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HERMITE POLYNOMIAL REPRESENTATION OF CHROMATOGRAPHY ELUTION CURVES

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SUMMARY

Elution curves for aqueous solutions of NaCl and β-lactoglobulin were measured for columns packed with porous polyacrylamide gel or non-porous glass particles. The elution curves were mathematically represented by series of Hermite polynomials in terms of the moments of the chromatographic pulses. Fitting the representation to skewed output pulses provides a criterion for trimming tails on elution curves.

INTRODUCTION

The 1965 chromatography theory of Kubin[1] and Kucera[2] presents a method for (a) determining mass transport parameters from a moment analysis of elution curves, and (b) predicting elution curves from a knowledge of mass transport parameters. The first part of the method has been applied to gas chromatography by Schneider and Smith[3], Suzuki and Smith[4], and Adrian and Smith[5], and to gel chromatography by Mehta *et al.*[6]. The second part was briefly explored by Kubin, who showed that Gaussian elution curves from packed beds of solid spheres were reasonably well-represented in terms of first and second moments. Kubin[1] proposed that four-term expansions in terms of Hermite polynomials be employed for exploring non-Gaussian elution curves. In this article it is shown how skewed elution curves may be represented in terms of their higher moments.

THEORETICAL TREATMENT

The moments of the elution curves are defined as time integrals of the concentration $c(t)$, *viz.* the zeroth moment,

$$m_0 = \int_0^\infty c(t)\,\mathrm{d}t \tag{1}$$

the normalized first absolute moment,

$$\mu_1' = \frac{1}{m_0}\int_0^\infty t c(t)\,\mathrm{d}t \tag{2}$$

and the nth central moments,

$$\mu_n = \frac{1}{m_0}\int_0^\infty (t-\mu_1')^n c(t)\,\mathrm{d}t \tag{3}$$

These moments have been expressed in terms of mass transport parameters (axial dispersion coefficient, internal diffusivity, fluid-to-particle mass transfer coefficient, adsorption constants, etc.) and bed properties (diameter, length, void fraction, particle size, etc.) for many cases of interest[1-6].

When convection is a major effect compared to dispersion, it is expected that an elution curve will be nearly Gaussian[7]. Then the concentration may be represented as a series in Hermite polynomials, which are chosen because of the e^{-x^2} weighting function in the orthogonality relation[8],

$$\int_{-\infty}^{\infty} H_m(x)H_n(x)\,e^{-x^2}\,dx = 2^n n!\pi^{\frac{1}{2}}\delta_{mn} \tag{4}$$

The Hermite polynomials $H_n(x)$ are defined[8] such that

$$\begin{aligned} H_0(x) &= 1 \\ H_1(x) &= 2x \\ H_2(x) &= 4x^2-2 \\ H_3(x) &= 8x^3-12x \\ H_4(x) &= 16x^4-48x^2+12 \end{aligned} \tag{5}$$

Letting $x=(t-\mu_1{}')/(2\mu_2)^{\frac{1}{2}}$, we represent a pulse as the series,

$$c(t) = m_0\,e^{-x^2}\sum_{n=0}^{\infty} a_n H_n(x). \tag{6}$$

Multiplying eqn. 6 sequentially by the Hermite polynomials (5) and integrating with the aid of eqn. 4, we obtain for the coefficients,

$$\begin{aligned} a_0 &= 1/(2\pi\mu_2)^{\frac{1}{2}} \\ a_1 &= 0 \\ a_2 &= 0 \\ a_3 &= \mu_3/2^2 3!\pi^{\frac{1}{2}}\mu_2{}^2 \\ a_4 &= 4(\mu_4/\mu_2{}^2-3)/2^4 4!\pi^{\frac{1}{2}}\mu_2{}^2 \end{aligned} \tag{7}$$

The series (6) can be used to represent a pulse in terms of its moments, as illustrated for experimental data below. Furthermore, if bed and mass transport parameters are known, the moments may be calculated from first principles, allowing eqn. 6 to be used to predict an output pulse in terms of an input pulse and operating conditions. As mentioned previously, the transport parameters themselves may be determined from moment analysis of pulse-response experiments if accurate pulse data are available.

EXPERIMENTAL AND RESULTS

The experimental method and materials have been described by Mehta *et al.*[6] and in detail by Mehta[9]. Briefly, the packed bed consisted of either a 40-cm length of hydrated polyacrylamide gel particles or an 85-cm length of non-porous glass beads packed in a 1.50-cm I.D. glass column or 1.27-cm I.D. acrylic column. Four different gel particle sizes of 510, 430, 230, and 130 μm diameter were studied. The diameter of the non-porous glass beads was 450 μm. The different non-adsorbing solutes used were sodium chloride, and a synthetic whey solution of NaCl and the protein β-lactoglobulin. The water flow-rates ranged from 3 to 25 ml/min. The signals from electroconductivity probes or ultraviolet absorption photometry cells were recorded on strip charts. Moments were calculated with eqns. 1–3 by numerical integration.

The more nearly Gaussian the elution curve, the fewer the number of terms in eqn. 6 needed for its representation. For the 85.0-cm column packed with 450-μm solid glass beads, the elution curves were quite symmetric with no tail or leading edge. For a trial at $v_0 = 0.185$ cm/sec (Fig. 1), the coefficients a_0, a_3, and a_4 were calculated from the numerically integrated moments μ_1', μ_2, μ_3, and μ_4. The predicted elution curve fits the experimental recorder output closely (Fig. 1). The effect of the third and fourth moments was nearly imperceptible for this case. Since the uncertainty of the data for the glass bead experiments is small, bed and transport parameters could be calculated from the moment data. A prediction of the elution curve from moments calculated from parameters determined from similar experiments is nearly as accurate as that in Fig. 1 (Ref. 6).

For input pulses of synthetic whey on 430-μm gel at $v_0 = 0.047$ cm/sec (Fig. 2), the output pulse of β-lactoglobulin is skewed and shows some tailing while the output pulse of NaCl is nearly symmetric. The tail was caused by backmixing in the UV detector cells, not by transport phenomena in the column, and therefore the tail was

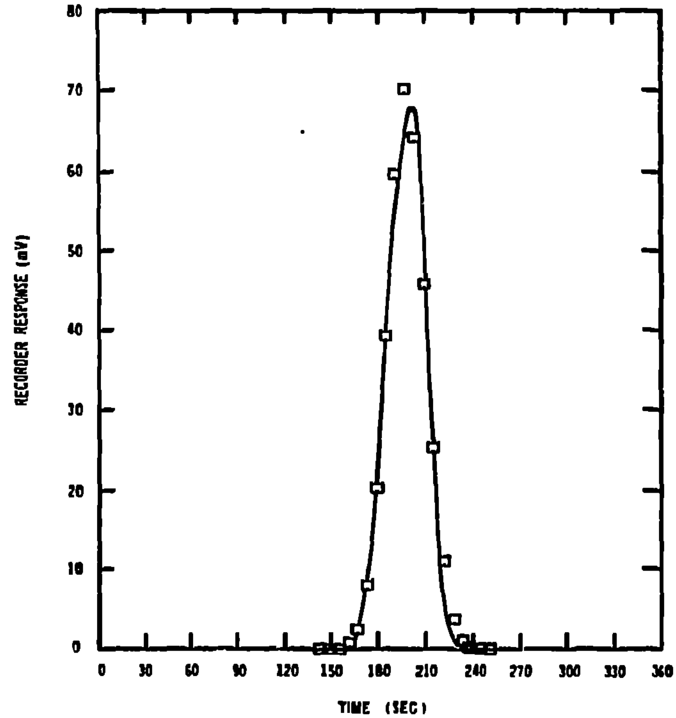

Fig. 1. Representation of an elution curve for NaCl on 450-μm non-porous glass beads. Column length, 85.0 cm. —, experimental curve; □, predicted points.

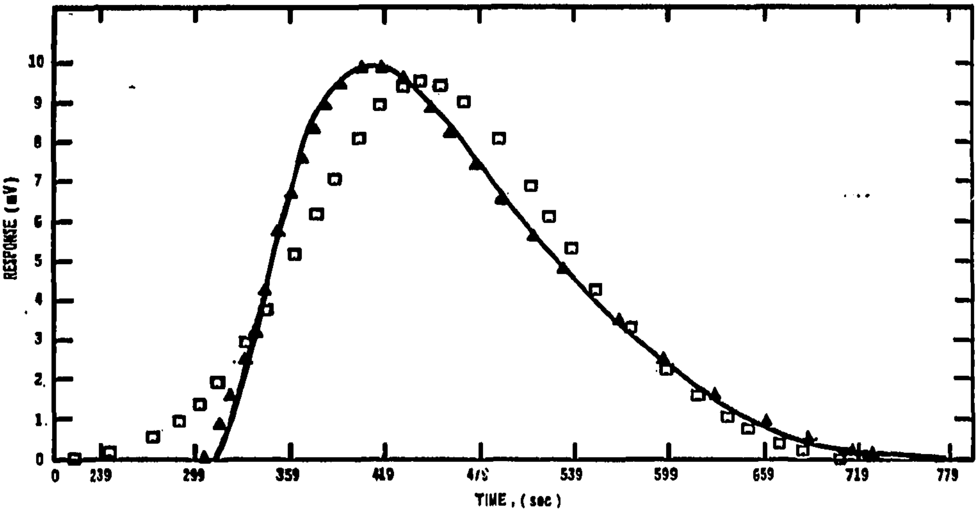

Fig. 2. Representation of an elution curve for β-lactoglobulin in synthetic whey on 430-μm gel. Column length, 39.8 cm. —, experimental curve; □, calculated points (with tail); – – –, tail trimmed; ▲, calculated points (with tail trimmed).

trimmed as in Fig. 2. The second moment and, even more so, the third moment are significantly distorted when calculated with the tail. Trimming the tail by eye (dashed line in Fig. 2) reduces μ_2 and μ_3 and yields a good fit of the Hermite polynomial representation with two terms in the series, *i.e.* with coefficients a_0 and a_3. Fig. 3 shows that the unaltered NaCl pulse, for which there was no extraneous backmixing, is represented accurately by the two-term series. This procedure illustrates a general method of correcting pulse data for column end effects and other factors not directly related to the chromatographic process.

Some of the NaCl output pulses demonstrated a leading edge due to channeling along the inner surface of the column. Our interpretation is that the elution curves

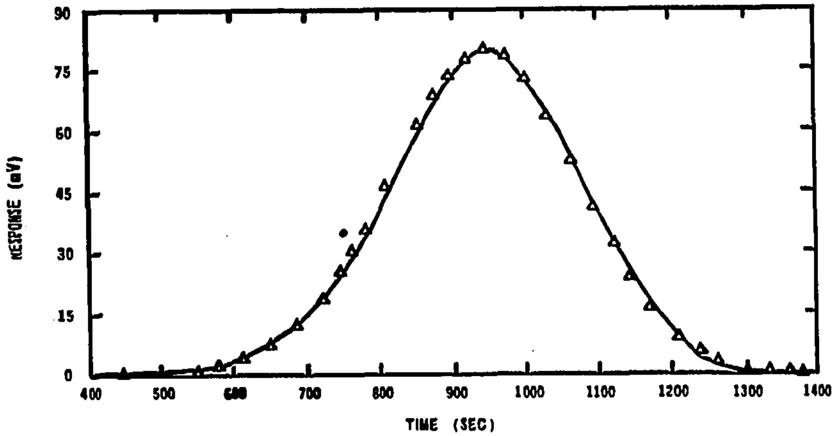

Fig. 3. Representation of an elution curve for NaCl in synthetic whey on 430-μm gel. Column length, 39.8 cm. —, experimental curve; △, predicted points.

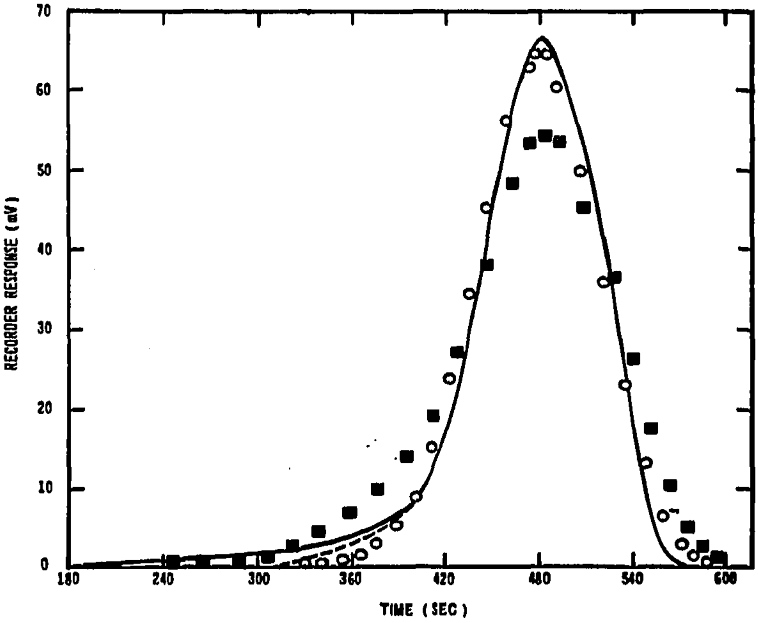

Fig. 4. Representation of an elution curve for NaCl on 230-μm gel. Column length, 37.4 cm. —, experimental curve; ■, calculated points (with leading edge); ---, leading edge trimmed; ○, calculated points (with leading edge trimmed).

in such cases involve two superimposed outputs: one due to the channeling and the other due to the chromatographic process itself. To show how a leading edge is trimmed we consider a NaCl pulse in the 37.4-cm plastic column packed with 230-μm gel and operated at $v_0=0.0787$ cm/sec (Fig. 4). Two terms in the series (6) were needed to satisfactorily fit the elution curve. Fourth moments had a negligible effect. With moments calculated without trimming the rather strong leading edge, the two-term series only roughly approximates the experimental curve. When the leading edge is curtailed by eye, as shown in Fig. 4, the calculated points agree reasonably with the elution curve corresponding to the chromatographic process.

Other experimental elution curves which were treated in the same manner as the curves discussed here provided similar agreement with the two-term Hermite polynomial series representation.

CONCLUSION

Two-term series in Hermite polynomials were fitted to chromatography output pulses of protein and NaCl. The fitting provides a method for judging the trimming of tails and leading edges of such pulses to correct for end effects and similar phenomena. In addition to this criterion for calculating moments of output pulses, an accurate representation of pulses may be useful for design and scale-up of chromatographic processes.

SYMBOLS

a_n =expansion coefficients in eqn. 6 given by eqn. 7, $\sec^{-1}$
c =concentration of solute in the interparticle space, mol/ml
e =2.303...
m_0 =zeroth moment defined by eqn. 1, mol sec/ml
m, n=indices, dimensionless
t =time, sec
v_0 =linear superficial velocity —(bed void fraction)×(volumetric flow-rate)/column cross section, cm/sec
x $=(t-\mu_1')/(2\mu_2)^{\frac{1}{2}}$, dimensionless
δ_{mn} =orthogonality variable, $\delta_{mn}=0$ for $m\neq n$, $\delta_{nn}=1$, dimensionless
μ_1' =normalized first absolute moment defined by eqn. 2, sec
μ_n =normalized nth central moment defined by eqn. 3, $\sec^n$, $n=2, 3, 4, \ldots$
π =3.14159...

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