

The Solution of Stiff Integro-Differential Problem of Isoelectric Focusing by the Tangent Method

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Abstract: The paper reports on the development of the methods for approximate analytical solution of stiff integro-differential problem on the example of modelling Isoelectric Focusing (IEF) in so-called 'anomalous' modes. While working on the model the integro-differential problem was analytically transformed to a compact form suitable for investigating by asymptotic methods. The asymptotic solution by applying the tangent method was obtained, allowing high accuracy approximation of concentration profiles of polygonal curves with the given parameters.

Key words: Stiff integro-differential problem . tangent method

INTRODUCTION

Isoelectric Focusing (IEF) is one of most effective and universal modern methods for protein characterization and fractionation. IEF has been widely used in many fields of modern chemistry and biology. The method is based on the ability of biopolymers or their fragments to form charged molecular complexes [1]. During one-dimensional IEF a mixture of ampholytes (amphoteric aminoacids having high buffer capacity) is placed in the electrophoretic chamber (EC) (the cylinder with length l and radius r). When exposed to one-dimensional IEF the pH gradient is formed ($\text{pH} = -\lg H$, where H is concentration of hydrogen ions H^+), with the fractionated components for certain fixed values of pH determined by their electrochemical properties having zero migration rate and being concentrated in the corresponding regions of EC. It is known as a stationary distribution of ampholytes. The distribution of ampholytes is invariable in any axial section of EC during one-dimensional IEF. The classical theory of electrophoresis the analytical concentrations of ampholytes are used to describe the system. Their graphs are called the ampholyte concentration profiles.

The founders of the mathematical theory of IEF built a basic mathematical model according to which the distribution of ampholyte concentration is determined by the Gaussian distribution density [2-8]. Many foreign researchers obtained the Gaussian distribution of ampholyte concentrations by the computer simulation of IEF [8-12]. On the other hand, they observed a distortion of the Gaussian distribution [10-14] which was called the 'anomalous' modes of IEF [15-17] (Fig. 1).

Using complex mathematical modeling of the IEF-systems by means of methods of mathematical physics [15-17] it was found that nonstationary boundary value problem becomes stiff at high current densities due to the presence of a small parameter in front of the derivatives. As a result the system enters the 'anomalous' mode. In the normal mode with the increase of the current density, a Gaussian curve of the concentration profile is stretched vertically and when it enters 'anomalous mode' its maximum seems to be limited by some kind of a graphical "ceiling" which limits its further growth and deforms it as the current density increases. At first the so called "plateaus" appear on tops of the curves, then the concentration profile takes the form of a rectangle or trapezoid.

Therefore, the questions arise: what is the mathematical interpretation of this phenomenon? How can one calculate the geometric parameters of the trapezoid (rectangles) into which initial Gaussian curves are transformed? The aim of the present investigation is to answer these questions.

Physical and mathematical formulation of the problem. The aqueous solution of N ampholytes is placed in the EC. For each ampholyte its dissociation constants of the reactions $K_1^{(k)}$, $K_2^{(k)}$, migration coefficient μ_k as well as the initial quantities m_k , $k = 1, 2, \dots, N$ are known. When exposed to the direct current with density J in the EC a distribution of ampholyte concentration is formed, resulting in stationary distribution of hydrogen ions H concentration. The dissociation reactions of k -ampholyte are supposed to be described by the following:



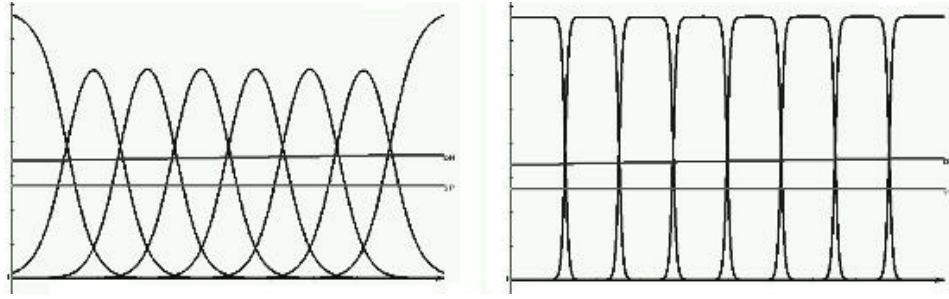


Fig. 1: Transformation of Gaussian curves to 'plateau-shaped' in 'anomalous' modes



where $\text{NH}\overset{\text{K}_1^{(k)}}{\text{R}}\text{COOH}^-$, $\text{NH}_2\text{R}\overset{\text{K}_2^{(k)}}{\text{COOH}}$ and $\text{NH}_2\text{R}\overset{\text{K}_0^{(k)}}{\text{COOH}}$ are positive, negative and neutral ampholyte ions. The molar concentration of the ions are ξ_1^k , ξ_{-1}^k , ξ_0^k . The analytical concentration of the ampholyte is: $\xi_k = \xi_1^k + \xi_{-1}^k + \xi_0^k$. In the equilibrium state the concentration of the analyzed ampholyte ions are related to their analytical concentration by the equations:

$$\xi_1^k = \alpha_1^k \xi_k \quad (3)$$

$$\xi_{-1}^k = \alpha_{-1}^k \xi_k \quad (4)$$

$$\xi_0^k = (1 - \alpha_1^k - \alpha_{-1}^k) \xi_k \quad (5)$$

where α_1^k and α_{-1}^k are the degrees of ampholyte dissociation. From reactions (1)-(2) based on the theory of the kinetics of electrochemical reactions we obtain: $\xi_0^k \text{H} = \text{K}_1^{(k)} \xi_1^k$, $\xi_{-1}^k \text{H} = \text{K}_2^{(k)} \xi_0^k$, where H is the concentration of hydrogen ions. Their transformation on account of (3)-(4) allows one to derive the formulas expressing the degree of ampholyte dissociation through its dissociation constant and the concentration of hydrogen ions:

$$\alpha_1^k = \text{H}^2 (\text{K}_1^{(k)} \text{K}_2^{(k)} + \text{K}_1^{(k)} \text{H} + \text{H}^2)^{-1} \quad (6)$$

$$\alpha_{-1}^k = \text{K}_1^{(k)} \text{K}_2^{(k)} (\text{K}_1^{(k)} \text{K}_2^{(k)} + \text{K}_1^{(k)} \text{H} + \text{H}^2)^{-1} \quad (7)$$

In addition to these reactions of ampholyte dissociation in aqueous solution the reaction of water autoprotolysis should be taken into account: $\text{H}_2\text{O} \Leftrightarrow \text{OH}^- + \text{H}^+$. For the mathematical description of the system, the following functions are used [18-20]: 1) ξ_k , $k = 1, 2, \dots, N$, analytical concentration of ampholytes (i.e. total concentrations of their positive, negative and

neutral ampholyte ions); 2) H, the concentration of hydrogen ions; 3) OH, the concentration of hydroxyl ions OH^- , connected with H by means of standard equation $\text{OH}^- = k_w^2 / \text{H}$, where $k_w^2 = 10^{-14}$ is a constant of water auto-dissociation; 4) E, electric field intensity. The above functions are the solutions of the one-dimensional problem, consisting of N+1 differential equations, one algebraic equation and N integral equations, replacing the boundary conditions:

$$-\varepsilon \frac{d\xi_k}{dx} + \xi_k (\alpha_1^k - \alpha_{-1}^k) E = 0, k=1, 2, \dots, N \quad (8)$$

$$J = \sum_{k=1}^N \left(-D_k \frac{d}{dx} ((\alpha_1^k - \alpha_{-1}^k) \xi_k) + \mu_k (\alpha_1^k + \alpha_{-1}^k) \xi_k E \right) - D_H \frac{dH}{dx} + \mu_H H E + D_{OH} \frac{d(OH)}{dx} + \mu_{OH} OH E \quad (9)$$

$$\sum_{k=1}^N (\alpha_1^k - \alpha_{-1}^k) \xi_k + \text{H} - \text{OH} = 0 \quad (10)$$

$$\pi a^2 \int_0^l \xi_k(x) dx = m_k \quad (11)$$

where $\varepsilon = RT/F$ is the standard electrochemical parameter (values R, T, F-absolute gas constant, temperature and Faraday constant, respectively; μ_H and μ_{OH} are the constants characterizing the mobility of ions H^+ and OH^- ; D_k , D_H and D_{OH} are the constants for diffusion coefficients of the ions, $D_k = \varepsilon \mu_k$.

The differential equations (8) are the equation of mass transport. The differential equation (9) is the Ohm's generalized law with the diffusion (the current density is the sum of the current densities of all the ions, including both hydrogen and hydroxyl ions). The algebraic equation (10) is the charge balance equation. Finally, integral equations (11) correspond to the mass conservation law (the total quantity of all forms of the ampholyte is constant and equal to m_k , $k = 1, 2, \dots, N$). The main mathematical difficulty of numerical integration of the system (8)-(11), which was called

integro-differential problem of IEF [15-17], is the necessity to determine the value H from the the implicit function (10) to solve differential equations (8). The author have transformed the system and managed to overcome this problem.

The analytical transformation of the system. Theorem 1. The system of equations (8)-(11) with reference to N+2 unknown functions H, E, $\xi_k(x)$, $k = 1, 2, \dots, N$, may be reduced to the boundary value problem with reference to N unknown functions $c_k(x)$, $k = 1, 2, \dots, N$:

$$\varepsilon \frac{dc_k}{dx} \frac{1}{c_k} = \frac{\phi'_k(\psi) J}{\phi_k(\psi) \sigma} \quad (12)$$

$$\sigma = \sum_{k=1}^n \mu_k c_k \left(\phi''_k(\psi) - \frac{(\phi'_k(\psi))^2}{\phi_k(\psi)} \right) + 2k_w \mu \operatorname{ch}(\psi - \psi_0) \quad (13)$$

$$\sum_{k=1}^n c_k \phi'_k(\psi) + 2k_w \operatorname{sh} \psi = 0 \quad (14)$$

$$\phi_k(\psi) = \delta_k + \operatorname{ch}(\psi - \psi_k) \quad (15)$$

$$\int_0^1 c_k(x) \phi_k(\psi) dx = M_k, M_k = \frac{m_k}{2\pi a^2} \quad (16)$$

The old and new unknown functions are connected by the relation:

$$\xi_k(x) = c_k(x) \phi_k(\psi) \quad (17)$$

$$H = k_w \exp(\psi) \quad (18)$$

Proof: At the first stage of the proof the new function ψ was introduced and considered, defined by the equation (def. as (18)): $H = k_w \exp(\psi)$. To simplify the equations new constants are introduced:

$$\psi_k = \frac{1}{2} \ln \left(K_1^{(k)} K_2^{(k)} / k_w^2 \right) \quad (19)$$

$$\delta_k = \frac{1}{2} \sqrt{K_1^{(k)} / K_2^{(k)}} \quad (20)$$

$$\psi_0 = \frac{1}{2} \ln (\mu_{OH} / \mu_H) \quad (21)$$

$$\mu = \sqrt{\mu_H \mu_{OH}} \quad (22)$$

In the new notation, the functions involved in (8)-(10), have taken the form:

$$e_k = \alpha_1^k - \alpha_{-1}^k = \operatorname{sh}(\psi - \psi_k) (\delta_k + \operatorname{ch}(\psi - \psi_k))^{-1} \quad (23)$$

In addition

$$\sigma_k = \alpha_1^k + \alpha_{-1}^k = \operatorname{ch}(\psi - \psi_k) (\delta_k + \operatorname{ch}(\psi - \psi_k))^{-1}$$

Besides, new functions and new current density are introduced: $\xi_k = 2k \xi_k^{\text{new}}$, $J = 2k J^{\text{new}}$. Now the system (8)-(10) can be rewritten as follows:

$$-\varepsilon \frac{d\xi_k^{\text{new}}}{dx} + \xi_k^{\text{new}} e_k E = 0 \quad (24)$$

$$J^{\text{new}} = \sum_{k=1}^N \mu_k \left(-\varepsilon \frac{d}{dx} (e_k \xi_k^{\text{new}}) + \sigma_k \xi_k^{\text{new}} E \right) + (-\varepsilon \nabla \psi + E) \mu \operatorname{ch}(\psi - \psi_0) \quad (25)$$

$$\sum_{k=1}^N e_k \xi_k^{\text{new}} + \operatorname{sh} \psi = 0 \quad (26)$$

At the second stage of the proof to the simplify the system, the new functions $\phi_k(\psi)$ are considered (def as (15)); then, $e_k = \phi'_k(\psi) (\phi_k(\psi))^{-1}$, $\sigma_k = \phi''_k(\psi) (\phi_k(\psi))^{-1}$. Let us represent the functions $\xi_k(x)$ as the product of the functions $\phi_k(\psi)$ by new unknown functions c_k^{new} : $\xi_k^{\text{new}}(x) = c_k^{\text{new}} \phi_k(\psi)$. With new variables the system of equations (24)-(25) takes the compact form, from which factor $(-\varepsilon \psi'_x + E)$ is excluded:

$$\varepsilon \frac{dc_k^{\text{new}}}{dx} \frac{1}{c_k^{\text{new}}} = \frac{\phi'_k(\psi) J^{\text{new}}}{\phi_k(\psi) \sigma^{\text{new}}} \quad (27)$$

$$\sigma^{\text{new}} = \sum_{k=1}^N \mu_k c_k^{\text{new}} \left(\phi''_k(\psi) - \frac{(\phi'_k(\psi))^2}{\phi_k(\psi)} \right) + \mu \operatorname{ch}(\psi - \psi_0) \quad (28)$$

The equation (26), in its turn, with new variables takes the form:

$$\sum_{k=1}^N c_k^{\text{new}} \phi'_k + \operatorname{sh} \psi = 0 \quad (29)$$

At the third stage of the proof let us return to the old analytical concentration $\xi_k = 2k_w \xi_k^{\text{new}}$ and the old current density $J = 2k_w J^{\text{new}}$. In accordance with (17) we introduce the new function $c_k(x)$, so that $\xi_k(x) = c_k(x) \phi_k(\psi)$. On account of $c_k^{\text{new}} = c_k / 2k_w$ as well as $\sigma^{\text{new}} = \sigma / 2k_w$, the system of equations (27), (28), (29) takes the form of (12), (13), (15) and integral condition (11)-the form of (17) Δ .

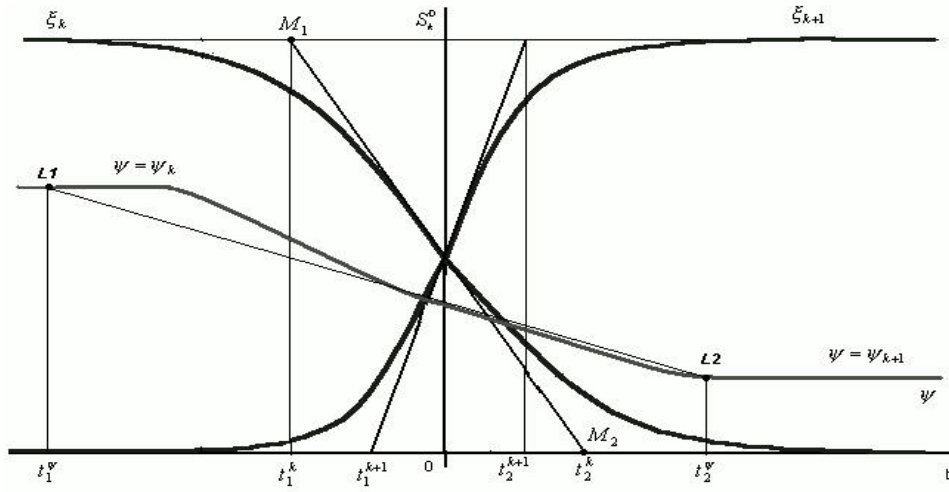


Fig. 2: The tangent to the profiles of two neighbouring ampholytes at the point of their intersection

Investigation of the system by tangent method. To solve the problem we used the tangent method which is based on the tension of a graph along the coordinate abscissa axis by replacing the variable: $t = x/\varepsilon$ (ε is a small value). The abscissa corresponding to the point of intersection of k and $k+1$ ampholyte profiles was taken as a new origin of coordinates (Fig. 2).

$$\xi_k(0) = \xi_{k+1}(0) \quad (30)$$

In the new coordinates the following assumptions are taken for the unknown functions:

$$\xi_k(-\infty) = S_k^0 \quad (31)$$

$$\xi_k(+\infty) = 0 \quad (32)$$

$$\xi_{k+1}(-\infty) = 0 \quad (33)$$

$$\xi_{k+1}(+\infty) = S_{k+1}^0 \quad (34)$$

where S_k^0 and S_{k+1}^0 are unknown parameters to be determined (parameters of IEF problem). Besides, for the function ψ the boundary conditions should be added:

$$\psi(-\infty) = \psi_k \quad (35)$$

$$\psi(+\infty) = \psi_{k+1} \quad (36)$$

where ψ_{k+1}, ψ_k are the constants to be determined.

Theorem 2: Functions $\xi_k(0), \xi_{k+1}(0)$ at $t = 0$ are defined by the equations:

$$\xi_k(t) = c_k(t)\phi_k(\psi), \xi_{k+1}(t) = c_{k+1}(t)\phi_{k+1}(\psi) \quad (37)$$

where functions $c_k(t), c_{k+1}(t)$ are determined from the boundary value problem, consisting of two differential and one algebraic equations:

$$\frac{1}{c_k} \frac{dc_k}{dt} = \frac{\phi'_k(\psi) J}{\phi_k(\psi) \sigma}, i = k, k+1 \quad (38)$$

$$\sigma = \sum_{i=k}^{k+1} \mu_i c_i (\phi_i''(\psi) - \frac{(\phi_i'(\psi))^2}{\phi_i(\psi)}) \quad (39)$$

$$c_k \phi'_k(\psi) + c_{k+1} \phi'_{k+1}(\psi) = 0 \quad (40)$$

with two initial conditions

$$c_k(0) = 0.5 S_k^0 / \phi_k(\psi(0)), i = k, k+1 \quad (41)$$

The value $\psi(0)$ in the formulas (41) is defined from algebraic equation:

$$\phi'_k(\psi(0))\phi_{k+1}(\psi(0)) + \phi'_{k+1}(\psi(0))\phi_k(\psi(0)) = 0 \quad (42)$$

Proof: At the first stage. Equations (12), (13), (14), on the basis of Fig. 2, are written for the two functions $c_k(t), c_{k+1}(t)$. At the second stage. Equation (14) under $t \rightarrow \pm\infty$, on account of (31)-(37) show that the term $2k_w \cdot \text{sh}(\psi_{k+1})$ can be neglected for being small. Consequently, equations (12), (13), (14) may be written in the form (38)-(40), in particular, the equation (40) in the general form:

$$\sum_{k=1}^n c_k \phi'_k(\psi) = 0 \quad (43)$$

The equation (43), in its turn, by the multiplication by ψ'_i , on the basis of (37), (38) and (43), we obtaine:

$$\xi_k + \xi_{k+1} = \text{const} \tag{44}$$

The conditions (30)-(34), (44) show that $S_k^0 + 0 = \text{const}, 0 + S_{k+1}^0 = \text{const}$. Consequently, in this assumption,

$$S_k^0 = S_{k+1}^0 = \text{const} \tag{45}$$

From the initial condition (30) we obtain the following equality: $2\xi_k = S_k^0$ and, consequently,

$$\xi_k(0) = \xi_{k+1}(0) = 0.5S_k^0 \tag{46}$$

At the third stage. Equations (30), (37) and (43), written for $t = 0$, provide the system of two linear homogeneous algebraic equations with reference to two unknowns $c_k(0)$ and $q_{k+1}(0)$. The system is joint if its determinant equals zero, which yields the equation (42) for determining the value $\psi(0)$. Hence, on the basis of (37) and (46) the initial conditions (41) are obtained Δ .

Now, let us draw the tangent to the profiles at the point $t = 0$ (Fig. 2). Obviously, they are set by the equations:

$$\xi_i(t) = \xi_i(0) + \xi'_i(0)t, i = k, k + 1 \tag{47}$$

$$\psi(t) = \psi(0) + \psi'(0)t \tag{48}$$

Theorem 3: In equations (47) and (48) the coefficients $\xi_k(0)$, $\xi_{k+1}(0)$ and $\psi(0)$ are determined by means of the obtained formulas (46) and (42) and slopes of the tangent are given by:

$$\xi'_k(0) = S_k^0 / \Delta t_k \tag{49}$$

$$\xi'_{k+1}(0) = -S_k^0 / \Delta t_k \tag{50}$$

$$\psi'(0) = 2\Phi_{k, k+1}(\psi(0)) / \Delta t_k \tag{51}$$

$$\Delta t_k = \frac{2\sigma}{J} \left(\frac{\Phi_k(\psi(0))}{\Phi'_k(\psi(0))} - \Phi_{k, k+1}(\psi(0)) \right) \tag{52}$$

$$\Phi_{k, k+1}(\psi(0)) = \left(\frac{\Phi'_{k+1} - \Phi'_k}{\Phi_{k+1} - \Phi_k} \right) \left(\frac{1 + \delta_k \Phi''_k}{\Phi_k^2} + \frac{1 + \delta_{k+1} \Phi''_{k+1}}{\Phi_{k+1}^2} \right) \Big|_{\psi=0} \tag{53}$$

Proof

1. Figure 2 shows that the tangent for $\xi_k(t)$ intersects the straight line $\xi = S_k^0$ at the point $M_1(t_1^k, S_k^0)$ and

abscissa axes $\xi = 0$ at the point $M_2(t_2^k, 0)$. On the basis of (47) the equality is obtained:

$$t_1^k - t_2^k = (\xi_k(-\infty) - \xi_k(+\infty))(\xi'_k(0))^{-1} \tag{54}$$

Similar relations for $\xi_{k+1}(t)$ and $\psi(t)$, on the basis of equations (47), (48) take the form:

$$t_1^{k+1} - t_2^{k+1} = (\xi_{k+1}(-\infty) - \xi_{k+1}(+\infty))(\xi'_{k+1}(0))^{-1} \tag{55}$$

$$t_1^\psi - t_2^\psi = (\psi(-\infty) - \psi(+\infty))(\psi'(0))^{-1} \tag{56}$$

We introduce the denotations

$$t_1^k - t_2^k = \Delta t_k, t_1^{k+1} - t_2^{k+1} = \Delta t_{k+1} \tag{57}$$

$$t_1^\psi - t_2^\psi = \Delta t_\psi, \psi_k - \psi_{k+1} = \Delta \psi_k \tag{58}$$

As a result, the equations (57)-(61), with the conditions (30)-(36), (45), take the form:

$$\xi'_k(0) = S_k^0 / \Delta t_k \tag{59}$$

$$\xi'_{k+1}(0) = -S_k^0 / \Delta t_{k+1} \tag{60}$$

$$\psi'(0) = \Delta \psi_k / \Delta t_\psi \tag{61}$$

Thus, the formulas (59)-(61) allow us to calculate the values $\xi'_k(0)$, $\xi'_{k+1}(0)$, $\psi'(0)$, if values Δt_k , Δt_{k+1} , Δt_ψ are known. The equation (37) shows that

$$\xi'_k(0) = (c'_k \Phi_k(\psi) + c_k \Phi'_k(\psi) \psi') \Big|_{t=0}$$

As a result, the equations (59), (60), using (38) can be given in the form:

$$S_k^0 = \Delta t_k c_k(0) \Phi'_k(\psi(0)) (J/\sigma + \Delta \psi_k / \Delta t_\psi) \tag{62}$$

$$S_k^0 = -\Delta t_{k+1} c_{k+1}(0) \Phi'_{k+1}(\psi(0)) (J/\sigma + \Delta \psi_k / \Delta t_\psi) \tag{63}$$

It is obvious, that $J/\sigma + \Delta \psi_k / \Delta t_\psi \neq 0$, otherwise magnitude S_k^0 would be zero. This means, that the system of equations (62), (63), with (76), leads to the important equality:

$$\Delta t_{k+1} = \Delta t_k \tag{64}$$

2. The equation of tangent for $\xi_k(t)$, written for the points M_1 and M_2 , gives a system of equations. Its

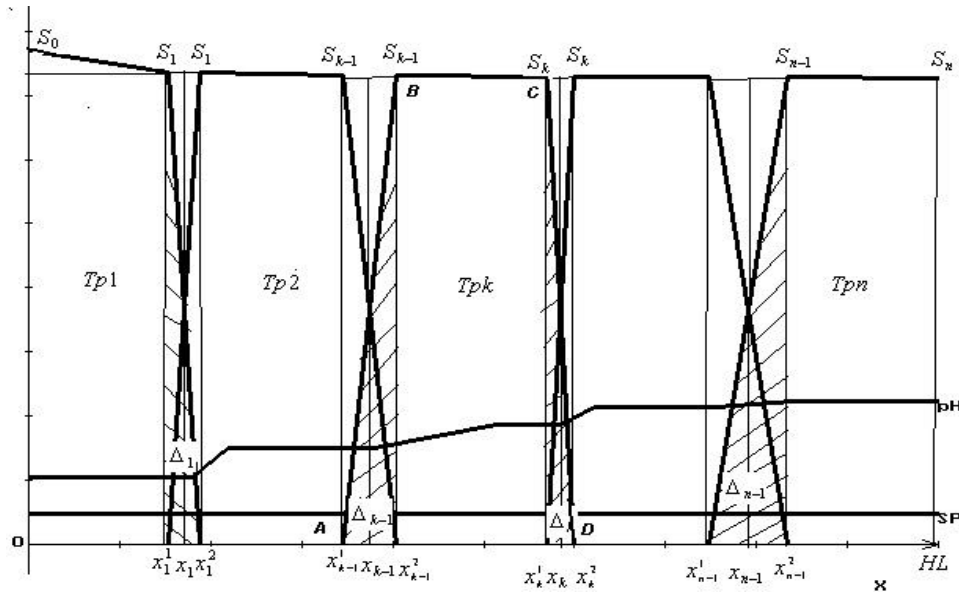


Fig. 3: Tangent approximation of the concentration profile of IEF

transformation with (44) and (58) leads to the equations:

$$t_1^k = 0.5\Delta t_k, \quad t_2^k = -0.5\Delta t_k \quad (65)$$

Similarly, the equation of tangent for $\xi_{k+1}(t)$ with (45) and (60) helps to obtain the equation:

$$t_1^{k+1} = 0.5\Delta t_k, \quad t_2^{k+1} = -0.5\Delta t_k \quad (66)$$

Consequently, $t_1^k = t_1^{k+1}, t_2^k = t_2^{k+1}$. Differentiation of (43) with (45), (59), (60) gives equation (51), (53). Substituting (51) in (62) with (41) gives equation (52).

- Figure 2 shows that tangent (48) for $\psi(x)$ intersect the straight line $\psi = \psi_k$ at the point $L_1(t_1^\psi, \psi_k)$ and straight line $\psi = \psi_{k+1}$ at the point $L_2(t_2^\psi, \psi_{k+1})$. Using the equation (48) at these points we obtain the formula:

$$t_1^\psi = 0.5\Delta t_k \frac{\psi_k - \psi(0)}{\Phi(\psi(0))}, \quad t_2^\psi = 0.5\Delta t_k \frac{\psi_{k+1} - \psi(0)}{\Phi(\psi(0))} \Delta \quad (67)$$

Let us consider the problem on the whole interval $[0,1]$. The following notations will be used: x_1 is the point of intersection of the 1st and 2nd ampholyte profiles; x_2 is the point of intersection of the 2nd and 3rd ampholyte profiles; x_{N-1} is the point of intersection of $(N-1)$ and N ampholyte profiles. Let us consider the graphical approximation of ampholyte concentration profiles by the trapezoid system (Fig. 3).

The Fig. 3 shows that k -profiles of concentration: 1) on the segment $[x_{k-1}^2, x_k^1]$ are approximated by means of a straight line passing through the points (x_{k-1}^2, S_{k-1}) and (x_k^1, S_k) ; 2) on the intervals $[x_{k-1}^1, x_{k-1}^2]$ and $[x_k^1, x_k^2]$ by means of tangents passing through the points $(x_{k-1}^1, 0)$, (x_{k-1}^2, S_{k-1}) and (x_k^2, S_k) , $(x_k^1, 0)$; 3) at all other points of the interval $[0,1]$ the concentration is assumed to be zero. The return to the initial variable x is realized on the basis of the formulas:

$$x_k^1 = x_k + 0.5\Delta t_k \cdot \varepsilon, \quad x_k^2 = x_k - 0.5\Delta t_k \cdot \varepsilon \quad (68)$$

The integral conditions (9) were applied to the functions ξ_k , $k = 1, 2, \dots, N$. Integration is realized by means of simple summation of the areas of trapezoids and leads to the following conclusion.

Theorem 4: Parameters of IEF problem S_k^0 , $k = 1, 2, \dots, N$ and x_1, x_2, \dots, x_N are determined by a system of $N+1$ linear algebraic equations:

$$\begin{cases} m_1 = \Delta x_1 \cdot S_1 + 0.5(S_0 + S_1)(x_1 - \Delta x_1) \\ m_k = \Delta x_{k-1} \cdot S_{k-1} + \Delta x_k \cdot S_k + 0.5(S_{k-1} + S_k)(x_k - x_{k-1} - \Delta x_{k-1} - \Delta x_k) \\ k = 2, 3, \dots, N-1 \\ m_N = \Delta x_{N-1} \cdot S_{N-1} + 0.5(S_{N-1} + S_N)(L - x_{N-1} - \Delta x_{N-1}) \end{cases} \quad (69)$$

and $N-1$ simplest (elementary) integral equation:

$$S_k = S_0 - 2k_w \int_0^{x_k} \text{sh}(\psi) \left(\frac{J}{\varepsilon \sigma} + \psi'_x \right) dx, \quad k = 1, N-1 \quad (70)$$

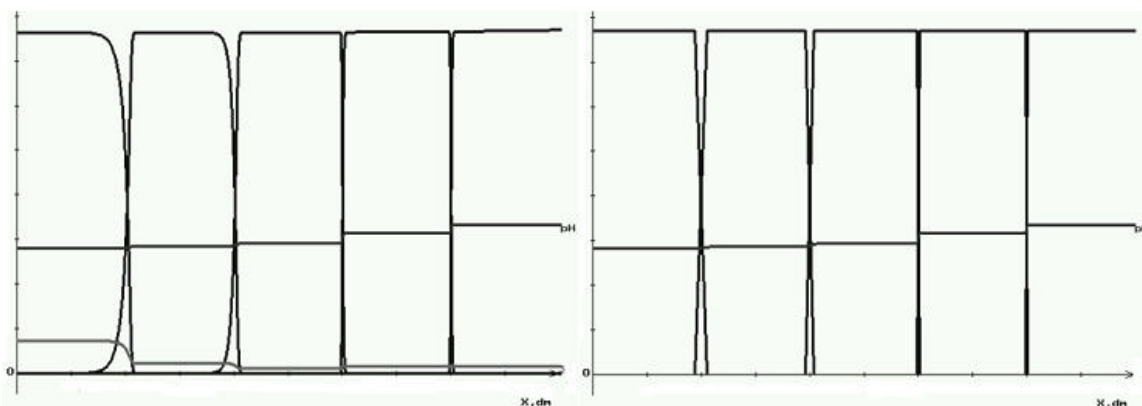


Fig. 4: Calculated and asymptotic concentration profiles the system with pH>7: His -His, His-Gly, His, β-Ala-His, Tyr-Arg, J = 0.539

Summing up the above, using the formulas (39), (41), (76), (51)-(53), (67), (68), the equations take the general form:

$$\xi_k = \begin{cases} 0, & x \in [0, x_{k-1}^1] \\ S_{k-1} \cdot \frac{(x - x_{k-1}^1)}{(x_{k-1}^2 - x_{k-1}^1)}, & x \in [x_{k-1}^1, x_{k-1}^2] \\ S_{k-1} + (S_k - S_{k-1}) \cdot \frac{(x - x_{k-1}^2)}{(x_k^1 - x_{k-1}^2)}, & x \in [x_{k-1}^2, x_k^1] \\ S_k - S_k \cdot \frac{(x - x_k^1)}{(x_k^2 - x_k^1)}, & x \in [x_k^1, x_k^2] \\ 0, & x \in [x_k^2, H] \end{cases} \quad (71)$$

$$x_k^1 = x_k + 0.5\Delta t_k \cdot \varepsilon, \quad x_k^2 = x_k - 0.5\Delta t_k \cdot \varepsilon, \quad i = k - 1, k$$

where values S_i^0 , x_k are determined by formulas (69), (70);

$$\Delta t_i = \frac{\Theta_i}{J} \left(\frac{\phi_i}{\phi_i'} - \phi_{i+1} \right) \Big|_{\psi=\psi(x_i)} \quad (72)$$

$$\Theta_i = \mu_i \frac{S_i}{\phi_i'} \left(\phi_i'' - \frac{(\phi_i')^2}{\phi_i} \right) + \mu_{i+1} \frac{S_{i+1}}{\phi_{i+1}'} \left(\phi_{i+1}'' - \frac{(\phi_{i+1}')^2}{\phi_{i+1}} \right) \Big|_{\psi=\psi(x_i)} \quad (73)$$

$$\Phi_{i,i+1}(\psi(x_i)) = \left(\frac{\phi_{i+1}'}{\phi_{i+1}} - \frac{\phi_i'}{\phi_i} \right) \left(\frac{1 + \delta_i \phi_i''}{\phi_i^2} + \frac{1 + \delta_{i+1} \phi_{i+1}''}{\phi_{i+1}^2} \right) \Big|_{\psi=\psi(x_i)} \quad (74)$$

the value $\psi(x_i)$ in the formulas (73)-(75) is derived from algebraic equation:

$$\phi_i'(\psi(x_i))\phi_{i+1}(\psi(x_i)) + \phi_{i+1}'(\psi(x_i))\phi_i(\psi(x_i)) = 0 \quad (75)$$

Accordingly, the function ψ is approximated by a broken line:

$$\psi = \begin{cases} \Psi_k, & x \in [x_{k-1}^\psi, x_k^\psi] \\ \Psi_{k+1} + (\Psi_k - \Psi_{k+1}) \cdot \frac{(x - x_k^\psi)}{(x_{k+1}^\psi - x_k^\psi)}, & x \in [x_k^\psi, x_{k+1}^\psi] \\ \Psi_{k+1}, & x \in [x_{k+1}^\psi, x_{k+2}^\psi] \end{cases} \quad (76)$$

$$x_k^\psi = x_k + \Delta t_k \frac{\Psi_k - \psi(x_k)}{\Phi(\psi(x_k))} \cdot \varepsilon$$

$$x_{k+1}^\psi = x_k + 0.5\Delta t_k \frac{\Psi_{k+1} + 0.5\psi(x_k)}{\Phi(\psi(x_k))} \cdot \varepsilon$$

Model testing. The calculations were carried out on the assumption that: the length of EC is $l = 2(\text{dm})$ and its radius is $r = 0.2(\text{dm})$. The current density is measured in A/sq.dm. The values of dissociation constants $K_1^{(k)}$, $K_2^{(k)}$ and migration coefficients are taken from [1]. The system of five standard ampholytes has been considered: His -His, His-Gly, His, β-Ala-His, Tyr-Arg. Asymptotic profiles have been constructed on the basis of formulas (72) (77). Fig. 4 shows that in ‘anomalous’ mode the calculated and asymptotic concentration profiles provide a high degree of consistency.

CONCLUSIONS

The asymptotic solution of the integro-differential problem of IEF has been obtained by using the tangent method. The concentration profiles are approximated by straight lines, whose coefficients are determined by the electrochemical parameters of the system. It has been found that the geometrical ‘ceiling’ for the system of concentration profiles is the broken line, with the parameters determined by the equations (58)-(59), plays the role of such a ‘ceiling’. The complex IEF model

developed in this paper has theoretical significance: using the suggested transformation methods and the asymptotic solution of stiff integro-differential problem, similar problems in mathematical physics, having large parameters, could be solved.

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