determined by the Maxwell distribution for relative velocities of molecules [4]:

$$\frac{\Delta n_D}{n} = \frac{\pi}{2} \left(\frac{m}{\pi k_B T} \right)^{3/2} \int_{v_D}^{\infty} \exp\left(-\frac{mv^2}{4k_B T}\right) v^2 dv, \quad (2)$$

where Δn_D is the number of molecules, having the relative velocities, leading to the destruction of water molecules due to their collisions, n is the numerical density of water molecules, m is the mass of water molecule, v is the relative velocity of motion between two molecules.

The minimal value of the relative velocity, sufficient for the self-dissociation of water molecule due to its collision with the nearest neighbor equals to:

$$v_D = \left(\frac{6kT_D}{m} \right)^{1/2}, \quad (3)$$

where T_D is the dissociation energy of water molecule in temperature units. One can verify, that the main contribution to the integral (2) is determined by the expression:

$$c_H^+ \approx \frac{2}{\sqrt{\pi}} \sqrt{\frac{3T_D}{2T}} \exp\left(-\frac{3T_D}{2T}\right). \quad (4)$$

Indeed, the expression (2) can be rewritten in the view:

$$\frac{\Delta n_D}{n} = \frac{4}{\sqrt{\pi}} \int_{x_D}^{\infty} e^{-x^2} x^2 dx, \quad x_D = 0.5v_D(m/k_B T)^{1/2}.$$

Since

$$\int_{x_D}^{\infty} e^{-x^2} x^2 dx \Rightarrow -\frac{1}{2} \int_{x_D}^{\infty} x de^{-x^2} \Rightarrow \frac{x_D}{2} e^{-x_D^2} + \frac{1}{2} \int_{x_D}^{\infty} e^{-x^2} dx$$

and

$$\int_{x_D}^{\infty} e^{-x^2} dx \ll \int_{x_D}^{\infty} e^{-x^2} x^2 dx,$$

we obtain with satisfactory accuracy the estimate:

$$\int_{x_D}^{\infty} e^{-x^2} x^2 dx \approx \frac{x_D}{2} e^{-x_D^2}.$$

Together with (3) it immediately leads to the formula (4).

As a result, the value of pH – index takes the view [5]:

$$pH = -\log \left(\frac{2}{\sqrt{\pi}} \sqrt{\frac{3T_D}{2T}} \exp \left(-\frac{3T_D}{2T} \right) \right). \quad (5)$$

In accordance with [6], the dissociation energy an isolated water molecule on ion H^+ and OH^- equals to $E_D = 117.8 \text{ kcal/mol}$ or $E_D = 0.82 \cdot 10^{-11} \text{ erg/particle} \rightarrow T_D = 59300 \text{ K}$. The dissociation energy obtained experimentally in [7] equals to $E_D = 41145.94 \text{ cm}^{-1}$. The close quantity is also determined by triple-resonance vibrational spectroscopy and *ab initio* calculations in [8]. The corresponding dissociation temperature equals to $T_D = 59200 \text{ K}$.

In liquid water the situation radically changes due to influence of screening effects. For this aim we can use the following dispersion law for the dielectric permittivity [6]:

$$\varepsilon(\omega) = \varepsilon_{\infty} + \frac{\varepsilon_0}{1 + (\omega\tau_D)^2},$$

where $\varepsilon_{\infty} \approx 2.5$ and $\tau_D \approx 0.5 \cdot 10^{-12} \text{ s}$

The value of the dissociation energy $E_D^{(w)}$ in liquid water can be reduced in comparison with its value for isolated water molecule. The same is also conserved for the dissociation energy in temperature units:

$$T_D^{(w)} = T_D / \varepsilon_{el}, \quad (6)$$

where $\varepsilon_{el} = \varepsilon(\omega = 1/\tau_D)$ is the dielectric permittivity of water on rotation frequencies [6,9]. By order of magnitude it takes values: $\varepsilon_{el} \approx 10 \div 20$. At $\varepsilon_{el} \approx 20$ we have an estimate: $T_D \approx 2965 \text{ K}$. This value is close to the H-bond energy [6,10,11], written in the temperature units.

The concentration of the hydrogen ions:

$$c_{H^+} = \frac{\Delta n_D}{n}, \quad (7)$$

estimated according to (4) and (6), is equal to:

$$c_H^+ \approx 0.855 \cdot 10^{-7} \quad (8)$$

This value is close to the standard one [1] observed at $T = 25^0 \text{ C}$:

$$pH = -\log(c_H^+) \approx 7. \quad (9)$$

1.2. Properties of proteins in aqueous solutions

In this Section we will consider the influence of water thermal motion on the electro-physical properties of Albumin and Fibrinogen. The main attention is focused on the behavior of their zeta potentials (see [12]).

a) Definition of the zeta potential (ZP)

The protein macromolecules of albumin and fibrinogen are important components of the blood plasma. They are able to attach to themselves the hydrogen ion H^+ and cations and also anions of type Na^+ and Cl^- . All these ions

joint to surface layers of protein macromolecules. The distribution of charges at the macromolecule surface **determines** the dynamics of ions in the surrounding interfacial region. The liquid layer surrounding the macromolecule is subdivided into two parts: an inner region (or the Stern layer), where surrounding water molecules and the ions are strongly bound with the protein macromolecule and an outer, diffusive region, where they are less attached. A protein macromolecules move together with surrounding them water molecules and ions from the Stern layer. In the diffusive region, the drift of macromolecules and surrounding water molecules and ions are unrelated. The distribution of charges at the boundary between the Stern and diffusive layers is characterized by the corresponding potential difference or the zeta potential (ZP).

In order to measure the ZP the electrophoretic light scattering technique is used.

Temperature and pH are most important factors affecting ZP. The important measurements of the ZP for albumin and fibrinogen had been presented in [12].

b) Albumin

The human serum albumin (HSA) is a single chain protein with 585 amino-acid residues with a predominant α -helical heart-shaped structure [13]. As noted above its dynamics depend on several factors like pH, temperature, etc []. Aqueous solutions with concentrations 1mg/ml for HSA and NaCl ions (0.075 mol/l, 0.15 mol/l, 0.225 mol/l) were investigated. The measurements were performed in the temperature interval 25–50°C with the 1°C step.

It was established that the values of the hydrodynamic radii remain practically constant in the temperature interval 30 – 50°C (Fig.1). The addition of NaCl ions changes the value of R_H in limits of 5 ± 0.3 nm.

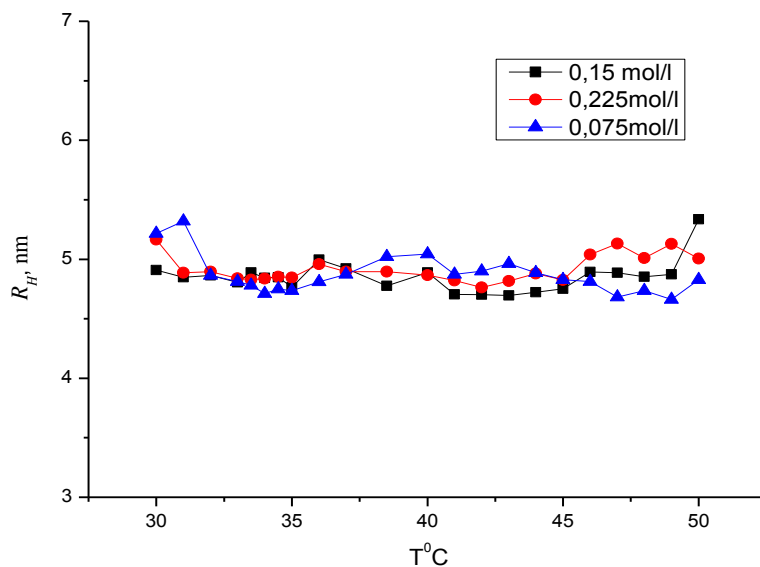


Fig.1. Temperature dependence of the hydrodynamic radius R_H for albumin at different concentrations of NaCl

The values of the ZP in the temperature range 25-70°C are presented in the Fig. 2. As we can see the ZP magnitude strongly increases from -27mV at the temperature 30°C up to zero around the temperature 42°C.

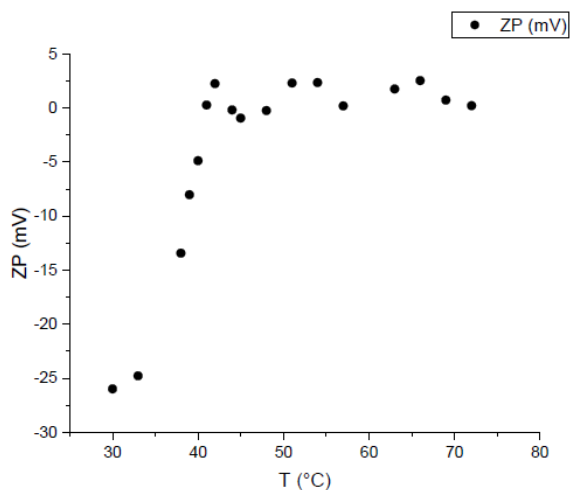


Fig.2. Temperature dependence of the ZP for aqueous solution of albumin at pH=7.4 and concentration 0.075 mol/l for NaCl.

Here it is necessary to note that the ZP takes zero value, characteristic for the isoelectric point (IEP), at proximity of 42°C. In works [14] it had been shown that

this temperature divides the region of liquid states for ordinary water on two intervals: $(T_r < T < T_r + 42^\circ)$ and $(T_r + 42^\circ < T < T_c)$. Within the first of them the thermal motion of water molecules has the crystal-like character, In the second interval water molecules move similarly to that in argon, i.e. the molecular motion has argon-like character.

As we can see, such a change of the character of thermal motion in water leads to considerable influence on the charge distribution of ions in aqueous solutions of albumin donated by salts of type $NaCl$. The system is not particularly stable in a region surrounding the condition of IEP.

Here it is necessary to pay attention that the behavior of the ZP near the 42°C is analogous to that for the magnetization m_z near the Curie-Weiss critical point T_{CW} of magnet [3,4]. Indeed,

$$m_z = \begin{cases} 0, & T > T_{CW}, \\ \neq 0, & T < T_{CW}. \end{cases} \quad (9)$$

The behaviour of the ZP, designated by ζ , is the same:

$$\zeta \approx \begin{cases} 0, & T > T_H, \\ \neq 0, & T < T_H, \end{cases} \quad (10)$$

where T_H is identified with 42°C and can be named as the peculiar point for the subsystem of ions reacting on the peculiarities of thermal motion in water.

c) Fibrinogen

A fibrinogen macromolecule consist of 2964 amino-acid and 4 carbohydrate residues. Each monomer unit consists of three non-identical polypeptide chains. The monomer units as well as polypeptide chains are linked with the disulfide bonds.

The measurements of R_H (Fig.3) and the ZP (Fig.4) have been carried out at the standard conditions: pH=7.4 and 0.15 mol/l concentration of $NaCl$.

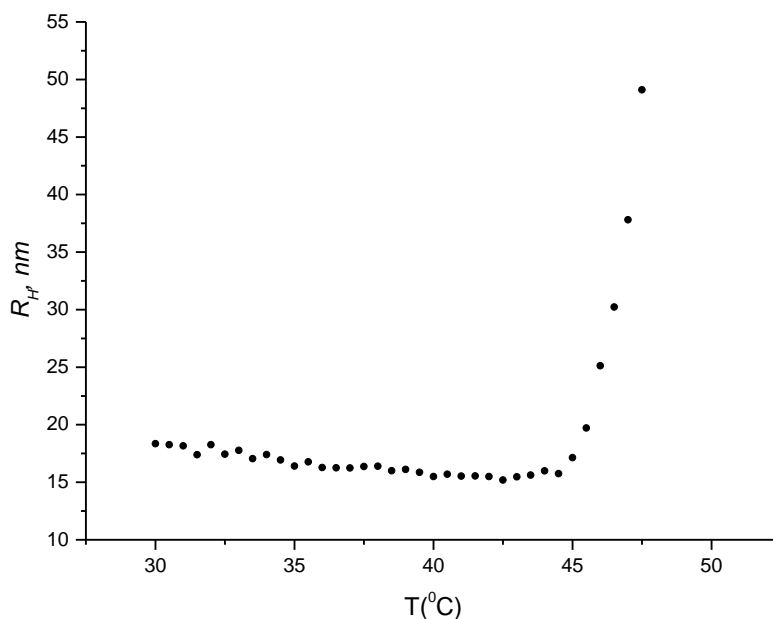


Fig.3. Temperature dependence of the fibrinogen hydrodynamic radius R_H at pH=7.4 and 0.15 mol/l concentration of $NaCl$.

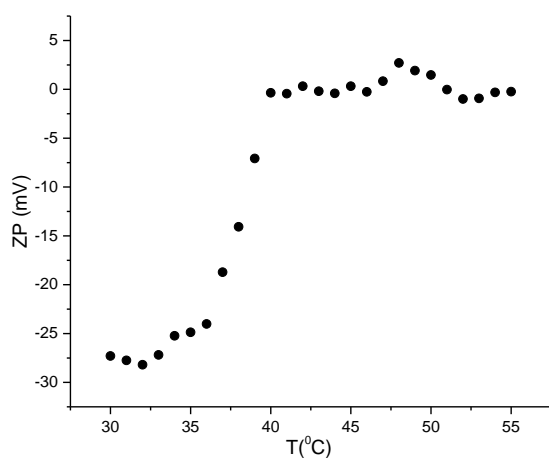


Fig.4. Temperature dependence of the ZP for a fibrinogen macromolecule.

As we can see the hydrodynamic radius of a fibrinogen macromolecule is practically constant within the temperature interval 30-45°C, whereas starting from 45°C the value of R_H considerably increases. However, the behaviour of the ZP reminds that for the albumin macromolecule. This indicates that the electro-

physical properties for different protein macromolecules are mainly determined by the peculiarities of thermal motion in water.

Such a behavior of the ZP for Albumin and Fibrinogen macromolecules testifies about their interconnection with the dynamic phase transition having place in water at 42°C [14]. More exactly, in [14] it had been shown that at 42°C crystal-like thermal motion in water transforms to argon-like thermal motion. At that, the practically fixed value of the albumin hydrodynamic radius indicates that only the charge distribution changes near this characteristic temperature. The analogous situation is observed near the Curie-Weiss critical point in the simplest magnets: in them the spin degrees of freedom are not practically connected with those responsible for the translational and rotational motions of ions. However, such an interconnection probably takes place for fibrinogen macromolecule. Due to this its hydrodynamic radius begins to increase above the peculiar temperature $T_H = 42^{\circ}\text{C}$.

The important role in similar phase transition can play water molecules forming H-bond bridges between segments of macro-molecules.

1.3. Zeta potential for the albumin macromolecules in dilute water-salt solutions

The main aim of this Section is 1) to define the notion of the Zeta potential (ZP) and 2) to calculate the ZP for albumin macromolecule in the Debye approximation.

Let us consider the dilute aqueous solution of the human serum albumin, donated additionally by the salt NaCl . Due to the thermal rotation the albumin macromolecule can be considered as the spherical object with the radius of magnitude 45Å [13]. Due to specific construction of the albumin macromolecule it can be attach to itself the hydrogen ion H^+ from surrounding water and also the cations and anions Na^+ and Cl^- appearing in water solution due to the dissociation of the salt molecules. All these ions are localized on the albumin surface, forming

so called the Stern layer. The ions of opposite sign form the diffusive electric layer in the surrounding solution around the albumin macromolecule. The surface charge of albumin is compensated by the opposite charge from the diffusive electric layer. There is the minimal spherical surface enveloping an albumin macromolecule and surrounding it the diffusive electric layer. Due to electro-neutrality the potential of electric field, created by all described charges, on this minimal surface equals to zero.

The zeta potential is determined as the difference of potentials between this surface and that having place on the surface of albumin macromolecule.

Let us to estimate the ZP in the case of not covering minimal surfaces for different albumin macromolecules.

The potential of the electric field inside of the diffusive layer satisfies the Poisson equation:

$$\Delta\varphi(r) = -4\pi\rho \quad (11)$$

The charge volume density is determined by the expression:

$$\rho(r) = \frac{1}{4\pi r_D^2} \varphi \quad (122)$$

Here r_D is the Debye radius having the meaning of effective thickness of the diffusive layer:

$$r_D = \left(\frac{\varepsilon k_B T}{8\pi e^2 n_{Na^+}} \right)^{1/2},$$

ε is the dielectric permittivity of the water solution, e is the electron charge, n_{Na^+} is the charge density for ions Na^+ .

On the surface of the albumin macromolecule having the radius r_a the potential satisfies the boundary condition:

$$\left. \frac{\partial\varphi(r)}{\partial r} \right|_{r=r_a} = 4\pi\sigma_s \quad (13)$$

The second boundary condition imposes on the minimal surface:

$$\varphi(r_M) = 0 \sim \varphi(r \rightarrow \infty) \rightarrow 0 \quad (14)$$

The potential satisfying the formulated boundary conditions is represented in the view:

$$\varphi(r) = \varphi_0(r_a) f(r) \quad , \quad (15)$$

where

$$\varphi_0(r_a) = \frac{4\pi\sigma r_a r_D}{\varepsilon(r_a + r_D)} \quad - \quad (16)$$

is the potential near the charged surface, and

$$f(r) = \frac{r_a}{r} \exp\left(-\frac{r-r_D}{r_D}\right) \quad (17)$$

is the function describing the behavior of the potential inside the diffusive electric layer.

In accordance with the definition given above for the zeta potential we get the following expression:

$$\zeta = \varphi_0(r_a) = \frac{4\pi\sigma r_a r_D}{\varepsilon(r_a + r_D)} \quad (18)$$

The dependence of the ZP vs. the ion density is presented in fig.3.1.

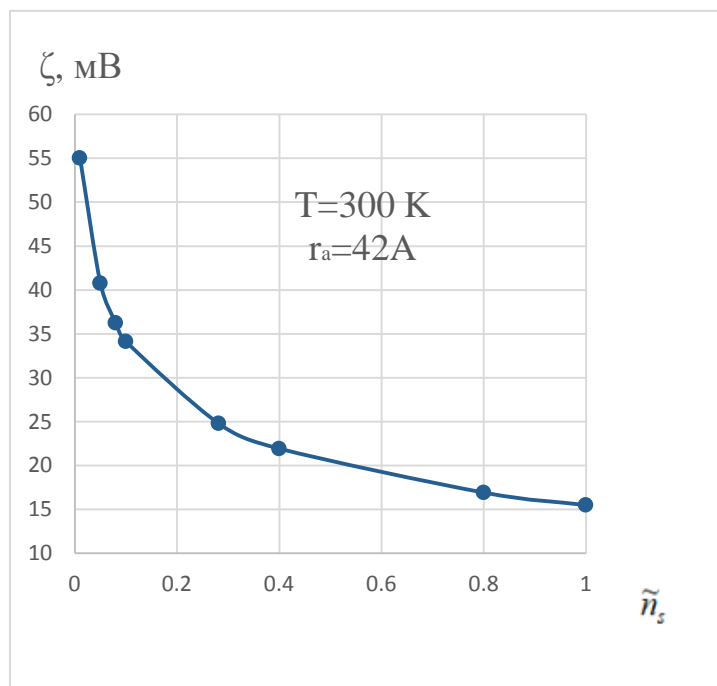


Fig.5. The ZP for albumin macromolecule vs. the ion density at T=300K.

1.4. A new problem – the influence of the pH-index on the Zeta Potential

The Diploma Project will be devoted to investigation of the Zeta potential ζ for albumin macromolecules placed in aqueous salt solutions as a function of the pH – index. Studying experimentally this question in the work [12] it had been shown that the dependence of ζ on the difference $pH - pH_0$ is similar to that for the magnetization m_z considered as a function of the magnetic field strength h for the simplest ferromagnetic. In this case

$$m_z(T, h) = th\beta h \quad (20)$$

where $\beta = T_*/T$ and T_* is so called the Curie-Weiss critical point.

In view of the similarity the ZP ζ can be described by the analogous expression:

$$\zeta = th\kappa(pH - pH_0). \quad (21)$$

This result is very surprising and it requires the physical explanation.

In order to understand the similarity mechanism for ZP and magnetization we apply to the Landau thermodynamic potential depending on the order parameter. Identifying the order parameter with the magnetization in the case of magnet and the ZP in the case of aqueous solutions of albumin we will construct the Landau thermodynamic potential, accepting the same structure for magnets and solutions.

Due to this we will get the natural basis for the explanation of the relation (21).

In connection with this we plan;

- to consider the physical nature of the pH – index;
- to acquaint with the notion of the dzeta potential;

- to discuss with the experimental relation connecting the zeta potential and pH –index;
- to study the behavior of the magnetization for ferromagnets and paramagnets near their Curie-Weiss critical points as a function of temperature and the magnetic field strength;
- to consider the behavior of zeta potential for albumin in aqueous solutions near $T_H = 42^{\circ} C$ as a function of temperature;
- to establish the similarity in the behavior of the zeta potential and magnetization;
- to discuss the fundamental relation between zeta potential and pH –index.

2. ζ -POTENTIAL AS A FUNCTION OF PH

2.1. Behavior of the zeta-potential for water solutions of albumin as function of their pH -index

The character of zeta-potential dependence on the pH -index for water solutions of albumin is studied in [15,16]. The corresponding dependences at different concentrations of the salt ($NaCl$), playing the role of third component in solution, are presented in Fig.1.

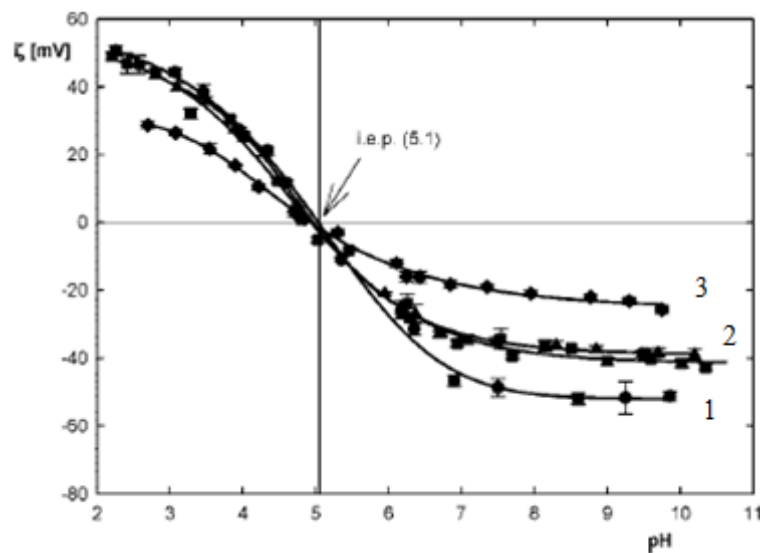


Fig. 2.1. Experimental values of the zeta-potential for human serum albumin at $T=300K$ and different salt concentrations:

1 - $n_s^{(1)} = 6 \cdot 10^{17} \text{ cm}^{-3}$, 2 - $n_s^{(2)} = 1.8 \cdot 10^{18} \text{ cm}^{-3}$, 3 - $n_s^{(3)} = 6 \cdot 10^{18} \text{ cm}^{-3}$.

As we can see, the character of these dependences reminds us the behavior of the magnetization versus the strength H of magnetic field [3]:

$$m_z = th\left(\frac{\gamma H}{k_B T}\right). \quad (22)$$

Here $thx = \frac{e^x - e^{-x}}{e^x + e^{-x}}$ is the hyperbolic tangent, $k_b T$ is the energy of thermal motion, γ is the parameter proportional to the number of the nearest neighbors and the interaction energy between them.

In accordance with (1) the behavior of the zeta potential versus pH – index is described by the similar formula:

$$\zeta = -\zeta_0 th \left(\kappa (pH - pH_0) \right) \quad (23)$$

Here it is necessary to add that the similar dependence first takes place on the right side from pH_0 . With suitable accuracy $pH_0 = 5.1$ and it is the same for all curves in the Fig.1. The values of κ and ζ_0 depend on the curve numbers and they are different for left and right branches of the same curve.

Table 1. Values of parameters κ_i and $\zeta_0^{(i)}$

Number of curve	Left branches		Right branches	
	κ_i	$\zeta_0^{(i)}$	κ_i	$\zeta_0^{(i)}$
1	0.54	53.3	0.54	53.3
2	0.39	60	0.63	40
3	0.45	35	0.54	23.5

The asymmetry degree of curves $\zeta_i = \zeta_i(pH - pH_0)$

Note, that left and right branches of the curves are not rigorously symmetrical. Indeed, considering the combination

$$\Delta \zeta_a(\text{pH} - \text{pH}_0) = \zeta_0^{(r)} \text{th} \zeta_r(\text{pH} - \text{pH}_0) - \zeta_0^{(l)} \text{th} \zeta_l(\text{pH} - \text{pH}_0)$$

as a function of $\text{pH} - \text{pH}_0$ we obtain the deviation degree from zero for every curve (Fig.2).

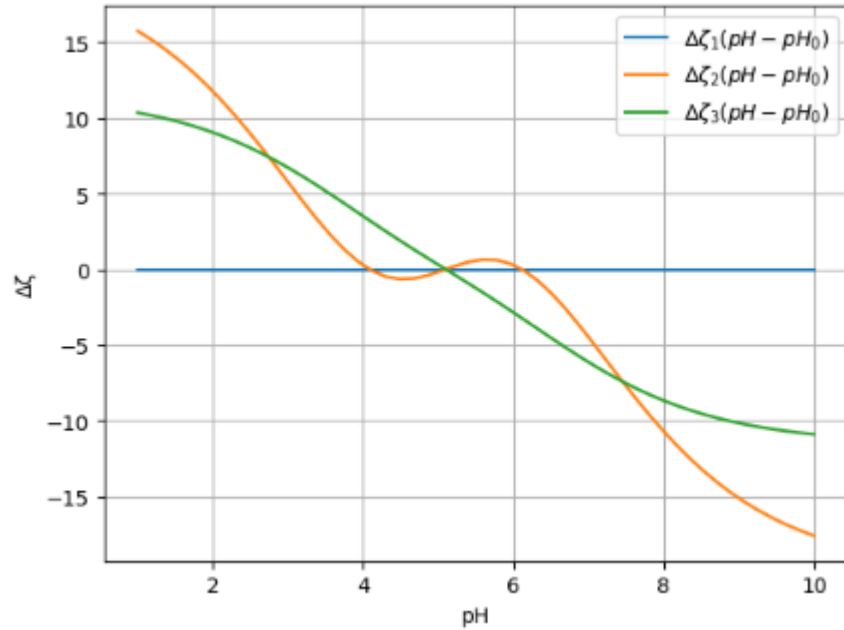


Fig.1.2. The behavior of $\Delta \zeta_a^{(i)}(\text{pH} - \text{pH}_0)$, $i=1,2,3$, vs. $\text{pH} - \text{pH}_0$.

As we can see, that 1) at the most low salt concentration ($n_s^{(1)} = 0.6 \cdot 10^{18} \text{ cm}^{-3}$) the deviation of the zeta-potential from (2) is practically absent and 2) the most considerable deviation from the curve 2 is observed at $n_s^{(2)} = 1.8 \cdot 10^{18} \text{ cm}^{-3}$, i.e. the

increase of the salt concentration leads to the non-monotonous deviation on the based curve (2). The relative deviation on the based curve (2) described by the formula:

$$\xi_a^{(i)} = \frac{\Delta \zeta_a^{(i)}(\text{pH} - \text{pH}_0)}{\left(\zeta_0^{(l)} + \zeta_0^{(r)} \right) / 2}$$

does not exceed 30% .

Thus, the applicability of the formula (2) to the description of zeta potential as a function of $\text{pH} - \text{pH}_0$ is quite satisfactory.

The physical nature for pH_0

The averaged concentration of albumin macromolecules in the blood plasma is about $c_a \approx 49.7 \text{ g/L}$ that is equivalent to their density $0.5 \cdot 10^{18} \text{ cm}^{-3}$. The numerical water density is: $n_w \approx 3 \cdot 10^{22} \text{ cm}^{-3}$. From here it follows that the molar concentration of the albumin macromolecules equals to:

$$c_a = n_a / n_w \approx 1.67 \cdot 10^{-5}$$

If an albumin macromolecule attaches only one ion H^+ we get the following value of the pH – index:

$$pH_1 = -\lg c_a = 5 - \lg 1.67 = 4.78$$

This value is close to the $pH_0 = 5.1$ characteristic for the iso-electric point observed for water solutions of albumin. It means that the macromolecule of albumin attaches $z_{H^+}^{(a)}$ ions, satisfying the inequality: $z_{H^+}^{(a)} < 1$.

From here it follows that the averaged number z_{H^+} of ions H^+ attached to an albumin macromolecule and corresponding to $pH_0 = 5.1$ equals to:

$$pH_0 = -\lg z_{H^+} - \lg c_a = 5.1$$

It leads to

$$z_{H^+} \approx 0.73$$

Thus, the zero value of the zeta potential corresponds to the charged albumin macromolecule (the seven hydrogen ions H^+ attach to ten albumin macromolecule). It is possible that this positive charge is compensated by the negative ions from salt solution which attach to an albumin macromolecule. Here

it is necessary to note that the distribution of potential has no the spherical symmetry for small charges on the macromolecule surface.

Hyperbolic tangent in the model expression for the zeta-potential

It is surprising that the zeta potential calculated within the cell model is also

proportional to the hyperbolic tangent. Indeed, in [17] it had be shown that the zeta potential equals to

$$\zeta(z, r_c, r_a, r_D) = \frac{ze}{\varepsilon r_a} r_D \frac{sh\left(\frac{r_c - r_a}{r_D}\right)}{r_a ch\left(\frac{r_c - r_a}{r_D}\right) + r_D sh\left(\frac{r_c - r_a}{r_D}\right)}.$$

Here r_a is the radius of sphere described the albumin macromolecule, r_c is the cell radius ($r_c > r_a$), r_D is the Debye radius ($r_D < (<<)r_c, r_a$), determining the decrease of the potential in diffusion part of double electric layer. This expression can be rewritten in the view:

$$\zeta(z, r_c, r_a, r_D) = \frac{ze}{\varepsilon r_a^2} r_D \frac{th\left(\frac{r_c - r_a}{r_D}\right)}{1 + \frac{r_D}{r_a} th\left(\frac{r_c - r_a}{r_D}\right)}$$

or

$$\zeta(z, r_c, r_a, r_D) = \frac{ze}{\varepsilon r_a^2} r_D th\left(\frac{r_c - r_a}{r_D}\right) \left(1 - \frac{r_D}{r_a} th\left(\frac{r_c - r_a}{r_D}\right) + \dots\right),$$

since $r_D / r_a \ll 1$

2.2. Critical phenomena in the simplest magnets

The very important peculiarity of critical phenomena in different systems is their isomorphism. So, the critical behavior of the simplest magnetics (paramagnetics, ferromagnetics) is similar to that in atomic liquids of the argon type. It means that these systems near their critical points are described by the same thermodynamic potentials, although outside the critical regions their thermodynamic potentials can be very different.

Let us consider this circumstance in more details.

Ferromagnetic near the Curie-Weiss critical point

The properties of the simplest ferromagnetic are usually described by the Ising model:

$$H = -J \sum_{\langle i,j \rangle} s_i s_j - h_0 \sum_i s_i, \quad J > 0, \quad (24)$$

where s_i is the lattice variable, describing the projection of electron spin on z -axis and taking values: $s_i = \pm 1$, J is the constant of exchanged spin-spin interaction, $\langle i, j \rangle$ is the symbol of summation on all pairs of the nearest neighbors, h_0 is strength of magnetic field directed along the z -axis. It is supposed that $1 \leq i, j \leq N$.

In accordance with (22) the interaction energy of two nearest spins depends on their directions:

$$\varepsilon_{\uparrow\uparrow} = \varepsilon_{\downarrow\downarrow} = -J, \quad \varepsilon_{\uparrow\downarrow} = \varepsilon_{\downarrow\uparrow} = J. \quad (25)$$

From here it follows that identical orientations of the nearest spins are energetically preferable. This is a prerequisite for the ordering of spins in a system.

Free energy for the Ising model

The free energy is determined by the standard expression:

$$F = -k_B T \ln Z, \quad Z = \sum_{\{s_i\}} \exp(-\beta H), \quad (26)$$

In which the symbol $\{s_i\}$ designates the summation on all possible spin configurations: $\uparrow\uparrow\uparrow \dots \uparrow$, $\downarrow\uparrow\uparrow \dots \uparrow$, $\uparrow\downarrow\uparrow \dots \uparrow$, $\downarrow\downarrow\uparrow \dots \uparrow$ and so on. In general the free energy depends only on temperature and the strength of external magnetic field:

$$F = F(T, h_0).$$

Due to equivalency of directions along and oppositely z -axis the free energy is the even function of h_0 :

$$F = F(T, h_0^2).$$

(4)

From here it follows that the magnetization M (directed along z -axis) of a system satisfies the equations:

$$M = -\frac{\partial F}{\partial h_0}, \quad (27)$$

and

$$M = -2h_0 \left. \frac{\partial F(T, h_0^2)}{\partial h_0^2} \right|_{h_0=0} = 0. \quad (28)$$

The second result reflects the symmetry property noted above. In particular it should be also observed at $T \rightarrow 0$. In order to obtain the ordered state at $T = 0$ it necessary to use the spontaneous symmetry violation (i.e. a weak magnetic field)[].

The approximation of averaged field

Let us introduced the averaged magnetic field:

$$H = -J \sum_{\langle i, j \rangle} s_i s_j - h_0 \sum_{i=1}^N s_i \Rightarrow -\sum_{i=1}^N s_i h_i,$$

where

$$h_i = h_0 + J \sum_{j=1}^z s_j^{(i)}$$

is the magnetic field created by z -nearest neighbors. If ($z \gg 1$), the values (8) can be approximated by the averaged expression:

$$J \sum_{j=1}^z s_j^{(i)} \Rightarrow zJ \langle s_i \rangle.$$

With the same accuracy:

$$h_i \Rightarrow h = h_0 + zJ \langle s_i \rangle. \quad (29)$$

In this approximation the statistical sum (23) transforms to:

$$Z \approx \sum_{\{s_i\}} \exp(\beta h \sum_{i=1}^N s_i) \Rightarrow \left(\sum_{s_1=\pm 1} \exp(\beta h s_1) \right)^N. \quad (30)$$

Since

$$\sum_{s_1=\pm 1} \exp(\beta h s_1) = 2ch(\beta h),$$

then the statistical sum takes the view:

$$Z \approx 2^N (ch(\beta h))^N. \quad (31)$$

The free energy per one spin equals to:

$$f = -\frac{k_B T}{N} \ln Z \Rightarrow -k_B T \ln(ch(\beta h)). \quad (32)$$

The averaged value of the magnetization per one lattice site: $m = \langle s_i \rangle$ and the free energy f should satisfy the thermodynamic identity [4,18]:

$$m = -\frac{\partial f}{\partial h_0}, \quad (33)$$

or in more details

$$m = th\beta h \Rightarrow th \frac{1}{t} \left(\frac{1}{t} + m \right) \tilde{h}_0 = h_0 / T_*. \quad (34)$$

Here

$$t = \frac{T}{T_*}, \quad T_* = \frac{zJ}{k_B},$$

has meaning of dimensionless temperature. In fact, the equation (15) can be considered as the equation of state for the magnetization.

In dependence of h_0 it leads to one, two or three solutions.

In particular, if $h_0 = 0$, the equation

$$m = th \left(\frac{m}{t} \right) \quad (35)$$

leads to the roots:

$$m(t) = \begin{cases} 0, & t > 1, \\ m_1 = 0, \quad m_{2,3} = \pm m_s, & t < 1. \end{cases} \quad (36)$$

The point

$$\left(\frac{1}{t}, h_c \right) \equiv \left(\frac{1}{t}, 0 \right), \quad (37)$$

corresponding to $t=1$ can be considered as **the critical point** for the spin subsystem of a ferromagnetic. In accordance with (17) the magnetization $m(t=1, h_0=0)=0$ at the critical point.

The magnetization near the critical point

Since $thx = x - \frac{1}{3}x^3 + \dots$, $x \ll 1$, the equation (17) near the critical point takes

the view:

$$m(t, h_0) = \frac{1}{t} \left(m_0 + m(t, \tilde{h}_0) \right) - \frac{1}{3} \frac{1}{t^3} \left(m_0 + m(t, \tilde{h}_0) \right)^3 + \dots \quad (38)$$

In zeroth magnetic field we get:

$$m \left(\tau + \frac{1}{3} m^2 + \dots \right) = 0. \quad (39)$$

where $t = 1 + \tau$ or $\tau = \frac{T - T_c}{T_c}$. Thus, the equilibrium values of the

magnetization are equal to:

$$m_1=0, \quad m_{2,3} = \pm\sqrt{-3\tau(1+\dots)}, \quad \tau < 0. \quad (40)$$

The equation

$$-\tilde{h}_0 + m\tau + \frac{1}{3}m^3 + \dots = 0 \quad (41)$$

is the generalization of (20) for $h_0 \neq 0$. It leads to the Landau free energy [4]

$$f_L(\tau, \tilde{h}_0, m) = -\tilde{h}_0 m + \frac{1}{2}am^2 + \frac{1}{4}am^4 + \dots, \quad a = \frac{1}{3}, \quad (42)$$

the minimization of which with respect to the magnetization generates the equation (22).

The linear totality, for which

$$h = 0 \quad \text{and} \quad \left. \frac{\partial h}{\partial m} \right|_{\tilde{m}=0} = 0, \quad (43)$$

corresponds to the system spinodal.

2.3. Landau potential for a simple liquid

In this Section we will show that the Landau potential for simple liquid in the vicinity of its critical point takes the same view as for magnetic.

The position of the critical point in liquid is determined by the equations [4]:

$$\left. \frac{\partial P}{\partial n} \right|_{T_c} = 0, \quad \left. \frac{\partial^2 P}{\partial n^2} \right|_{T_c} = 0, \quad (44)$$

and the additional condition:

$$\left. \frac{\partial^3 P}{\partial n^3} \right|_{T_c} < 0. \quad (45)$$

Considering the pressure as a function of the reduced temperature $\tau = \frac{T - T_c}{T_c}$

and density $\varphi = \frac{n - n_c}{n_c}$, we get the following expansion, satisfying to (25) and

(26):

$$P = P_c + q\tau + \alpha\tau\varphi + \gamma\tau\varphi^2 + a\varphi^3 + , \quad (46)$$

The corresponding Landau thermodynamic potential equals to

$$f_L = -h\varphi + \frac{1}{2}\alpha\tau\varphi^2 + \frac{1}{3}\gamma\tau\varphi^3 + \frac{1}{4}a_4\varphi^4, \quad h = P - P_c - q\tau. \quad (47)$$

The Landau free energy (28) for a simple liquid differs from that (23) for ferromagnetic by the contribution $\frac{1}{3}\gamma\tau\varphi^3$, non-invariant about the transformation: $\varphi \rightarrow -\varphi$. Near the critical point its role is small since the coefficient at φ^3 tends to zero. Due to this the Landau free energy of simple liquid is equivalent to that for the simplest magnetic.

At the same time the weak non-invariance about the transformation $\varphi \rightarrow -\varphi$ leads to the specific effect – the weak asymmetry of the branches for binodal and spinodal:

$$\varphi_{\pm}^{(s)} = \pm \left(-\frac{\alpha\tau}{3a_4} \right)^{1/2} - \frac{\gamma}{3a_4}\tau + \dots \quad (48)$$

2.4. Similarity of water-protein solutions and paramagnetics

In the Section **I2** it had been noted that the ZP near the peculiar point $T_H = 42^\circ C$ behaves itself similarly to the magnetization near its critical point.

In the theory of phase transitions the magnetization is accepted to name by the order parameter. The last is designated as φ . Its dependence on temperature and magnetic field is determined by the Landau thermodynamic potential (fluctuation effects have separate interest):

$$f_L(\tau, h, \varphi) = -h\varphi + \frac{1}{2}\tau\varphi^2 + \frac{1}{4}a\varphi^4 + \dots, \quad (49)$$

where $\tau = \frac{T - T_p}{T_p}$, and the characteristic temperature T_p coincides with the Curie-

Weiss critical one, h takes the same sense as \tilde{h}_0 (see (15)).

The behavior of φ is determined from the minimum of the Landau thermodynamic potential. It is reduced to the equation:

$$\frac{\delta f_L(\tau, h, \varphi)}{\delta \varphi} = 0 \Rightarrow -h + \tau\varphi + a\varphi^3 + \dots = 0 \quad (50)$$

At the absence of magnetic field:

$$\varphi(\tau) = \begin{cases} 0, & \tau > 0, \\ \pm \sqrt{-\tau/a}, & \tau < 0. \end{cases}$$

Due to similarity in the behavior of the magnetization and the ZP, the last will be also identified with the order parameter φ . We also accept that the corresponding Landau potential takes the view (4.1) and the characteristic temperature T_p coincides with the peculiar point $T_p = T_H = 315K$ ($42^\circ C$). In accordance with (4.3) it leads to the temperature dependence of the ZP:

$$\zeta(\tau) = \begin{cases} 0, & \tau > 0, \\ \pm \sqrt{-\tau/a}, & \tau < 0. \end{cases} \quad (51)$$

Comparing the branch

$$\zeta(\tau) = -\sqrt{-\tau/a}, \quad (52)$$

with temperature dependence of the ZP in [] we can find the coefficient a .

The role of the magnetic field in (4.1) plays the difference of the pH - factors:

$$h = pH - pH_0. \quad (53)$$

The analog of (5) with good accuracy takes view []:

$$\zeta(h) \approx th\beta \left(pH - pH_0 \right) \quad \beta = T_*/T. \quad (54)$$

CONCLUSIONS

1. In the work it is shown that the temperature dependence of the zeta-potential for the albumin macromolecule near the temperature T_H of the dynamic phase transition in ordinary water is similar to that for the magnetization in the vicinity of the Curie-Weiss critical point for the simplest magnets;
2. It had been concluded that the ZP can be considered as the order parameter for the Landau thermodynamic potential having the same structure as for the simplest magnets near their Curie-Weiss critical points;
3. To guarantee the similarity of magnetic and polarization properties we conclude the difference $pH - pH_0$ of the pH - index takes the sense of the field conjugated to the order parameter, i.e. is the analogue of the magnetic field for magnets;
4. Assuming that the similarity of magnetic and polarization properties has place not only near their peculiar points, but also in the large enough range enveloping the temperature T_H of the dynamic phase transition, we get the relation:

$$\zeta = th\kappa(pH - pH_0), \quad (C)$$

observed experimentally;

5. The physical meaning of pH_0 is established. This value corresponds to the number $z_{H^+} = 0.72$ of hydrogen ions attached to the albumin macromolecule. The iso-electrical point arises if this charge is compensated by negative charges of ions Cl^- ;
6. The applicability region for the relation (C) is investigated. It is shown that deviations of the experimental values of ZP from those giving by the expression (C) do not exceed 30%.

Author's signature _____

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SUMMARY

Zhang Wei. «pH as an indicator of phase transitions in water-protein solutions » - Thesis to obtain a master's degree in specialty 104 – physics and astronomy. Odesa I. I. Mechnicov National University. - Odesa, 2024

The research of the master's thesis is devoted to the study of the changes in the main properties of blood depending on the pH-index value. The basic component of blood - an aqueous solution of albumin (the main protein of its plasma) was taken as the object of the study. Some electrophysical properties of protein macromolecules are more adequately described using the so-called zeta potential. This is a local characteristic of electric fields inside and outside macromolecules. In contrast, the pH index is a global characteristic of ion distribution. In this situation, establishing the relationship between the potential and the index is a very important issue. His experimental research showed that the corresponding equation takes the form of a hyperbolic tangent characteristic of paramagnets.

The paper concludes that the zeta potential can be considered as an order parameter for the Landau thermodynamic potential, which has the same structure as for the simplest magnets near their Curie-Weiss critical points, and shows its relationship with the number of ions attached to the macromolecule and pH index.

Key words: water, proteins, albumin, zeta-potential solutions, pH-index.

АНОТАЦІЯ

Чжан Вей. «pH as an indicator of phase transitions in water-protein solutions» - Кваліфікаційна наукова робота на правах рукопису. Робота на здобуття наукового ступеня магістра за спеціальністю 104-фізика та астрономія. Одеський національний університет імені І.І. Мечникова. Одеса, 2024.

Дослідження магістерської роботи присвячено важливій проблемі зміни головних властивостей крові в залежності від показника рН. За об'єкт дослідження взято базовий компонент крові – водний розчин альбуміну (головного протеїну її плазми). Деякі електрофізичні властивості макромолекул протеїну більш адекватно описуються за допомогою так званого дзета-потенціалу. Це локальна характеристика електричних полів усередині та поза макромолекулами. На відміну від нього, рН-індекс є глобальною характеристикою розподілу іонів. У цій ситуації встановлення взаємозв'язку між потенціалом та індексом є дуже важливим питанням. Його експериментальне дослідження показало, що відповідне рівняння набуває вигляду характерного для парамагнетиків – гіперболічного тангенсу.

У роботі роблено висновок, що дзета-потенціал можна розглядати як параметр порядку для термодинамічного потенціалу Ландау, який має таку саму структуру, як і для найпростіших магнітів поблизу їх критичних точок Кюрі-Вейса, та показано його зв'язок з кількістю приєднаних до макромолекули іонів та рН-індексом.

Ключові слова: вода, протеїни, альбумін, розчини дзета-потенціал, рН-індекс.