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Stump-like mathematical model and computer simulation on dynamic separation of capillary zone electrophoresis with different sample injections

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ABSTRACT

In this paper, a novel mathematical model of stump-like peak was constructed for alternative computer simulation of capillary zone electrophoresis (CZE) by using Haarhoff–Van der Linde (HVL) function. Unlike a classical model of Gaussian peak, the developed model contains both Gaussian and plateau concentration distributions of analytes. Based on the model, the relevant computer software was developed and implemented in Borland Delphi 7 environment. The relevant results revealed that (i) the software could freely simulate the plateau and Gaussian distribution peaks; (ii) the simulator could simulate a dynamic process of CZE properly; and (iii) the program could display the final electropherogram of numerous analytes in CZE. We further conducted the relevant experiments and compared them with the simulations. The comparisons demonstrated the high agreement between the simulation results and the experiments as well as those cited from references. In addition, the software could calculate effective mobility, diffusion coefficient and concentration of analytes based on the physico-chemical parameters input by users. The developed model and software have evident significance for understanding of electrophoretic separation, conditional optimization and basic computation on physico-chemical parameters of analytes in CZE.

1. Introduction

Computer simulation is a powerful tool to display the vivid electrophoretic process and to economically provide the optimization on experimental conditions of electrophoretic separation [1]. Various mathematical models and their computer programs have been developed for simulations on isotachophoresis (ITP), isoelectric focusing (IEF), capillary zone electrophoresis (CZE) and online sample concentration in capillary electrophoresis (CE).

There have been numerous well-developed mathematical models and computer programs for ITP simulation so far. Beckers et al. in 1972 [2] advanced the simple model of ITP for computer simulation, with which up to eight metal ions can be visually and simultaneously separated in their given electrophoretic system. In 1984, Hirokawa [3] described a computer program for the simulation on ITP separation of fourteen lanthanoid metal ions using three electrolyte systems. Radi [4] in 1985 and Shimao [5,6] in 1986 advanced the numerical simulation for complex ITP systems (e.g., three systems and protein systems etc), revealing the behavior of ITP and counter ion components in the steady state of ITP. In 1992, Heinrich et al. [7] developed a versatile model and computer program for the rapid optimization of ITP (as well as CZE and continuous flow electrophoresis) conditions, such as buffer, ionic strength, temperature, Joule heat, activity coefficients and concentration, etc. Caslavska et al. [8] in 1993 performed a simple simulation of ITP evaluation using a commercial, inexpensive, computerized data acquisition system. In 1995, Schafer–Nielsen [9] advanced the time-based simulation of ITP with free definition on boundary conditions for handling n constituents with n pK-values and calculating constituent concentrations and derived parameters as a function of time. Schwer et al. [10] in 1993 described Simul 4 for the numerical simulation on ITP and Hruska et al. [11] further developed Simul 5 for the dynamic simulation of ITP on inspecting system peak, stacking analytes and optimizing separation conditions.

Almost at the same time, a series of IEF simulations have also been developed. In 1979, Murel et al. [12] developed a simple model and computer program for the illustration of pH gradient instability (e.g., drifting and plateau phenomena) in IEF run. During 1981–83, Bier et al. [1,13] advanced a steady state IEF model for the simulation on concentration profile, pH value, conductivity and potential gradient. They [14,15] in 1986 developed their software for the dynamics of IEF. In 2000, Mao et al. [16] developed a fine IEF program for the dynamics simulation with high resolution. With the assistance of the software, Mosher et al. [17] in 2002 restudied the post-separation stable phase in IEF and Thormann et al. [18,19]

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investigated the dynamics of protein during an IEF and pH gradient mobilization after steady-state IEF run. Shimao [20–22] also conducted the numerical simulation of protein separation in IEF, which was treated as zero velocity ITP. In 2009, Jin et al. [23,24] developed the mathematical model and software of moving reaction boundary (MRB), and further revealed the relation between IEF and MRB via the results of simulation and experiment.

Furthermore, various mathematical models and programs have been described for CZE simulation hitherto. In 1994–1999, Reijenga et al. [25] developed a computer program for the simulation on migration, dispersion of samples and the influence of different injection in CZE. Cifuentes and Poppe [26] in 1994 and Janine et al. [27] in 1999 performed the simulation of separation and mobility mapping of 58 peptides that varied in size from 2 to 39 amino acids and in charge from 0.65 to 7.82. Gas et al. [28] in 1995 simulated the peak dispersion, including wall absorption, and in 2002 they greatly developed the PeakMaster for the optimization of electrophoretic conditions (e.g., running buffer, pH value, concentration and electric field as well as effective length of capillary) in CZE [29]. Erny et al. [30] in 2001–2003 discussed how to use Haarhoff–Van der Linde (HVL) equation to simulate the peak in CZE. In 2008, Hsu and Hung [31] conducted the simulation of charged ion migration in CZE. Recently, Hruska et al. [32,33] extended the linearized model of electromigration by calculation of nonlinear dispersion and diffusion of zone and introduced a computer implementation of the mathematical model of CZE which can predict the shapes of the system peaks even for a complex injected sample profile, such as a rectangular plug.

Unlike the models of CZE mentioned above, this paper tried to propose a novel stump-like HVL mathematical model of electrophoresis which contains both Gaussian and plateau concentration distributions of analytes, to develop the relevant computer program for simulation on plateau peak and the dynamic separation process of CZE. At the same time, the relevant experiments were performed for the demonstrations on the validity of developed stump-like model and its relevant simulation results. The developed software supplies an alternative choice for computer simulation on CZE. Below are the developed HVL model, a versatile computer program, the dynamic simulation results and the relevant experimental demonstrations.

2. Theoretical

2.1. Mathematical model of peak

Fig. 1A shows an idealized Gaussian peak of analyte which can be quantitatively described by the HVL equation. Evidently, under the same conditions except sample injection, the model of Gaussian peak could not explain plateau peak in CZE which accompanied with long sample injection [24,33]. Fig. 1B reveals the modified HVL model, called as stump-like HVL model. As shown in Fig. 1, the Gaussian peak in Panel A is cleaved into two parts, viz., the left and right halves of a Gaussian peak. Then a rectangle peak is set between the left and right halves. As a result, a stump-like HVL model is created as shown in Panel B. The rectangle length is determined by sample injection time in CE. The whole stump-like HVL model symbolizes a plateau-like peak if an abundant sample injection is given. Obviously, the modified model turns into an idealized Gaussian peak when the injection time is short. Under the condition of Panel A, the original HVL equation is modified as [34]

$$f(t)=\frac{a_0}{a_2\sqrt{2\pi}}\exp\left[-\frac{1}{2}\left(\frac{t-a_1}{a_2}\right)^2\right] \tag{1}$$

where, a_0 is the area of peak ($a_0=\int_{-\infty}^{+\infty}f(t)dt$), a_1 is the center of peak ($a_1=\int_{-\infty}^{+\infty}t\times f(t)dt/a_0$), a_2 is the variance of peak ($a_2=\int_{-\infty}^{+\infty}(t-a_1)^2f(t)dt/a_0$), and t is a time variable and can be rewritten as a distance variable x via mathematical conversion.

Suppose cross-sectional area of capillary is S, the amount of analyte M in a simulation can be computed with

$$M=\int_{-\infty}^{+\infty}Sf(t)dt \tag{2}$$

Thus, a_0, a_1 and a_2 in Eq. (1) respectively become

$$a_0=\int_{-\infty}^{+\infty}f(t)dt=\frac{M}{S}=cL \tag{3}$$

$$a_1=\frac{L_{\text{eff}}}{E\left(\mu_{\text{eff}}+\mu_{eof}\right)} \tag{4}$$

$$a_2^2=2Dt \tag{5}$$

where, L is the total length of capillary, L_{eff} is the effective length of capillary, E is the electric field intensity, μ_{eff} is the effective mobility, μ_{eof} is the electro-osmotic flow (EOF) mobility, D is the diffusion constant, and c is the concentration of analyte.

If the simulation is to display dynamic separation process of analytes (see the bottom column in Fig. S1B), the variable is a displacement (x), rather than the time (t). If there is the condition of $x_{\text{center1}}<x_{\text{center}}<x_{\text{center2}}$, there appears a plateau peak. And the model of plateau peak ought to be described with

$$f(x)=\frac{\int_{-\infty}^{+\infty}f(x)dx}{a_2\sqrt{2\pi}}\exp\left(-\frac{(x-x_{\text{center1}})^2}{2{a_2}^2}\right) \tag{6}$$

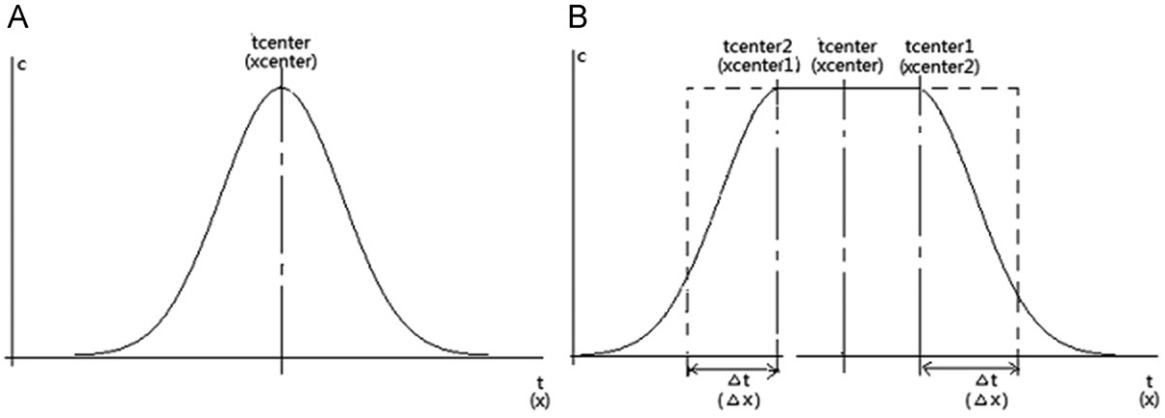

Fig. 1. Diagram of peak shape of Gaussian peak (A) and stump-like plateau peak (B). x-axis means running time (t) or distance from the inlet (x), y-axis means concentration of analytes.