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Determination of rate constants in a liquid chromatographic reactor by means of a fitting algorithm

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ABSTRACT

Based on the exponentially modified Gaussian profile, a new equation for the evaluation of product peaks of liquid chromatographic first-order reaction chromatograms is given. It is shown that this equation is able to fit reaction chromatograms corresponding to the linear model of chromatography.

INTRODUCTION

If chromatographic equipment is applied for the determination of rate constants, several methods can be used [1]. It seems that the so-called inert standard method is the most widespread, in which an inert standard is added to the reactant, and then the reactant is converted into one or more products, which are separated from the reactant. The conversion of the reaction can be evaluated from the ratio of the pulse area of the reactant and the inert standard. By variation of the flow-rate of the mobile phase, the duration of the reaction can be varied, and from the correlation between the retention time and the conversion an apparent rate constant can be found.

On the other hand, it may be time consuming to look for a suitable standard. Moreover, the method is suitable only for simple first-order reactions. For complex reactions only a composite rate constant can be determined. Even with a sim-

ple first-order reaction, the area of the reactant pulse must be corrected, as it is not possible to separate the reactant and the product completely from each other. Especially in liquid chromatography there may be the problem of comparable rate constants for the chemical reaction and the mass transfer, which makes the determination of statistical moments necessary [2,3].

For these reasons, we decided to develop an analytical function that represents the product curve for simple first-order reaction and for parallel reactions. Unfortunately, the situation becomes more complicated for consecutive reactions, and this aspect will be treated in a subsequent paper.

The derivations were based on the exponentially modified Gaussian (EMG) profile [4], because it is useful for many applications in chromatography [5] and Naish and Hartwell [6] showed its special advantage for liquid chromatography.

MATHEMATICAL MODELLING

The product peak formed by the simultaneous occurrence of chemical reaction and the chro-

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matographic process (dynamic partitioning between the stationary and mobile phases) is the sum of differential product pulses, which are formed one after the other as the reactant pulse passes the column.

The product concentration, which appears at the end of the column at time t, is the sum of those concentration elements dc which are leaving the column together at time t. Every concentration element dc is related to an amount element dm, which is produced when the reactant passes the length coordinate x of the column. The concentration elements can be evaluated from the amount elements by a distribution or peak shape equation, the moments of which (first moment, second and third central moments) in linear chromatography are related to the moments of the pure substances by a linear equation (a list of symbols is given at the end of the paper):

$$dc_P(t, x) = dm_P(x)\Psi_P[\mu_i(x), t]$$

$$= -\frac{dm_R(x)}{dx} \cdot \Psi_P[\mu_i(x), t]\, dx \qquad (1)$$

$$\mu_i(x) = \frac{x}{l} \cdot \mu_{iR} + \frac{l-x}{l} \cdot \mu_{iP} \qquad (2)$$

In a simple first-order reaction, we obtain for an amount element dm_P:

$$dm_p = k\, e^{-kt_0(x/l)}\, dx = k'\, e^{-k'(t-\mu_{1P})}\, e^{k'(\mu-t)} \qquad (3)$$

In a parallel reaction we find a very similar term:

$$dm_p = k_1\, e^{-kt_0(x/l)}\, dx = k_1'\, e^{-k'(t-\mu_{1P})}\, e^{k'(\mu-t)}$$
$$k = k_1 + k_2 \qquad (4)$$

Therefore, it will be possible to transfer the following results given for simple first-order reactions to product peaks from parallel reactions.

Introducing the EMG distribution:

$$\Psi_P(\mu, t) = \frac{1}{\tau}\, e^{-\frac{1}{2}\left(\frac{\sigma}{\tau}\right)^2}\, e^{-\frac{\sigma}{\tau}z} \int_{-\infty}^{z} \frac{e^{-\frac{y^2}{2}}}{\sqrt{2\pi}}\, dy$$
$$z = \frac{t - \mu}{\sigma} - \frac{\sigma}{\tau} + \frac{\tau}{\sigma} \qquad (5)$$

for the peak shape equation in eqn. 1, we already have an EMG-based equation for the

product curve of irreversible first-order reactions:

$$c_p = k'\, e^{-k'(t-\mu_{1p})}\, \frac{\sigma}{\tau}\, e^{-\frac{1}{2}\left(\frac{\sigma}{\tau}\right)^2}\, e^{k'\sigma\left(\frac{\sigma}{\tau} - \frac{\tau}{\sigma}\right)}\, I$$

$$I = \int_{z(\mu_{1R})}^{z(\mu_{1P})} e^{k_\sigma z} \int_{-\infty}^{z} \frac{e^{-\frac{y^2}{2}}}{\sqrt{2\pi}}\, dy\, dz \qquad (6)$$

$$k_\sigma = k'\sigma - \left(\frac{\sigma}{\tau}\right)$$

There remains, two problems however: first, there is a contradiction between eq. 2 for the moments of the product peak and the moments of the EMG pulse [4]:

$$\mu_2 = \sigma^2 + \tau^2$$
$$\mu_3 = \frac{\tau^3}{2} \qquad (7)$$

It is not possible to fulfil both eqs. 2 and 7 at the same time. The second problem is of a numerical nature: it is not possible to simplify eqn. 6 as long as it is assumed that both σ and τ depend on the length coordinate or, which means the same, as long as it is assumed that σ and τ of the product and the reactant differ markedly. On the other hand, it is not possible to assume simply that they are always equal, because then it will not be possible to fit real reaction chromatograms.

Investigating eqn. 6, it turned out that a larger part of the product curve between the μ_{1R} and the μ_{1P} values is nearly independent of σ and τ as long as the σ and τ values do not differ dramatically. Therefore, we suggest the following procedure. The concentration of the product is evaluated first with the pure σ and τ of the reactant and second with the pure σ and τ of the product. The final concentration will be found by a weighted average according to the equation

$$c_P = t_m c_P(\tau_R, \sigma_R) + (1 - t_m)c_P(\tau_P, \sigma_P)$$
$$t_m = \frac{t - \mu_{1P}}{\mu_{1R} - \mu_{1P}} \qquad (8)$$

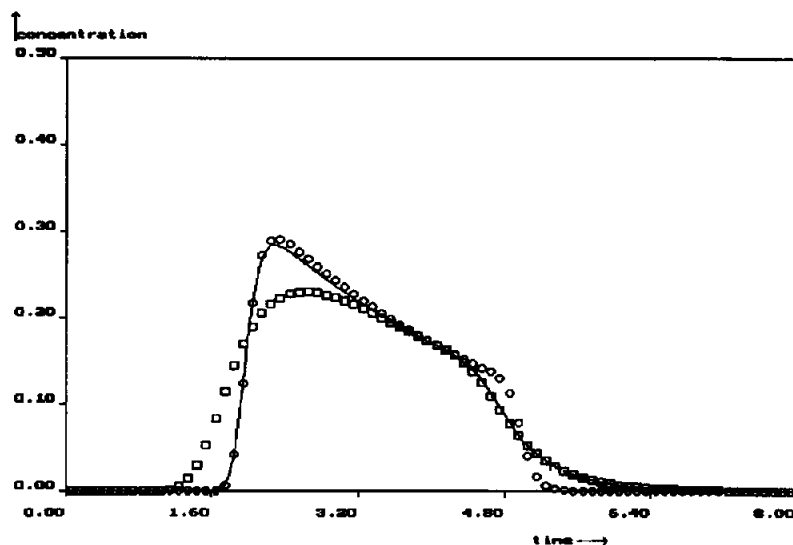Then the integral I in eqn. 6 can be simplified:

Fig. 1. Composition of the resulting product peak (line) from the product peak with the shape parameters of the reactant (squares) and the product peak with the shape parameters of the product (circles).

$$I = \frac{1}{k_\sigma} (e^{k_\sigma z(\mu_{1P})} \, F[z(\mu_{1P})] - e^{k_\sigma z(\mu_{1R})} \, F[z(\mu_{1R})]$$

$$- e^{\frac{k_\sigma^2}{2}} \{F[z(\mu_{1P})] - F[z(\mu_{1R})]\}) \qquad (9)$$

$$F[z] = \int_{-\infty}^{z} \frac{e^{-\frac{y^2}{2}}}{\sqrt{2\pi}} \, dy$$

The Gaussian integral function in these terms can easily be calculated by several polynomial approaches [7]. Fig. 1 displays the comparision of the final product peaks according to eqn. 8.

NUMERICAL EVALUATIONS

As there are nearly always reaction chromatograms obtained in which both the reactant and the product are present, the fitting equation has to be a sum of the shape equation for the reactant and the product peak taking into account that there can be different molar detector responses for both species. Therefore, we obtain the following fitting equation:

$$y = f_P(f_R c_R + c_P)$$

$$c_R = e^{-kt_0} \, \psi(\mu_R, \tau_R, \sigma_R, t) \qquad (10)$$

It is obvious that it will not be very simple to fit this nine-parameter equation to the chromatograms. Fortunately, some initial values for the parameters can be taken from the chromatogram (cf., Fig. 2).

The response factors f_P and f_R are calculated from the area ratio of the fitting equations and the chromatogram for selected parts of the chromatogram (in Fig. 2: $t_{22} - t_{23}$ for f_P and $t_{21} - t_{11}$ for f_R). The fitting itself starts then with the selection of the magnitude of the rate constant. Then the parameters are systematically varied using the sequence k, μ_{1P}, σ_P, τ_P, μ_{1R}, σ_R, τ_R.

We used a Turbo PASCAL program for the implementation of this algorithm on a personal computer.

In order to see if our approach meets the model of linear chromatography, we used the method of finite differences to solve the partial differential equations of the linear liquid chromatographic reactor and fitted our equation to the chromatogram numerically evaluated. Fig. 3 shows the very good agreement between the numerical chromatogram and our fitting equation. The results for the moments and the rate constant are given in Table I. There is only one greater deviation concerning the values for the
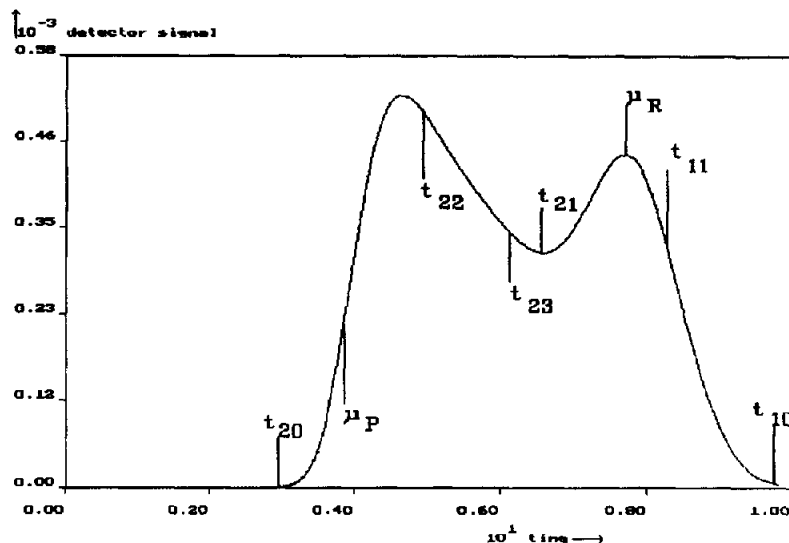
Fig. 2. Essential points in the reaction chromatogram for the estimation of initial values for several parameters t_{20} = Beginning of the fit; μ_P = initial value for μ_{1P}; initial value for σ_P, $\sigma_P = (\mu_P - t_{20})/2$; $t_{22} - t_{23}$ = region for the evaluation of f_P; $t_{21} - t_{10}$ = region for the evaluation of f_R; μ_R = initial value for μ_{1R}; t_{11}, $\sigma_R = t_{11} - \mu_R$.

third moment of the product, but this is due to the fairly symmetric shape of the product pulse.

We can conclude that our equation is well suited for the fitting of reaction chromatograms which are produced by linear chromatographic processes.

EXPERIMENTAL AND RESULTS

We used a modular liquid chromatographic system from GAT (Berlin, Germany), equipped with a 5μm RP-18 column and a GAT PHD 601 UV detector. The hydrolysis of acetic anhydride
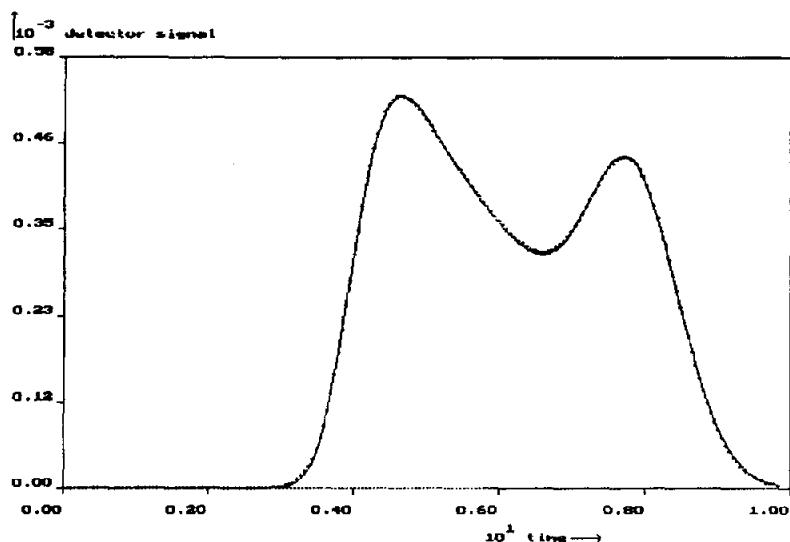

Fig. 3. Best fit (points) of eqn. 10 to a chromatogram numerically evaluated by a finite difference method.

TABLE I

RESULTS OF FITTING EQN. 10 TO A NUMERICAL
CHROMATOGRAM

	μ_{1R}	$10\,\mu_{2R}$	$10\,\mu_{3R}$	μ_{1P}	$10\,\mu_{2P}$	$10\,\mu_{3P}$	k
Num.[a]	7.92	3.78	2.08	4.00	1.44	1.04	1.40
Fit.[a]	7.92	3.91	2.15	4.02	1.42	0.08	1.42

[a] Num. = from numerical chromatogram by integration;
Fit. = from fitting eqn. 10 to the chromatogram.

was used for the investigation of a first-order
reaction. With pure water as the eluent we
obtained extremely skewed peaks, which obvi-
ously will not be in accordance with the assump-
tions of linear chromatography. Therefore, we
added 20% of methanol to reduce the peak
tailing. We used amounts of 0.3 μl of acetic
anhydride and varied the flow-rates.

As can be seen from Figs. 4–6, the reactant is
contaminated by impurities, which especially
interfere with the product pulse. It is not surpris-
ing that one of them is obviously acetic acid, as
the reaction with the eluent will begin within the
sample loop. Because of this distortion of the
product peak flank we could not fit the first
moment and the EMG peak shape parameters of

the product, but took the values from the chro-
matograms assuming that the acetic acid pulse is
nearly a Gaussian.

The essential results of the fittings are summa-
rized in Table II. It can be seen that the
apparent rate constants are in agreement over a
relatively wide range of conversion. In addition
to the results of the numerical evulations, this
shows that the application of an EMG-based
product profile leads to reasonable results even
in difficult cases.

SYMBOLS

c concentration
f_P molar detector response of the product
f_R ratio of molar dectector response of reactant
    and product
k apparent rate constant
k' $kt_0/(\mu_{1R} - \mu_{1P})$
l column length
m concentration–time area of the peak
P   product
R   reactant
t time
t_0 dead time
x length coordinate
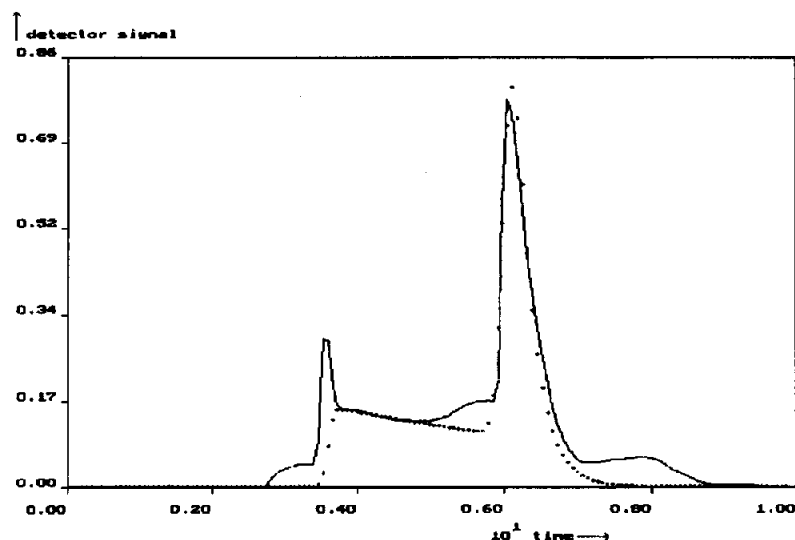ψ peak shape function

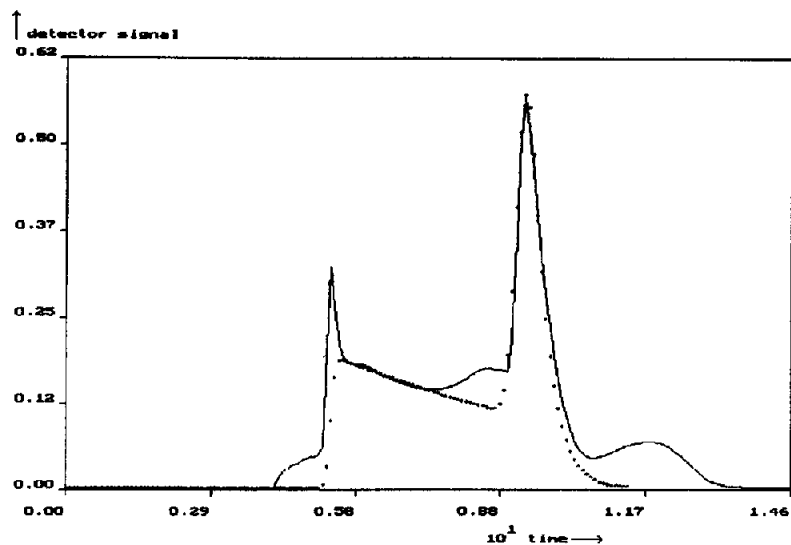Fig. 4. Hydrolysis of acetic anhydride at a flow-rate of 0.3 ml/min. Points: best fit according to eqn. 10.

Fig. 5. Hydrolysis of acetic anhydride at a flow-rate of 0.2 ml/min. Points: best fit according to eqn. 10.
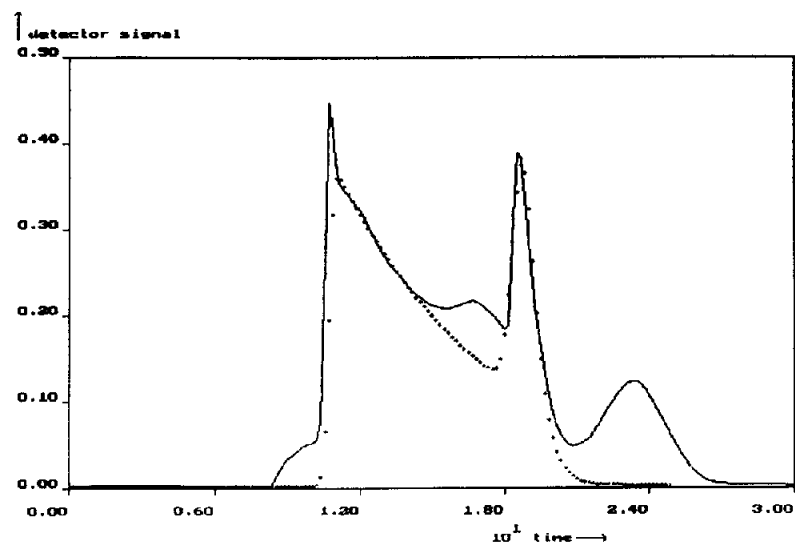

Fig. 6. Hydrolysis of acetic anhydride at a flow-rate of 0.1 ml/min. Points: best fit according to eqn. 10.

TABLE II

RESULTS OF FITTING EQN. 10 TO CHROMATO-
GRAMS FOR THE HYDROYLSIS OF ACETIC ANHY-
DRIDE

Flow-rate (ml/min)	Conversion (%)	k (fit)(min^{-1})
0.3	ca. 35	0.072
0.2	ca. 50	0.071
0.1	ca. 70	0.070

μ_i moment of the peak under normal chromato-
graphic conditions:
  $i = 1$: first absolute moment
  $i = 2$: second central moment
  $i = 3$: third central moment
σ standard deviation parameter of the EMG
function
τ skew parameter of the EMG function

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