PHYSICAL SCIENCES

MATHEMATICAL EXPRESSION OF THE THEORY OF MULTIPHASE SYSTEMS

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Abstract

A deeper study of many biological processes occurring in the body and the metabolism of substances transported by blood is one of the urgent issues facing biophysical science. In order to study these processes in depth, the requirements imposed by the food, pharmacological and medical industries on the separation and purification of mixtures of biological particles in order to study each of their components separately are constantly increasing. Therefore, a number of special methods have recently been developed for the purification of biological substances. The most effective, simple and economically viable method for the separation and purification of biological materials is the method of uneven distribution of substances in water-polymer two-phase systems. The requirements for the purification and separation processes of biological materials force this method to be further improved. It is obvious that the results obtained for two-phase systems are also used for various purposes. Thus, the results obtained allow us to understand the mechanism of the distribution of substances in biological systems and lead to the idea of viewing a living organism as a multiphase system in equilibrium with each other. In the presented work, an attempt was made to improve the method of uneven distribution of substances in water-polymer two-phase systems and to apply this theory to multiphase systems. At the same time, a mathematical expression for multiphase systems was obtained based on the mathematical expression used for two-phase systems and obtained from experiments. Finally, the advantages of this new method were emphasized.

Keywords: Biological processes, water-polymer two-phase systems, multiphase systems, partition coefficient, non-uniform distribution method.

İnstroduction. The process of separating and purifying any substances, including biologically active substances themselves and their components, from mixtures is a difficult process requiring great sensitivity, and the requirements placed on this area by the food, pharmacological and medical industries are constantly increasing. The numerous methods available for the separation and purification of chemical substances are not suitable for the purification of biological substances, and biological materials, as they are easily denatured under the influence of various factors, lose their biological activity. Therefore, a number of special methods have recently been developed for the purification of biological substances. However, these methods are very complex and relatively expensive. Recently, a simple, inexpensive and effective method for the separation and purification of biological materials has been developed - the method of uneven distribution of substances in two-phase water-polymer systems. This method is based on the separation of a mixture of aqueous solutions of two polymers with different chemical properties into two phases at a certain value of the concentration of the components. At the end of the 19th century, Bayerik observed that mixtures of aqueous solutions of gelatin with aqueous solutions of both agar and starch separated into two phases at certain values of the concentration of the components. (Figure1) [1].

Figure 1.

This experimental fact, which remained unnoticed by experts, attracted the attention of scientists again 40 years later when studying the compatibility (or incompatibility) of polymer pairs in a common solvent. When studying phase equilibria in polymer-water systems, Dobri found that only 4 out of 35 pairs of polymers formed homogeneous solutions [6]. Studies of water-soluble polymers have shown that phase separation is a common phenomenon in such systems. It should be noted that phase separation is observed not only when two polymers are dissolved in a common solvent, but also in mixtures of solutions of one polymer with organic or inorganic salts. Polymer-water two-phase systems formed by various types of polymers were first systematically re-examined by the Swedish scientist Albertson [3,4]. Albertson's monograph showed a large number of different polymer pairs forming two-phase systems. After the publication of this monograph, it attracted the attention of biologists and biochemists, who saw that the method of uneven distribution of these substances in two-phase aqueous polymer systems would be a highly effective method for the separation and purification of various biological materials. Note that the solvent in the phases is water and constitutes the basis of both phases (~70-95%). When a mixture of proteins or cells is introduced into this type of two-phase system, one protein and cell accumulate more in one phase and less in the other [2]. Such uneven distribution is due to the individual properties of the biological particles and the distribution conditions (nature of polymers, concentration, additives, etc.). In some cases (this can be called an ideal case), when distributing a mixture of several types of proteins in two-phase systems, all of the mentioned proteins accumulate in one phase, and the rest in the other phase. Given that the solvent in both phases of the system is water, proteins, nucleic acids, viruses, cells, various cell organelles, etc. can be separated and purified in this system. These objects are unevenly distributed in a two-phase aqueous polymer system without losing their intact properties [6]. It should be noted that any unstable (sensitive) biological materials are not damaged and do not lose their biological activity when distributed in such a two-phase polymer-water system. Any pair of natural and synthetic polymers can be used to create two-phase water-polymer systems. Currently, the most widely used polymer pair to create two-phase systems in the world is dextran-polyethylene glycol [8]. These polymers are artificial blood substitutes. One of the most important advantages of the method of distribution in water-polymer two-phase systems (compared to other methods used for separating and purifying biological objects) is that this method can be implemented seamlessly from laboratory to industrial conditions and using simple equipment. It should be noted that recently, in addition to the purification of biological particles, two-phase systems have also been used for the analytical analysis of natural compounds. Calculations show that the distribution and purity control of biological substances, including drugs, in two-phase water-polymer systems is approximately 3-5 times cheaper than ultrafiltration and other existing methods [2].The widespread application of the distribution method in two-phase water-polymer systems in industry, despite all its advantages, has been hampered for many years as a result of the formation of two-phase systems and the incomplete understanding of the mechanisms of distribution of substances in these systems. Due to the lack of a scientific basis for the method, the solution of all technological issues, the selection of phase-forming polymers, etc. was carried out empirically. It should be noted that in all the various two-phase systems selected and used in practice, the phase separation medium is water, and one of the components forming the system is of a macromolecular nature. We have noted that the main medium carrying substances in these systems is water. Analysis of the results obtained from experiments shows that a pair of polymers with different chemical natures are more compatible. This contradicts the generally accepted rule that substances dissolve better in substances similar to themselves. This contradiction shows that in order to understand the incompatibility of two polymers, that is, the mechanism of phase separation, it is necessary to take into account all the specific interactions of the polymers with each other and with the solvent of any of them [8]. Let us touch on some characteristics of two-phase systems. As we have seen, water-polymer two-phase systems resemble blood-tissue fluid, blood-lymph, etc. systems, that is, they can be considered as their models. Note that in such a system, the distribution coefficient (k) of the substance is determined by the ratio of its concentrations in the phases (C1 , C2) (Fig. 2) [1,5]:

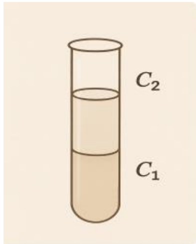


Figure 2.

$$k = \frac{C_1}{C_2} \qquad (1)$$

Since the free energy of phase transition of a substance is small compared to the energy of thermal motion, if we use the Bolsmann distribution and the equality of the chemical potentials of the components of the phases, we can calculate the distribution coefficient

$$k = \frac{C_1}{C_2} = e^{-\frac{\Delta G}{kT}} \qquad (2)$$

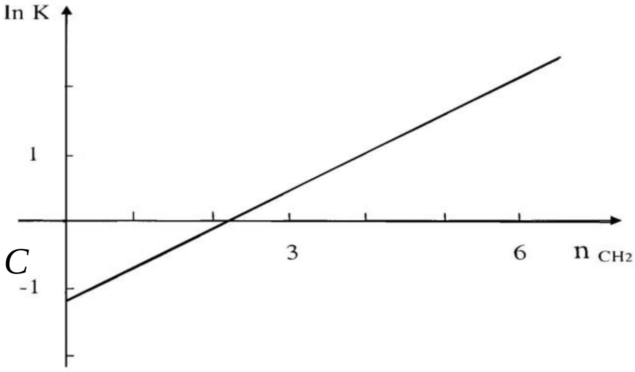
We can write it as. From here, for the logarithm of the distribution coefficient

$$\ln k = -\frac{\Delta G}{RT} \qquad (3)$$

and for the free energy of interphase transition,

$$\Delta G = -RT \ln k \qquad (4)$$

We can write the expression. As can be seen, lnk-can characterize the relative hydrophobicity or water avidity of the substance. The distribution coefficient of some marker substances from the same homologous series in a two-phase system depends on the number of CH2 groups (n_{CH_2}) The dependence is shown in the figure. As can be seen from the figure $\ln K$ □ n_{CH_2} addiction



Şəkil 3. Dependence of the logarithm of the partition coefficient in two-phase systems on the number of CH2 groups in amino acids lnK~ n(CH2)

$$\ln K = C + E \cdot n_{CH_2} \quad (5)$$

is described by the linear equation. Here, the physical meanings of E and C are the constants known below. If we multiply each side of equation (5) by RT

$$RT \ln K = RTC + RTE \cdot n_{CH_2} \quad (6)$$

we get. According to (4) $RT \ln k = -\Delta G$ Considering that in (6)

$$\Delta G^{mad}_{II \to I} = -RTEn - RTC \quad (7)$$

can be. E-is the free energy of the transition. These results obtained for two-phase systems are successfully used for various purposes. Thus, the results obtained allow us to understand the mechanism of distribution of substances in biological systems and lead to the idea of viewing a living organism as a multiphase system in equilibrium with each other. It should be noted that the distribution of substances between the blood and tissues of the body corresponds to the distribution of substances, for example, between the phases of multiphase systems. Taking into account the importance of two-phase systems and the advantages of the method of unequal distribution in Water-Polymer two-phase systems and using some theories, it is possible to improve this method. The organism is a very complex system that is multiphase, multicomponent, and in equilibrium with each other[2]. Therefore, there will be many advantages to using multiphase systems. These advantages will mainly be time saving and a reduction in the error rate. In the metabolic process of a living organism, substances are constantly transported from the membrane in one direction or another due to the concentration gradient. There is a continuous transport of substances from the cell environment through the double membrane into the cell, and then to the cell organelles - the nucleus, mitochondria, ribosomes, and the Holci complex. The transported substance is then distributed in a multiphase system, and its concentrations in the phases can be represented as C1, C2,, C3, and C4. As we mentioned above, if we take into account that water plays the main role in the transport of substances and based on the Flory-Huggins theory, we can say that the energies spent on the entry and exit of substances will be equal: E = -E. Taking into account these things, it is possible to simplify the model of a multiphase system. It is convenient to study the processes occurring in such systems by modeling them. Thus, living organisms can be viewed as multiphase, multicomponent systems, and the processes occurring there occur analogously to the processes occurring in multiphase systems. As we know, equation (6) is satisfied only for two-phase systems. Therefore, it is necessary to simplify the mathematical expression characterizing multiphase systems in such a way that equation (6) is satisfied for them as well. For this, let us treat the phases with concentrations C1, C2, C3 as the general 1st phase, and the last phase with concentration C4 as the 2nd phase. Let us denote the general concentration of the 1st phase we have adopted by C'. The only problematic issue will be to find the value of the concentration C'. We can reduce the existing problem by taking the value of the concentration C' as the numerical average of these three concentrations (Figure 4).

$$C' = \frac{C_1 + C_2 + C_3}{3} \quad (8)$$

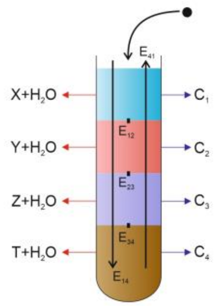


Figure 4

Since we analyze multiphase systems as two-phase systems based on this model, equation (5) will be satisfied.

$$\ln K_{14} = RTC + RT \cdot n_{CH_2} E_{14} \quad (9)$$

Since matter expends energy each time it transitions to a new phase, the total transition energy will be equal to the sum of these energies:

$$E_{14} = E_{12} + E_{23} + E_{34} \quad (10)$$

The graph of linear equation (9) will be as shown in Figure 3. Taking this into account, we can write equation (6) for the multiphase system under consideration.

$$RT \ln K_{24} = RTC + RT \cdot n_{CH_2} \cdot E_{14}$$

$$RT \ln \frac{C'}{C_4} = RTC + RT \cdot n_{CH_2} \left(E_{12} + E_{23} + E_{34}\right) \quad (11)$$

Considering expression (8) in (11),

$$RT\ln = \frac{C_1 + C_2 + C_3}{3C_4} = RTC + RT \cdot n_{CH_2}\left(E_{12} + E_{23} + E_{34}\right)$$

is obtained. Of course, the organism is very complex, that is, it cannot be limited to 4 phases. Therefore, it is necessary to generalize this expression for a system with an arbitrary number of phases. Taking into account the above facts and the sequence in expression (12), we obtain:

$$RT\ln = \frac{C_1 + C_2 + ... + C_{n-1}}{(n-1)C_n} = RTC + RT \cdot n_{CH_2}\left(E_{12} + E_{23} + ... + E_{(n-1)n}\right)$$

The last mathematical expression we obtained is an analytical expression of the uneven distribution of substances in multiphase systems.

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