Translated from *Uspekhi Khimii*, 47, 2134-2159 (1978) U.D.C. 541.49

# Methods of Mathematical Treatment of the Results of Physicochemical Studies on Complex Compounds

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The general principles of the determination of the equilibrium constants and the physicochemical parameters of complexes under the conditions of their dissociation are examined. The possibilities of approximate computational methods and direct analytical procedures for the solution of systems of the corresponding equations are analysed. Various methods involving the simultaneous determination of the equilibrium constants and physicochemical parameters of complexes, based on the statistical principle of maximum probability, are compared. The ways of the most rational employment of computer techniques in the study of involved complex-formation reactions by various physical methods are discussed.
The bibliography includes 226 references.

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## I. INTRODUCTION

The problem of coordination interaction has been attracting much attention by investigators working in different fields because this type of intermolecular interaction plays a major role in many physical, chemical, and biological phenomena. The range of energies of coordination interactions is extremely wide, starting with the formation of weak self-associated species in liquids and vapours and extending as far as the formation of fairly stable complexes (various molecular complexes, hydrogen-bonded complexes, complexes of ions with various ligands, etc.).

The advances made in recent years in the study of the nature of the coordinate bond and the characteristics of the formation and the properties of complex compounds have been to a large extent due not only to the employment of modern physical research methods but also to improvement of the mathematical procedures used in the interpretation of the experimental results[1-11]. Many physical research methods such as spectrophotometry, NMR, measurements of dipole moments, calorimetry, etc. require that the experiment be carried out in the liquid phase, in solution, or in the vapour phase, i.e. under conditions where there is a possibility of the dissociation of the complexes into the initial components. Any measured property of the solution or vapour is then an overall characteristic of the equilibrium mixture of the initial components and the complexes formed in the system. In order to determine particular parameters of the complexes, it is necessary to know the composition of the equilibrium mixture and hence the stability constants of the complexes. The latter can be determined in an individual experiment, for example, by measuring the colligative properties of the solutions, i.e. properties which depend only on the concentrations of the components of the equilibrium mixture and are independent of the physical characteristics of these molecules. However, even when the equilibrium constants for multistage complex-formation reactions are known, the calculation of equilibrium concentrations is an extremely complex task, since it requires the simultaneous solution of a system of non-linear equations corresponding to the Law of Mass Action and the material balance equations.

The development of a mathematical description of the chemistry of equilibrium processes leads to the possibility of determining the equilibrium constants and the physicochemical parameters of the complexes formed in a given experiment. Methods which permit the determination of the parameters of the complexes without isolating the latter in a pure state are of special interest. The formulation of the experiment under these conditions reduces to the measurement of a physicochemical property of the solution or vapour as a function of the overall concentration of the initial components, mixed in various molar proportions [titration and isomolar series (continuous variations) methods]. In the vast majority of cases the simultaneous determination of the physical parameters and stability constants of complexes in a single experiment is virtually impossible without the use of a computer.

Thus the realisation of the potential possibilities of even extremely informative and accurate physical methods, which require that the experiment be carried out in the liquid or gas phases, depends to a large extent on the reliability of the method of mathematical treatment of the results of the measurements.

The first studies on these lines were carried out towards the end of the 1940s and the beginning of the 1950s, i.e. at a time when computer technology had not developed sufficiently. Different versions of analytical and graphical extrapolations based on approximate equations were widely used. It is noteworthy that, in the analysis of data obtained by these methods, no account is frequently taken of the degree of approximation of the equations employed and attempts are actually made to solve approximate equations by means of a computer. Clearly such a procedure cannot be regarded as rational. Further development of computer technology led to a rigorous solution of the problem under consideration.

In this review an attempt is made to analyse the present state of methods for the mathematical treatment of the results of physicochemical studies of complex formation

reactions, to demonstrate the advantages and disadvantages of many computational methods used, and to discover the most rational ways of employing computers for a rigorous solution of the problem of the simultaneous determination of the equilibrium constants and physical parameters of complexes.

## II. GENERAL PRINCIPLES OF THE DETERMINATION OF THE PARAMETERS OF DISSOCIATING COMPLEXES

The methods for the treatment of the results of physicochemical experiments designed to determine the parameters of complexes are based on the following relations: (1) the equation relating the measured property of the solution to the parameters of the components of the equilibrium mixture and their concentrations; (2) the Law of Mass Action equation; (3) the material balance equation.

An experimentally measured physicochemical property of a system containing an equilibrium mixture of the initial components and the complexes formed is a function of the parameters of all the components of the mixture and their equilibrium concentrations. The measured property $X$ can be represented by the following additive function with a degree of approximation which is adequate for many methods [12]:

$$X = X_z + L\left(x_A C_A + x_B C_B + \ldots + \sum_{i=1}^{n} x_i C_i\right), \qquad (II.1)$$

where $x_A$, $x_B$, ..., $x_i$ are the parameters of the initial compounds A, B, ..., and the $i$th complex respectively, $c_A$, $c_B$, ..., $c_i$ are their equilibrium molar concentrations, $n$ is the number of complexes in the mixture, $L$ is a constant whose magnitude and dimensions depend on the physical method used and the experimental conditions, and $X_Z$ is the corresponding property of the medium (solvent).

For example, in spectrophotometry the measured property of the solution is the optical density $D$ at a given wavelength $\lambda$. Eqn. (II.1) then assumes the form of Eqn. (II.2). In order to synthesise the formulation of this and subsequent equations, we shall assume that the system contains only two initial components A and B:

$$D = l\left(\varepsilon_A C_A + \varepsilon_B C_B + \sum_{i=1}^{n} \varepsilon_i C_i\right) + D_z, \qquad (II.2)$$

where $l$ is the optical pathlength, $\epsilon_A$, $\epsilon_B$, and $\epsilon_i$ are the molar extinction coefficients of A, B, and the $i$th complex, and $D_Z$ is the optical density of the solvent.

In the determination of the dipole moments of complexes by the Debye method the measured dielectric constants $\epsilon$ and the densities $d$ of the solution may be represented by the following functions [12]:

$$\begin{aligned} \varepsilon &= \alpha_A C_A + \alpha_B C_B + \sum_{i=1}^{n} \alpha_i C_i + \varepsilon_z, \\ d &= \gamma_A C_A + \gamma_B C_B + \sum_{i=1}^{n} \gamma_i C_i + d_z, \end{aligned} \qquad (II.3)$$

where $\alpha_A$, $\alpha_B$, $\alpha_i$ and $\gamma_A$, $\gamma_B$, and $\gamma_i$ are parameters linked to the dipole moments of the corresponding molecules by the expressions

$$P_{i,\infty} = \frac{\varepsilon_S - 1}{\varepsilon_S + 1} \cdot \frac{1}{d_S}\left(M_i - 1000\gamma_i + \frac{3000}{(\varepsilon_S + 2)^2}\alpha_i\right)$$

$$\mu_i = 0.01283\sqrt{(P_{i,\infty} - P_A - P_E)\,T}$$

Here $P_{i,\infty}$ is the molar polarisation of the substance at infinite dilution, $P_A$, and $P_E$ are the atomic and electronic polarisations (it is usually assumed that $P_A + P_E = R_i$, $R_i$ being the molar refraction of the substance for the sodium $D$ line), and $T$ is the absolute temperature.

In high-resolution NMR spectroscopy (under the conditions of rapid exchange) one usually measures the chemical shift of the averaged signal $\delta$, whose position depends on the contributions of all the components of the equilibrium mixture containing the resonating nucleus. If the molecules of A and B incorporate respectively $y$ and $z$ atoms with the resonating nucleus, then Eqn. (II.1) becomes [13,14]

$$\delta = \frac{1}{yC_{A_0} + zC_{B_0}}\left(y\delta_A C_A + z\delta_B C_B + \sum_{i=1}^{n} \delta_i C_i\right), \qquad (II.4)$$

where $\delta_A$, $\delta_B$, and $\delta_i$ are the chemical shifts of the signals due to the nuclei in the corresponding molecules.

In calorimetric measurements the amount of heat $Q$ evolved as a result of the complex formation reaction is related to the enthalpies of formation $\Delta H_i$ of the complexes from the components as follows [6-10]:

$$Q = v\sum_{i=1}^{n} \Delta H_i C_i, \qquad (II.5)$$

where $v$ is the volume of the solution (litres). It is readily seen that Eqn. (II.5) is also a special case of Eqn. (II.1) in which $x_A = x_B = 0$, $x_i = \Delta H_i$, $L = v$, and $X_Z = 0$.

The quantities $x_A$, $x_B$, and some of the $x_i$ may be zero not only in calorimetric measurements but also in studies by other physicochemical methods. For example, in spectrophotometry zero values are assumed by the parameters of those substances which have no absorption bands in the experimental frequency range; in NMR spectroscopy the characteristics of the molecules without resonating nuclei are zero.

Methods based on the measurement of colligative properties of the system are used frequently to determine the equilibrium constants. These properties are independent of the physical parameters of the molecules present in the equilibrium mixture, which makes it possible to assume that $x_A = x_B = x_i = \ldots = x_n = 1$. In this case Eqn. (II.1) becomes

$$X = L\left(C_A + C_B + \sum_{i=1}^{n} C_i\right) + X_z. \qquad (II.6)$$

This simplified form of the general equation (II.1) may be used to interpret data obtained by cryoscopic, ebullioscopic, tensimetric, gas–liquid chromatographic, etc. methods.

The concentrations of the components of the equilibrium mixture are related to the equilibrium constants of the complex formation reactions by the Law of Mass Action equations. Assuming that the test solutions or the gas mixture are ideal (the activity or fugacity coefficients are unity), the equilibrium constant of the reaction

$$pA + qB \overset{K}{\rightleftarrows} A_pB_q, \qquad (II.7)$$

can be formulated in the following form:

$$K = [A_pB_q]/[A]^p \cdot [B]^q. \qquad (II.8)$$

If the assumption of ideality is invalid, the concentrations in Eqn. (II.8) must be replaced by the activities. $K$ depends on the way in which the concentration is

expressed. At concentrations expressed on the molar scale, Eqn. (II.8) becomes

$$K = \frac{C_{A_pB_q}}{(C_A)^p (C_B)^q} \quad \text{or} \quad C_{A_pB_q} = K (C_A)^p (C_B)^q . \qquad \text{(II.9)}$$

The complex $A_pB_q$ with $p > 1$ and(or) $q > 1$ is as a rule formed in stages. The equilibrium mixture can then contain complexes having different compositions. Furthermore if the initial molecules A and B show a tendency towards self-association, then the mixture may contain also associated species of the type $A_m$ and $B_n$.[9] The stepwise formation of the complex $AB_n$ can be represented schematically thus:

$$\begin{gathered} A + B \overset{K_1}{\rightleftarrows} AB,\ C_1 = K_1 C_A C_B; \\ AB + B \overset{K_2}{\rightleftarrows} AB_2,\ C_2 = K_2 C_1 C_B = K_1 K_2 C_A C_B^2; \\ \cdots\cdots\cdots\cdots\cdots\cdots \\ AB_{n-1} + B \overset{K_n}{\rightleftarrows} AB_n,\ C_n = K_n C_{n-1} C_B = K_1 K_2 \ldots K_n C_A C_B^n . \end{gathered} \qquad \text{(II.10)}$$

The mechanism of the same reaction can be formulated as follows:

$$\begin{gathered} A + B \overset{\beta_1}{\rightleftarrows} AB,\ C_1 = \beta_1 C_A C_B; \\ A + 2B \overset{\beta_2}{\rightleftarrows} AB_2,\ C_2 = \beta_2 C_A C_B^2; \\ \cdots\cdots\cdots\cdots\cdots \\ A + nB \overset{\beta_n}{\rightleftarrows} AB_n\ C_n = \beta_n C_A C_B^n . \end{gathered} \qquad \text{(II.11)}$$

Thus we have for the stepwise formation of complexes $AB_i$

$$c_i = K_i C_{i-1} C_B = K_1 K_2 \ldots K_i c_A c_B^i = \beta_i c_A c_B^i, \qquad \text{(II.12)}$$

where $\beta_i = \prod_{l=1}^{i} K_l$ is the overall stability constant of the complex $AB_i$.

The mechanism of the involved reaction whereby the complex $A_mB_n$ is formed can be formulated, for example, as follows when account is taken of the self-association of component A:

$$\begin{gathered} A + A \overset{K_1}{\rightleftarrows} A_2,\ C_1 = K_1 C_A^2; \\ A + B \overset{K_2}{\rightleftarrows} AB,\ C_2 = K_2 C_A C_B; \\ AB + A \overset{K_3}{\rightleftarrows} A_2B,\ C_3 = K_3 C_A C_2 = K_2 K_3 C_A^2 C_B; \\ AB + B \overset{K_4}{\rightleftarrows} AB_2,\ C_4 = K_4 C_2 C_B = K_2 K_4 C_A C_B^2; \\ AB_2 + A \overset{K_5}{\rightleftarrows} A_2B_2,\ C_5 = K_5 C_4 C_B = K_2 K_4 K_5 C_A^2 C_B^2; \\ A_2B_2 + B \overset{K_6}{\rightleftarrows} A_2B_3,\quad C_6 = K_6 C_5 C_B = K_2 K_4 K_5 K_6 C_A^2 C_B^3. \\ \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots \end{gathered}$$

In the general case the equilibrium concentration of the complex formed in the $i$th stage of any involved reaction is a function of the equilibrium constant of the $i$th and preceding reaction stages and the equilibrium concentrations of the corresponding complexes in the mixture:

$$C_i = f_i (C_A, C_B, \ldots, C_1, \ldots, C_{i-1}, K_i) = \varphi_i (C_A, C_B, \ldots, K_1, \ldots, K_i). \qquad \text{(II.13)}$$

The form of the functions $f_i$ and $\varphi_i$ depends on the stoichiometry of the reaction investigated.

The most general and convenient method of representing the mechanisms of involved chemical reactions is based on their formulation with the aid of numerical matrices of stoichiometric coefficients. The most general method of such formulation has been proposed by Temkin[15] and Aris[16]. The equation for the $i$th stage of the reaction

$$p A + q B + \ldots \rightleftarrows p' E + q' D + \ldots$$

can be formulated in the following way by transferring all the terms to the left-hand side:

$$\sum_{l=1}^{m+s} \alpha_{il} A_l = 0,\ i = 1, 2, \ldots, n,$$

where $m$ is the number of reaction products, $s$ the number of reactants, $n$ the number of stages, and $\alpha_{il}$ the stoichiometric coefficient of the component $A_l$ in the $i$th reaction stage, which can be any integer (positive, negative, or zero).

The stoichiometric mechanism of an $n$-stage reaction is a matrix of integers:

$$\| \alpha_{il} \|;\ i = 1, \ldots, n;\ l = 1, \ldots, m + s. \qquad \text{(II.14)}$$

The number of columns in this matrix is equal to the number of all the substances involved in the reaction and the number of rows is equal to the number of reaction stages. If any of the reaction components does not participate in the $i$th stage, the corresponding element in the $i$th row of the matrix (II.14) is assumed equal to zero. A matrix of type (II.14) is used in the interpretation of data on the kinetics of involved chemical reactions[17-19].

An abbreviated version of the matrix (II.14) rather than the matrix itself is usually employed for complex formation reactions. If each reaction stage is formulated in terms of the dissociation of the complex into its components:

$$A_{p_i}B_{q_i}D_{r_i} \ldots \overset{\beta_i}{\rightleftarrows} p_i A + q_i B + r_i D + \ldots,$$

then part of the matrix (II.14), which is made up of the stoichiometric coefficients of the complexes, will always be an $n \times n$ unit matrix. Tobias and coworkers[20] and Sillén and coworkers[21-23] do not write out this unit matrix and formulate the reaction scheme solely in terms of the matrix of the stoichiometric coefficients of the initial components A, B, D, ...:

$$\| p_i q_i r_i \ldots \| = \| p_{il} \|\ i = 1, \ldots, n;\ l = 1, \ldots, s. \qquad \text{(II.15)}$$

A matrix of type (II.15) has been widely used in calculations of the equilibria of involved complex-formation reactions in two-component[24-29] and multicomponent[30-42] systems.

The matrix (II.15) makes it possible to formulate the equation of the Law of Mass Action in a general form[20-23]:

$$c_i = \beta_i (C_A)^{p_i} (C_B)^{q_i} (C_D)^{r_i} \ldots . \qquad \text{(II.16)}$$

We may note that the formulation of stoichiometric schemes for involved complex-formation reactions in terms of matrices of type (II.15) makes it possible to calculate only the overall equilibrium constants $\beta_1$, $\beta_2$, ..., $\beta_n$ corresponding to, for example, scheme (II.10). Another method of the matrix formulation of a stoichiometric scheme for a multistage reaction has been proposed[13,43]. It permits the determination of both the overall equilibrium constants and the constants for each stage. It is assumed that each reaction stage involves the formation of a single complex from two reactants:

$$m_{i1} D_{m_{i2}} + m_{i3} D_{m_{i4}} \overset{K_i}{\rightleftharpoons} m_{i5} D\, m_{i6}, \qquad \text{(II.17)}$$

where $m_{i1}$, $m_{i3}$, and $m_{i5}$ are the stoichiometric coefficients of the $i$th reaction, $m_{i2}$, $m_{i4}$, and $m_{i6}$ are the numbers of substances D participating in the given stage, which may be the components A, B, ... and the complexes formed in preceding stages. The substances are numbered as follows: the numbers 1, 2, ..., $s$ are assigned to the initial components A, B, ... and the numbers $i + s$ are assigned to the complexes formed in the $i$th stage. The

scheme for an $n$-stage reaction is formulated by means of a matrix of the following form:

$$M = \| m_{i1} m_{i2} m_{i3} m_{i4} m_{i5} m_{i6} \|, \; i = 1, \ldots, n, \qquad \text{(II.18)}$$

where the number of rows is equal to the number of reaction stages and the number of columns is six.

The equation of the Law of Mass Action can be written in the following form using the elements of the matrix (II.18):

$$C_i = C_{m_{i6}} = [K_i (C_{m_{i2}})^{m_{i1}} (C_{m_{i4}})^{m_{i3}}]^{1/m_{i5}}, \qquad \text{(II.19)}$$

where $C_{m_{i2}}$, $C_{m_{i4}}$, and $C_{m_{i6}}$ are the equilibrium concentrations of the corresponding substances.

It is noteworthy that, when matrices of types (II.15) and (II.18) are used, a stoichiometric reaction scheme can be usefully set up in such a way that the complex of the given composition is formed solely in one reaction stage. This makes it possible to obtain a system of independent Law of Mass Action equations[15-19].

For a complex formation reaction with participation of $s$ initial components A, B, ..., one can formulate $s$ material balance equations with respect to each component separately:

$$C_{A_0} = C_A + \sum_{i=1}^{n} p_i C_i,$$
$$C_{B_0} = C_B + \sum_{i=1}^{n} q_i C_i, \qquad \text{(II.20)}$$

where $C_{A_0}$ and $C_{B_0}$ are the overall concentrations of substances A, B, ... Equations for the calculation of $p_i$ and $q_i$ from the matrix (II.18) have been published[13,43].

Simultaneous solution of Eqns. (II.1), (II.13), and (II.20) permits the simultaneous calculation of the stability constants $K_1, \ldots, K_n$ of the complexes formed and the required parameters $x_1, \ldots, x_n$.

If the reaction investigated has $n$ stages and $s$ initial components are involved in the interaction, then one can write $n + s + 1$ equations for each $j$th experiment and the total number of equations for $N$ experiments is $N(n + s + 1)$. The unknowns which must be determined using the above system of equations are as follows: $C_A, C_B, \ldots; C_1, \ldots, C_n; K_1, \ldots, K_n; x_1, \ldots, x_n$. The total number of unknowns is $(n + s)N + 2n$. By comparing the number of equations with the number of unknowns, it is easy to determine the minimum number of experiments $N$ necessary to solve the problem formulated:

$$N \geqslant 2n. \qquad \text{(II.21)}$$

Thus even the study of complex-formation reactions with not unduly complicated stoichiometric ($n \geqslant 2$) necessitates the solution of a system of non-linear equations with a fairly large number of unknowns.

There exist various approaches to the solution of the problem of the determination of the parameters of the complexes from the results of a physicochemical experiment. In terms of mathematical procedures, they can be divided into three groups.

1. Approximate methods involving linear graphical extrapolation or a simplified analytical calculation.
2. Methods based on the exact solution of the system of equations.
3. Methods involving the search for the parameters on the basis of the statistical principle of maximum probability.

These methods of calculation will be discussed below.

Any physicochemical method permitting the determination of equilibrium constants over a temperature range can be used to determine the thermodynamic parameters of the complex formation process: $\Delta G^\circ$, $\Delta H^\circ$, and $\Delta S^\circ$. The free energy $\Delta G^\circ$, enthalpy $\Delta H^\circ$, and entropy $\Delta S^\circ$ of a given reaction under standard conditions are related to the equilibrium constants $K$ as follows:

$$\Delta G^0 = -RT \ln K = \Delta H^0 - T\Delta S^0. \qquad \text{(II.22)}$$

$\Delta H^\circ$ and $\Delta S^\circ$ are usually calculated from the relation between $\ln K$ and $1/T$ as the linear coefficients of Eqn. (II.22) written in the following form[2,5,6,44,45]:

$$\ln K = -\Delta H^0/RT + \Delta S^0/R. \qquad \text{(II.23)}$$

In principle it is not obligatory to calculate initially the equilibrium constants for each given temperature and then evaluate $\Delta H^\circ$ and $\Delta S^\circ$ from Eqn. (II.23).[46] As suggested by the present authors[47], $\Delta H^\circ$ and $\Delta S^\circ$ may be adopted as the required parameters and Eqns. (II.1), (II.13), (II.20), and (III.23) may be solved simultaneously.

In order to determine the enthalpies and entropies of formation of complexes from the temperature variation of the equilibrium constants, one usually begins with the hypothesis that $\Delta H^\circ$ and $\Delta S^\circ$ are independent of temperature. This assumption is more or less valid when $\Delta H^\circ$ and $\Delta S^\circ$ are determined from data obtained over a comparatively narrow temperature range and close to standard conditions[48]. However, in studies over a wide temperature range, where the heat capacity of the system may change significantly, one must take into account the possible temperature dependence of $\Delta H^\circ$ and $\Delta S^\circ$.[49-51] This applies particularly to tensimetric measurements, which are carried out, as a rule, at a high temperature (200° to 600°C) over a range of the order of 100–200 K.[51-53] The values of $\Delta H^\circ_T$ and $\Delta S^\circ_T$ obtained from such measurements are difficult to adjust to standard conditions owing to the lack of data for the heat capacities of the complexes.

## III. APPROXIMATE METHODS FOR THE CALCULATION OF THE PARAMETERS OF COMPLEXES BASED ON A LINEAR GRAPHICAL EXTRAPOLATION

In order to simplify the solution of the system of non-linear equations (II.1), (II.13), and (II.20), one frequently uses particular approximations or limitations are imposed on the experimental conditions. This makes it possible to convert the equations into a form convenient for the graphical determination of the required parameters.

For a single-stage complex-formation reaction, where only one complex $A_pB_q$ is formed in solution [Eqn. (II.7)], the equilibrium concentration $C_c$ and the stability constant of the latter can be expressed[1,6] in the following form on the basis of Eqns. (II.1), (II.9), and (II.20):

$$C_c = \Delta X/\Delta x, \qquad \text{(III.1)}$$

where

$$\Delta X = X - X_z - L(x_A C_{A_0} + x_B C_{B_0}) \text{ and } \Delta x = L(x_c - px_A - qx_B).$$

The above symbols ($\Delta X$ and $\Delta x$) will be used also in subsequent equations.

$$K = C_c/(C_{A_0} - pC_c)^p (C_{B_0} - qC_c)^q. \qquad \text{(III.2)}$$

For 1 : 1 complexes ($p = q = 1$), the following expression may be obtained on the basis of Eqns. (III.1) and (III.2):[6]

$$\frac{1}{K} = \frac{C_{A_0}C_{B_0}}{\Delta X}\Delta x - (C_{A_0} + C_{B_0}) + \frac{\Delta X}{\Delta x}. \qquad \text{(III.3)}$$

For highly dissociated complexes, where $C_C = \Delta X/\Delta x \ll (C_{A_0} + C_{B_0})$, the last term in Eqn. (III.3) may be neglected, which yields

$$\frac{1}{K} = \frac{C_{A_0}C_{B_0}}{\Delta X}\Delta x - (C_{A_0} + C_{B_0}). \qquad \text{(III.4)}$$

After certain rearrangements, it is easy to obtain the following relations from the simplified Eqn. (III.4):[6]

$$C_{A_0}C_{B_0}/\Delta X = (C_{A_0} + C_{B_0})/\Delta x + 1/K\Delta x, \qquad \text{(III.5)}$$

$$C_{A_0}C_{B_0}/\Delta X\,(C_{A_0} + C_{B_0}) = 1/K\Delta x\,(C_{A_0} + C_{B_0}) + 1/\Delta x. \qquad \text{(III.6)}$$

Equations of type (III.5) and (III.6) are used widely for the graphical determination of the parameters of highly dissociated molecular complexes [1,2,5,6,54-81]. According to Eqn. (III.5), based on experimental data, the plot of $C_{A_0}C_{B_0}/\Delta x$ against $(C_{A_0} + C_{B_0})$ should be a straight line whose slope is $1/\Delta x$ and the intercept on the ordinate axis is $1/K\Delta x$ (Fig. 1). Hence it is possible to obtain the values of $K$ and $\Delta x$ and to calculate $x_C = \Delta x/L + x_A + x_B$ for known values of $x_A$ and $x_B$ [see Eqn. (III.1)] with $p = q = 1$. The same parameters may be obtained when the experimental data are represented by a plot of $C_{A_0}C_{B_0}/\Delta X(C_{A_0} + C_{B_0})$ against $1/(C_{A_0} + C_{B_0})$. According to Eqn. (III.6), the plot should be a straight line which makes an intercept on the ordinate axis equal to $1/\Delta x$ and has a slope equal to $1/K\Delta x$.

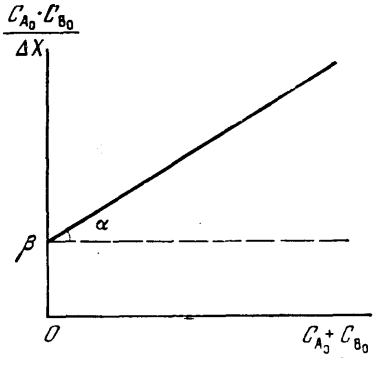



Figure 1. Determination of the parameters $x_C$ and $K$ from a linear plot corresponding to Eqn. (III.5); $\tan\alpha = 1/\Delta x_C$; $\beta = 1/K\Delta x_C$.

This method for the simultaneous determination of the stability contants and the physical parameters of 1 : 1 complexes was proposed for the first time by Benesi and Hildebrand[54] for the interpretation of spectrophotometric data. Apart from the condition $C_C \ll (C_{A_0} + C_{B_0})$, a further two conditions are imposed on the formulation of the experiment: firstly, there must be a large excess of one of the components, i.e. $C_{A_0} + C_{B_0} \simeq C_{B_0}$ and, secondly, the experiment must be carried out at a wavelength where only the complex absorbs. Under these conditions, one can obtain the following expression from Eqns. (III.4), (III.1), and (III.5):

$$C_{A_0}l/D = 1/K\varepsilon_C C_{B_0} + 1/\varepsilon_C. \qquad \text{(III.7)}$$

Under the same conditions, Eqns. (III.6) readily yield Scott's equation[55]:

$$C_{B_0}C_{A_0}l/D = C_{B_0}/\varepsilon_C + 1/K\varepsilon_C. \qquad \text{(III.8)}$$

Subject to the condition $C_{A_0} = \text{const.}$, Foster and coworkers[5,56] obtain the equation

$$D/C_{B_0} = -KD + KC_{A_0}\varepsilon_C. \qquad \text{(III.9}$$

from the Benesi–Hildebrand equation. According to Eqn. (III.9), $K$ and $\epsilon_C$ may be determined from a linear plot of $D/C_{B_0}$ against $D$, whose slope is $-K$ and whose intercept on the ordinate axis is $KC_{A_0}\epsilon_C$.

Together with its various modifications, the Benesi–Hildebrand method has been used widely in the interpretation of not only spectrophotometric data[5,6,54-72] but also of results obtained by other physical methods: NMR [5,6,72-79] calorimetry[5,6,8,9], dielectric measurements[6,8], etc.

Graphical methods for the simultaneous determination of $K$ and $x_C$, based on equations of type (III.5)–(III.9), suffer from significant disadvantages, which have been widely discussed in the literature[5,6,8,9,58-73,81]. These are primarily the restriction of their application solely to systems where one 1 : 1 complex AB is formed, i.e. where $p = q = 1$. With increase of $p$ and $q$, the degree of Eqn. (III.2) increases, which makes it virtually impossible to convert it into a form permitting the construction of linear plots.

Furthermore, the use of equations of type (III.5)–(III.9) yields satisfactory results only subject to the condition $C_C \ll (C_{A_0} + C_{B_0})$. However, in order to test the validity of this condition, it is necessary to know at least the order of magnitude of $K$; such information is as a rule lacking in the study of new types of complexes. Significant errors in the determination of $K$ and $x_C$ may arise owing to the possible formation in the test system of complexes having compositions other than 1 : 1.

Certain methods of improving the accuracy of the required parameters of the complexes A and B when the use of Eqns. (III.5)–(III.9) leads to large errors for one reason or another have been proposed in a number of studies [82,83]; sometimes attempts were made to employ a computer in order to introduce appropriate corrections [84-86]. For example, in a study of fairly stable 1 : 1 complexes, Tamres and coworkers[82] suggested the use of linear regression models and an iterative procedure in order to refine with the aid of a computer the parameters $K$ and $x_C$ obtained from approximate relations. Such ways of developing computational methods involving the use of approximate equations with subsequent refinement of the parameters obtained are apparently irrational. If the approximations adopted do not satisfy the experimental conditions, it is necessary to employ more rigorous computational methods.

In order to determine the compositions and parameters of complexes $A_pB_q$ which are relatively little dissociated in solution [reaction (II.7)], graphical extrapolation of linear sections of curves obtained by the molar ratios (titration) or continuous variations (isomolar series [1,2,6,

[12,87,88]) methods is used widely. One then begins with the assumption that the linear sections of $X-C_{B_0}/C_{A_0}$ titration curves (with $C_{A_0}$ = const.; see Fig. 2) or $X-C$ isomolar series curves, where $C = C_{A_0}/(C_{A_0} + C_{B_0})$ (with $C$ = const.; see Fig. 3), correspond to complete binding, i.e. a complete displacement of equilibrium (II.7). This eliminates the necessity for the employment of the non-linear Law of Mass Action equation (II.9) in order to estimate the equilibrium concentrations of the mixture components, which are related solely by the material balance equations (II.20). The composition of the complex and its parameter $x_C$ can be found by extrapolating the linear sections of the experimental curve on the basis of the so-called point of "equivalence" [6] (see Figs. 2 and 3). Knowing $x_C$ it is possible to calculate by Eqns. (II.1) and (III.2) the equilibrium constant for the given reaction from data referring to the part of the experimental curve where the complex dissociates into components (sections KL in Figs. 2 and 3).

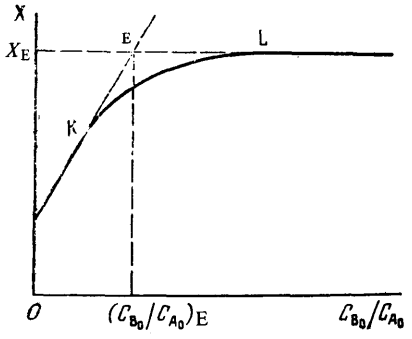



Figure 2. Determination of the composition and parameters of complexes $A_pB_q$ by the titration method. At the equivalence point E we have $(C_{A_0}/C_{B_0})_E = p/q$ and $x_C = (X_E - X_Z)p/L(C_{A_0})_E = (X_E - X_Z)q/L(C_{B_0})_E$. Along the section KL of the experimental curve, the complex dissociates into components.

A common disadvantage of the method based on linear graphical extrapolation is the absence of a reliable criterion which would make it possible to infer that the condition of the formation in the system of only one complex, which has been adopted in this procedure, does indeed hold. The linearity of sections of the curve, frequently adopted as evidence for the validity of the assumptions made, cannot be regarded as a sufficiently reliable criterion, because, owing to the scatter of experimental points on the graphs, one cannot always detect the curvature which might be a sign of the formation of more than one complex in the system [6,84,85].

If several complexes having different compositions are formed simultaneously in the system, the problem of the determination of their parameters becaomes extremely more complex. The conversion of the computational equations into a form suitable for linear graphical extrapolation or calculation by hand then requires even more drastic approximations than those quoted above for single-stage reactions. In the interpretation of the results of the study of multistage complex-formation reactions it is frequently assumed that, under particular experimental conditions, the solution or vapour contains mainly only one of the complexes formed [1,2,6,12,89-99]. However, this hypothesis can be valid only in relation to complexes with limiting compositions, i.e. complexes containing the maximum or minimum number of the molecules of A and B. The latter is sometimes achieved in the presence of a large excess of the corresponding initial component.

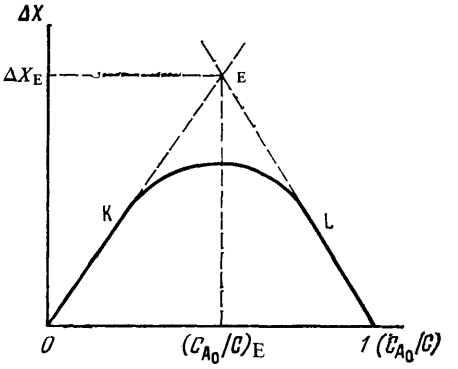



Figure 3. Determination of the compositions and parameters of complexes $A_pB_q$ by the method of continuous variations ($C_{A_0} + C_{B_0} = C$ = const.); at the equivalence point we have $p/q = (C_{A_0}/C)_E/[1 - (C_{A_0}/C)_E]$ and $x_C = \Delta X_E(p + q)/CL$. Along the section KL, the complex dissociates into components.

The available approximate methods for the interpretation of the results of the study of multistage complex-formation reactions are as a rule extremely cumbersome and insufficiently reliable [1,2,6,12,89-95]. We believe that the use of a computer in order to simplify and refine approximate methods of calculation [90,91,98,99] is undesirable, because computer technology permits a rigorous solution of the problems under consideration.

## IV. METHODS FOR THE DIRECT SOLUTION OF THE SYSTEM OF EQUATIONS RELATING THE PARAMETERS OF COMPLEXES TO EXPERIMENTAL DATA

Owing to the approximations adopted in the derivation of the corresponding equations, the linear graphical extrapolation methods discussed in the previous section are applicable solely in the study of either comparatively weak or extremely strong complexes. The interpretation of the results of the physicochemical study of complexes of the most common type, i.e. with moderate stabilities, requires the use of more rigorous computational methods.

For single-stage complex-formation reactions, methods for the solution of the system of four equations, comprising Eqns. (II.1), (II.9) and two equations (II.20) without

the introduction of any approximations, have been examined[100-118]. Simultaneous solution of these four equations eliminates the equilibrium concentrations of mixture components, which depend on the experimental conditions ($c_A$, $c_B$, $c_C$), and yields only one equation [Eqn.(IV.1)], which contains two unknowns ($x_C$ and $K$) and the experimental data ($X$, $C_{A_0}$, and $C_{B_0}$):

$$K = \frac{\Delta X/\Delta x}{(C_{A_0} - p\Delta X/\Delta x)^p (C_{B_0} - \Delta X/\Delta x)^q}. \qquad (IV.1)$$

In principle, the solution of two equations (IV.1) for two experimental points makes it possible to find the parameters $x_C$ and $K$.[100] However, the possible experimental errors necessitate the determination of the parameters $x_C$ and $K$ on the basis of data referring to a number of experimental points significantly larger than two. It is necessary to solve a system of non-linear equations (IV.1) for all the pairs of experimental points[100-105]. This method of solution is extremely cumbersome and in practice is possible only with the aid of a computer[100,102]. For the simplest case with $p = q = 1$, methods have been proposed[106-116] for the determination of the parameters $x_C$ and $K$ which replace the procedure involving the solution of a system of non-linear equations (IV.1). Having specified an arbitrary set of values of one of the parameters to be determined, the second parameter is determined from experimental data. Eqns.(IV.1) are then written in a form convenient for the calculation of one parameter from the specified values of the other:

$$K = \frac{\Delta X/\Delta x}{(C_{A_0}\Delta x - \Delta X)(C_{B_0}\Delta x - \Delta X)}, \qquad (IV.2)$$

$$x_K = x_A + x_B + \frac{\Delta X}{2L}/(R - \sqrt{R^2 - 4C_{A_0}C_{B_0}}), \qquad (IV.3)$$

where $R = C_{A_0} + C_{B_0} + 1/K$.

The solution of the problem is found by studying the relation $K = f(x_C)$ or $x_C = f'(K)$, or $K = \varphi(C_{A_0}, C_{B_0})$, or $x_C = \varphi'(C_{A_0}, C_{B_0})$. Bearing in mind that the system must have a unique solution for $x_C$ and $K$, these parameters can be found graphically from the coordinates of the points of intersection of the lines of the $K = f(x_C)$ or $x_C = f'(K)$ series, plotted for each experimental point[106].

Since the equilibrium constants and the physical parameters of the complexes are independent of the experimental conditions, $K$ and $x_C$ may be found by varying arbitrarily one of the parameters until a value is obtained for which the second parameter remains constant regardless of the initial concentrations $C_{A_0}$ and $C_{B_0}$.[114-116] The last pair of values of $x_C$ and $K$ is a solution of the problem.

Olofson and coworkers[117,118] proposed a method for the solution of Eqn.(IV.1) with $p = q = 1$ on a computer. Eqn. (IV.1) is written as follows:

$$\frac{C_{A_0}C_{B_0}}{\Delta X}\Delta x - (C_{A_0} + C_{B_0} + 1/K) + \frac{\Delta X}{\Delta x} = \varphi_j = 0. \qquad (IV.4)$$

Values of $x_C$ and $K$ for which the functions $\varphi_j$ become zero are solutions of Eqn.(IV.4). Owing to experimental errors, the required parameters are found from the pair of values of $x_C$ and $K$ corresponding to the minimum in the function $\sum_{j=1}^{N} |\varphi_j|$, where $j$ and $N$ are the ordinal number of the experiment and the total number of experiments respectively. For complexes $A_pB_q$ with compositions more complex than 1 : 1, the use of such procedures in order to solve equations of type (IV.4) involves considerable difficulties owing to the increasing degree of Eqn.(IV.1).

A method has been proposed[119] for the solution of Eqns. (IV.1) for complexes $A_pB_q$ with any values of $p$ and $q$ by means of the following equation:

$$x_C = px_A + qx_B + \frac{\Delta X}{2LC_{A_0}} \frac{a \pm \sqrt{a^2 - 4bC_{A_0}\Delta X'(q\Delta X - C_{B_0}\Delta X')}}{q\Delta X - C_{B_0}\Delta X}, \qquad (IV.5)$$

where $a = [p(p-1)C_{B_0} + q(q-1)C_{A_0}]\Delta X' + pq\Delta X$,
$b = pq(p+q+1)$, $\Delta X' = (\partial X/\partial C_{B_0})_{C_{A_0}} - x_B L$.

Eqn.(IV.5) was obtained by differentiating Eqn.(IV.1) with respect to $C_{B_0}$ subject to the condition $(\partial K/\partial C_{B_0})C_{A_0} = \text{const.} = 0$. The derivative $(\partial X/\partial C_{B_0})C_{A_0}$ in Eqn.(IV.5) may be found from the experimental dependence of $X$ on $C_{B_0}$ by any of the known methods for the determination of a derivative with respect to a specified function. Knowing $x_C$, it is easy to calculate $K$ from Eqn.(IV.1). Such calculations may be performed also by hand, but this requires a considerable amount of time. A program has been devised[43] for calculations by Eqn.(IV.5) on a Minsk-22 (or Minsk-32) computer. The derivatives $(\partial X/\partial C_{B_0})C_{A_0}$ are then calculated by fitting a second-degree polynomial to sections of the experimental $X - C_{B_0}$ curve[43,120]. The use of a computer greatly reduces the time required for calculation.

In the general case of an $n$-stage complex-formation reaction, the number of equations is $n + 3$: one equation (II.1), $n$ equations (II.9), and two equations (II.20). When the equilibrium concentrations of the mixture components ($C_A$, $C_B$, ..., $C_1$, ..., $C_n$) are eliminated by the simultaneous solution of these equations, then in principle it is possible to obtain one equation relating the parameters of the complexes $x_1$, ..., $x_n$, $K_1$, ..., $K_n$ to be determined to the experimental $X$, $C_{A_0}$, $C_{B_0}$ data. Simultaneous solution of the system of equations for $2n$ experiments makes it possible to find all $2n$ unknowns.

However, with increase of the number of reaction stages and of the complexity of the composition of the complexes formed, there is an increase not only of the number of equations to be solved simultaneously but also of their degree. As a result of this, the rearrangements associated with the elimination of equilibrium concentrations from Eqns.(II.1), (II.9), and (II.20) become much more laborious. Even in the simplest case involving the simultaneous formation of only two complexes, having 1 : 1 and 1 : 2 compositions, the solution of a system of not less than four cubic equations is necessary[100,124,125]. There are no literature data concerning the use of such procedures for the interpretation of the results of studies on complex-formation reactions involving more than three stages[100,121-125].

Thus the procedure involving the direct solution of a system of non-linear equations, particularly in the study of multistage complex-formation reactions (even with the aid of a computer), appears to be relatively unsuitable, primarily because of its extremely cumbersome nature. For a rigorous determination of the parameters of the complexes from physicochemical experimental data, it is apparently more rational to employ computational methods based on the statistical principle of maximum probability.

## V. METHODS OF CALCULATION BASED ON THE STATISTICAL PRINCIPLE OF MAXIMUM PROBABILITY

Methods of computer calculations based on the principle of maximum probability[126] consist in seeking a set of parameters $x_1$, ..., $x_n$, $K_1$, ..., $K_n$ to be determined

which gives the best description of the experimental data, i.e. the dependence of the measured property of the solution (or vapour) $X$ on the initial concentrations $C_{A_0}$, $C_{B_0}$, ... In essence, all these methods reduce to seeking a minimum in the function reflecting the deviation of the experimental quantities $X_{exp}$ from the values $X_{calc}$ calculated by Eqns. (II.1), (II.13), and (II.20) using arbitrarily specified and varied values of the required parameters [127]. The principle of least squares, which is most widely used in such calculations, yields fairly reliable results [12-14,20-47,128-203].

Methods of calculation in accordance with the principle of least squares involve the seeking of a minimum in the function

$$F = \sum_{j=1}^{N} (X_{exp\,j} - X_{calc\,j})^2. \qquad (V.1)$$

The calculation of the quantity $F$ [Eqn. (V.1)] from the specified set of parameters $x_1, \ldots, x_n, K_1, \ldots, K_n$ consists of three stages.

1. Starting with the specified equilibrium constants $K_1, \ldots, K_n$ and the experimental values of $C_{A_0 j}$ and $C_{B_0 j}$, one calculates the equilibrium concentrations of all the mixture components $C_A, C_B, \ldots, C_1, \ldots, C_n$ by the simultaneous solution of the system of non-linear Law of Mass Action equations (II.13), (II.15), or (II.19) and the material balance equations (II.20).

2. Using the values of $C_A, C_B, \ldots, C_1, \ldots, C_n$ obtained and the specified set of physical parameters of the complexes $x_1, \ldots, x_n$, the values of $x_{calc\,j}$ are calculated from the linear equations (II.2)-(II.6) or (II.1).

3. Having determined the $X_{calc\,j}$ for all the $N$ experiments and using the corresponding values of $X_{exp\,j}$, one calculates $F$ by Eqn. (V.1).

By varying the arbitrarily specified set of parameters $x_1, \ldots, x_n, K_1, \ldots, K_n$, one finds a minimum in the function $F$. As a first approximation, one can use parameters obtained with the aid of approximate methods of calculation. The set to which corresponds a minimum in $F$ is regarded as a probable set of parameters $x_1, \ldots, x_n, K_1, \ldots, K_n$ to be determined.

In order to find the minimum in the function $F$ of $2n$ variables, various methods for seeking an extremum in a function are used [17,204-212]. In particular, in the study of single-stage processes, the simplest method of "trial and error" is sometimes employed [141,142,177,179,195]. The method of successive sorting of variables and the method of "descents along coordinates" are frequently used [147,157,174-176,189]. At the same time, various types of iterative procedures are widely employed to seek the minimum in the function $F$: gradient methods [33-36,134], Newton's method and its versions (the Newton-Raphson method [14,21-25,37-39] and the Gauss-Newton method [20,27,30-32,40,152,160]), and the Davidson-Fletcher-Powell (DFP) method [41,165].

The function $F$ [Eqn. (V.1)] is "pit-like" [210-212], i.e. near the minimum it is represented by an extended narrow "pit". For this reason, in seeking the minimum in $F$ one frequently employs special so-called "pit mapping" methods [13,43,47,156]. The possibilities and disadvantages of various methods used in seeking the minimum in $F$ are compared in the Table.

The derivatives $\partial F/\partial x_i$ and $\partial F/\partial K_i$ required in the search for the minimum in $F$ are usually calculated by the approximate finite difference method [17,204]. A method involving a rigorous analytical calculation of these derivatives with the aid of Jacobi matrices has been proposed [13,43]. The minimum in $F$ may be sought both with respect to all $2n$ variables [155-157,161,176,195] and with respect to $n$ variables $K_1, \ldots, K_n$ [12-14,22,25,141,147,165-170,185,189].

The fact that the parameters $x_1, \ldots, x_n$ enter into Eqns. (II.1)-(II.6) as coefficients of the equilibrium concentrations of the complexes $c_1, \ldots, c_n$ makes it possible to reduce the number of variables with respect to which the search is made from $2n$ to $n$. This leads to the possibility of calculating, by the method of least squares which is applicable to linear equations [213], the parameters $x_1, \ldots, x_n$ giving the best description of the experimental data for a specified set of $K_1, \ldots, K_n$ [10,13].

Comparison of the methods for seeking the minimum in $F$.

| No. | Method | Advantages of method | Disadvantages of method |
|---|---|---|---|
| 1 | Construction of networks of schematic maps (tabulation) | Method is complete and accurate | Requires much computer time |
| 2 | Newton-Raphson method | Method requires little computer time | Method does not distinguish saddle points and minima. The quadratic approximation method can be both positively and negatively defined. The region of convergence is small |
| 3 | Gauss-Newton method | Method locates only minima. The quadratic approximation matrix is always positively defined. The region of convergence is larger than in method 2 | Method requires more computer time than method 2. |
| 4 | Davidon-Fletcher-Powell (DFP) method | Method locates only minima. The region of convergence is larger than in methods 2 and 3 | Method requires approximately 25% more computer time than method 2. Its computation algorithm is more complex |
| 5 | "Pit mapping" method | Method locates only minima. The region of convergence is larger and the "ravine" direction is better defined than in methods 2, 3, and 4. The method requires a smaller amount of computer memory | Method requires more computer time. Near the minimum its execution is slower than that of methods 2, 3, and 4 |

The required parameters $x_1, \ldots, x_n$ and $K_1, \ldots, K_n$ may differ significantly in magnitude, which complicates the search for the minimum in $F$ and frequently requires a special scaling procedure, which is extremely difficult for the $K_i$ [129-131]. In addition, in seeking $F_{min}$ some of the values of $K_1, \ldots, K_n$ may fall within the region of negative values, which has no physical significance and this also complicates the search for $F_{min}$ and requires the use of a special computational algorithm [129,130]. The use of the $\ln K_i$ instead of the $K_i$ as the mapping variables makes it possible to overcome these difficulties [10,12,13,20,23].

In the calculation of the equilibrium concentrations $C_A, C_B, \ldots, C_1, \ldots, C_n$ from the specified $K_1, \ldots, K_n$ the system of equations consisting of $n$ non-linear Law of Mass Action equations and $s$ material balance equations (see Section II) is reduced by simultaneous solution to $s$ equations with $s$ unknown $C_A, C_B, \ldots$ On solving the resulting system of $s$ non-linear equations by one or other iterative procedure [214-216], the values of $C_A, C_B, \ldots$ are found; Newton-Raphson procedure, which is fastest, is most frequently employed for this purpose [22,27,43,215]. It has been suggested in a number of studies [12,22,43]

that a satisfactory initial approximation to $C_A$, $C_B$, ... required for the iterative method be calculated on a computer for each $j$th experiment by means of special algorithms. On the basis of the values of $C_A$, $C_B$, ... obtained, the equilibrium concentrations of the complexes $C_1$, $C_2$, ..., $C_n$ are calculated with the aid of the Law of Mass Action equations. The algorithms proposed in the literature for the calculation of equilibrium concentrations are frequently based on the employment of Law of Mass Action equations (II.13) in which the functions $f_i$ or $\varphi_i$ assume different forms depending on the stoichiometry of each stage of the given reaction. This approach requires the development of individual programs for different types of complex-formation reactions [141-146,153-155,161,173-190,202].

A unique program, applicable to any involved complex-formation reaction, can be devised by resorting to the matrix formulation of the reaction stoichiometry and correspondingly to the Law of Mass Action equations expressed in form (II.15) [14,20-42,156,165,166] or (II.18).[13,43,47,168-170,191,194]

Complexes are studied by various physical methods, so that procedures for the interpretation of experimental results in terms of the principle of least squares and on the basis of specific equations of type (II.2)-(II.6), applicable only to each specific physical method separately, have been developed extensively. Methods have been described for the interpretation of the results of calorimetric [25,28,33,38,161-173], spectrophotometric [22,141-160],

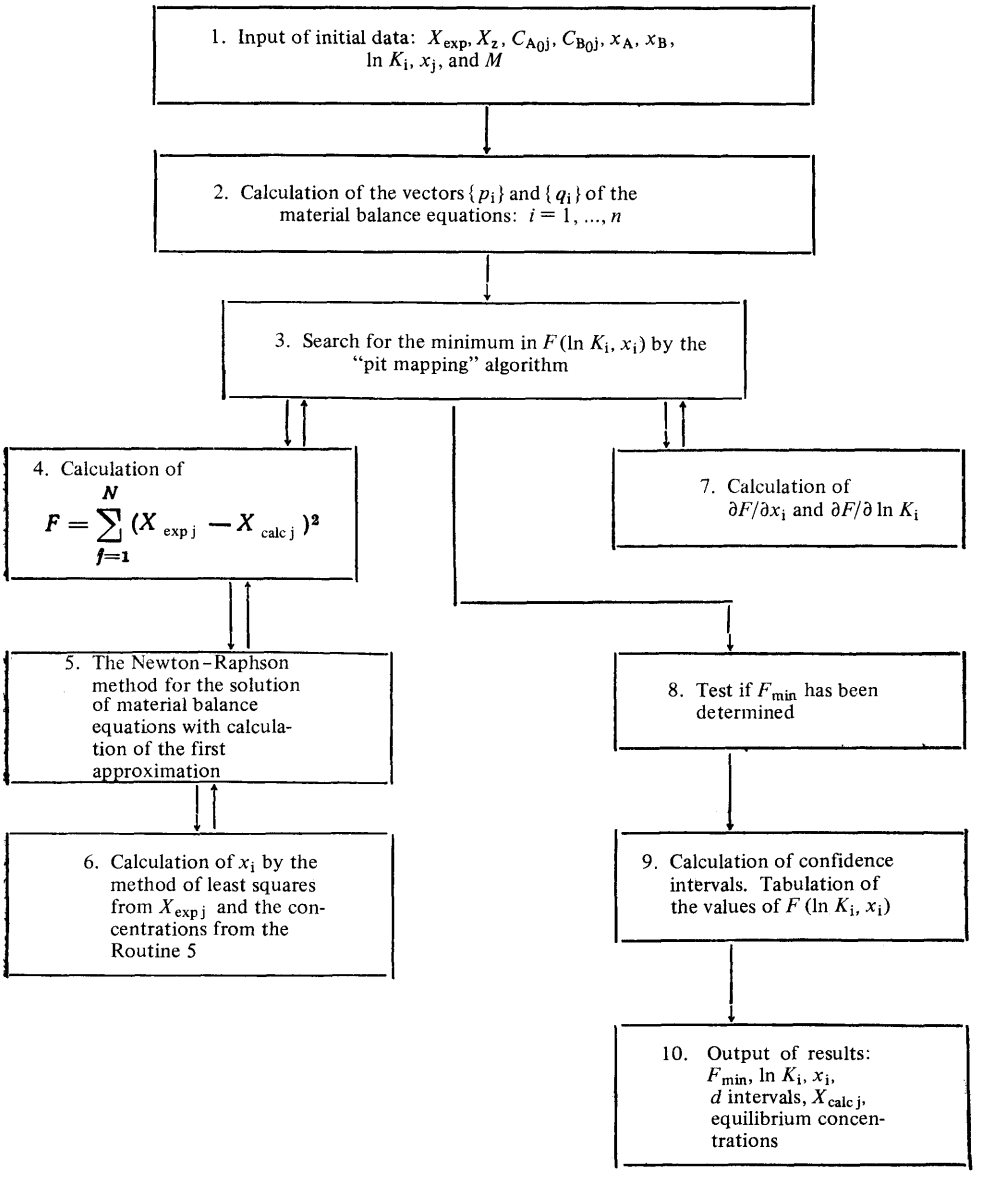



**Figure 4.** Flow diagram of the computer program for the calculation of the parameters of complexes.

NMR,[14,174-191] dielectric constant[12,192-196], potentiometric[20-23,26-36,39-42,128-140], tensimetric[197-201], and cryoscopic[24,202] measurements. Thus, when several methods are used, a whole library of programs is required. It appears more rational to develop general programs applicable to any research technique.

Such a program, consisting of individual routines, each of which can be used when necessary and can be supplemented by other routines, was proposed for the first time by Sillén and Ingri[22-25,129-131]. A more general and convenient program has been proposed by the present authors[13,43]. The program is based on the general functional relation (II.1), which, as shown above (Section II), is applicable with adequate approximation to the majority of physical methods which are most informative and most widely used in the study of complexes.

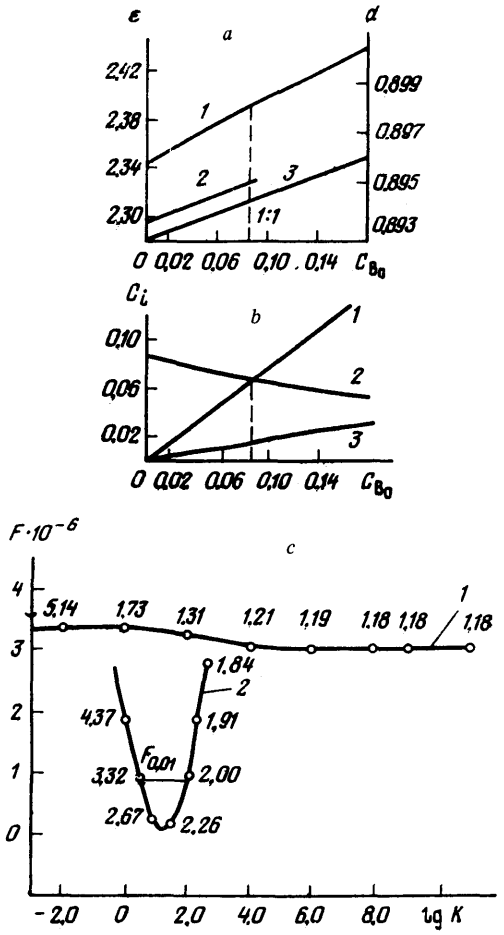



Figure 5. *a*) Experimental $\epsilon - C_{B_0}$ (curves *1* and *2*) and $d - C_{B_0}$ (curve *3*) plots; $B = (C_6H_5)_2S$ [$C_{A_0}$: 1) and 3) 0.085; 2) 0.028]; *b*) equilibrium concentration distribution diagram [1) $(C_6H_5)_2S$; 2) $TeCl_4$; 3) $TeCl_4.(C_6H_6)_2S$; $C_{A_0} = 0.085$]; *c*) $F = \ln K$ tabulation graphs for a dielectric constant study of the reaction $TeCl_4 + (C_6H_5)_2S \overset{K}{\rightleftharpoons} TeCl_4.(C_6H_5)_2S$ in benzene [$C_{A_0}$: 1) 0.028; 2) 0.085]; $\ln K = 1.25 \pm 0.75$; $\alpha = 2.4 \pm 0.4$; the numerals opposite the points in the figure represent the values of $\alpha$; $F_{0.01}$ is the $F$ level for $p = 0.01$.

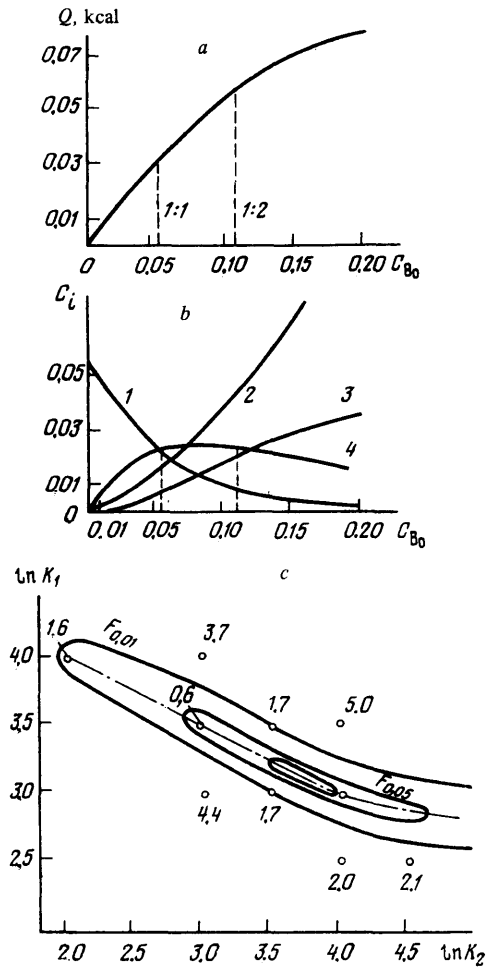



Figure 6. *a*) Experimental $Q - C_{B_0}$ curve; B = (iso-$C_4H_9)_2SO_2$; *b*) equilibrium concentration distribution diagram ($C_{A_0} = 0.055$) [1) $SnCl_4$; 2) (iso-$C_4H_9)_2SO_2$; 3) $SnCl_4.2$(iso-$C_4H_9)_2SO_2$; 4) $SnCl_4.$(iso-$C_4H_9)_2SO_2$; *c*) $10^{-6} F$ tabulation plot in the $\ln K_1 - \ln K_2$ plane for a calorimetric study of the reactions $SnCl_4 + (iso\text{-}C_4H_9)_2SO_2 \overset{K_1}{\rightleftharpoons} SnCl_4.(iso\text{-}C_4H_9)_2.SO_2$ and $SnCl_4.(iso\text{-}C_4H_9)_2SO_2 + (iso\text{-}C_4H_9)_2SO_2 \overset{K_2}{\rightleftharpoons} SnCl_4.2(iso\text{-}C_4H_9)_2SO_2$ in benzene; $F_p$ are the $F$ levels for $p = 0.01$ and 0.05.

A general computational algorithm was developed on the basis of the general equation for the measured property [Eqn. (II.1)], the matrix formulation of the stoichiometric reaction scheme [Eqn. (II.18)], and the "pit mapping" procedure for seeking the minimum in the function $F$.

It makes it possible to employ a single program in order to interpret the results of studies on various types of complex-formation reactions by ultraviolet and NMR spectroscopic methods, dielectric measurements, and calorimetric, cryoscopic, and any other methods for which the measured property obeys the rule of additivity of contributions. A brief flow diagram of the program is illustrated in Fig. 4. Together with the parameters $x_1, \ldots, x_n, K_1, \ldots, K_n$ to be determined, the program generates the minimum in $F$ ($F\min$), the values of $X\,\text{calc}$, and the equilibrium concentrations of the components corresponding to all the points on the experimental curve. The values of $C_A, C_B, \ldots, C_i, \ldots, C_n$ at each point on the experimental $X = f(C_{A_0}, C_{B_0})$ curve can be used to plot diagrams illustrating the distribution of the equilibrium concentrations (Figs. 5*b*, 6*e*, and 7*b*). The values of $X\,\text{calc}\,j$ make it possible to compare clearly (graphically) the experimental results with the calculation (Figs. 5*a*, 6*a*, and 7*a*). $F\min$ is used to estimate the reliability of the results obtained.

The determination of the parameters $x_1, \ldots, x_n, K_1, \ldots, K_n$ by seeking the minimum in $F$ is not the final stage of the calculation. A necessary condition for the solution of problems on the basis of the statistical principle of maximum probability is the estimation of the reliability of the results. This is particularly important when the functions $X$ are non-linear [Eqn. (II.1)] and when $F$ [Eqn. (V.1)] can have several minima and only one of these must correspond to a unique solution of the problem. Various procedures have been described in the literature [13,33,43,129,161,164] for describing the reliability of the parameters of the complexes obtained. It has been suggested [13,43] that the Fischer statistic be used:

$$\sigma^2/\sigma^2_{\text{exp}} \leqslant F_{\nu_1,\nu_2,p}, \qquad \text{(V.2)}$$

where $\sigma$ and $\sigma_{\text{exp}}$ are the variances of the calculation and the experiment respectively, $\nu_1$ and $\nu_2$ are the numbers of degrees of freedom in the numerator and denominator of Eqn. (V.2), and $p$ is the level of significance of the statistic. This statistic is fairly well founded only for linear problems [126,217–220], but, owing to the lack of other statistics, it is usually employed also for non-linear relations.

The quantity $\sigma$ may be calculated from $F\min$:

$$\sigma^2 = F_{\min}/(N-2n). \qquad \text{(V.3)}$$

On the basis of Eqns. (V.2) and (V.3), we obtain the condition for the reliability of the results:

$$F_{\min} \leqslant F_{\nu_1,\nu_2,p}\sigma^2_{\text{exp}}\,(N-2n),$$

or

$$\tau = F_{\min}/[F_{\nu_1,\nu_2,p}\sigma^2_{\text{exp}}\,(N-2n)] \leqslant 1. \qquad \text{(V.4)}$$

The validity of condition (V.4) shows that the proposed stoichiometric reaction scheme and the parameters $x_1, \ldots, x_n, K_1, \ldots, K_n$ obtained correspond to the true values with a probability close to $1-p$, where $p$ is the chosen level of significance (usually $p = 0.01$, 0.05, and 0.5). When the reaction stoichiometry has been incorrectly formulated, the condition (V.4) is not as a rule fulfilled [43,47,168–170,194,221]. Thus the above criterion of reliability can be used to establish the stoichiometry of the reaction investigated.

The confidence limits serve as an indication of accuracy. The determination of confidence limits for $x_1, \ldots, x_n$ and $K_1, \ldots, K_n$ is a fairly complex task. In a number of studies [27,33,36,129,155–157,163] the confidence limits are determined using the information matrix [126,217–220], which is constructed on the basis of the quadratic approximation to the function $F$ at the minimum.

A more rigorous procedure for estimating the confidence limits for the parameters to be determined involves the construction of confidence regions using the Fischer statistics [13,43]. The confidence region ($d$ region) is made up of all the sets of parameters satisfying the condition

$$F(x_1, \ldots, x_n, K_1, \ldots, K_n) \leqslant F_{\nu_1,\nu_2,p}\sigma^2_{\text{exp}}\,(N-2n). \qquad \text{(V.5)}$$

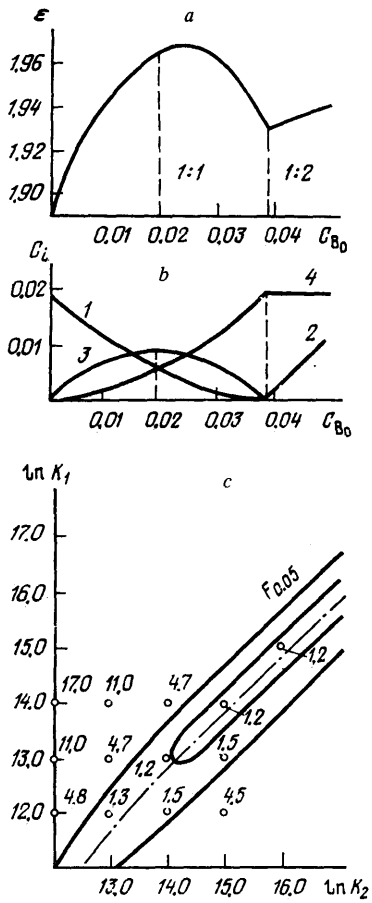



**Figure 7.** *a*) Experimental $\epsilon - C_{B_0}$ curve; B = $(C_4H_9)_3PO$; *b*) equilibrium concentration distribution diagram ($C_{A_0}$ = 0.019) [1) $SnCl_4$; 2) $(C_4H_9)_3PO$; 3) $SnCl_4.(C_4H_9)_3PO$; 4) $SnCl_4.2(C_4H_9)_3PO$]; *c*) $10^{-5}$ $F$ tabulation graph in the $\ln K_1 - \ln K_2$ plane for a dielectric constant study of the reactions $SnCl_4 + (C_4H_9)_3PO \overset{K_1}{\rightleftharpoons} SnCl_4.(C_4H_9)_3PO$ and $SnCl_4.(C_4H_9)_3PO + (C_4H_9)_3PO \overset{K_2}{\rightleftharpoons} SnCl_4.2(C_4H_9)_3PO$ in hexane; $F_{0.05}$ is the $F$ level for $p = 0.05$.

The true values of the parameters are located with a probability $\sim(1-p)$ within the limits of this region. The standard deviations for the parameters found (the set corresponding to $F\min$) are obtained from the largest and smallest values of each of the required parameters in the $d$ region.

*d* regions can be constructed by a tabulation procedure, i.e. one involving the calculation of $F$ for a series of values of the required parameters varying within the specified region in specified steps. For $n \leq 2$, it is possible to construct tabulation graphs (Figs. 5*c*, 6*c*, and 7*c*) and find the confidence regions by plotting lines corresponding to constant values of $F$ for each of the selected levels of significance. The same procedure can be used to investigate the behaviour of the functions $F$ in the particular region of variation of the mapping variables [13,43,221]. It is noteworthy that the dimensions of the confidence regions and correspondingly of the confidence limits for the parameters obtained are greater the less sensitive the function $F$ to changes in the mapping variables [43,221-225]. The sensitivity of $F$ to mapping variables depends on the amount of information yielded by the experiment [43,225] and, in particular, on the choice of the initial concentrations $C_{A_0}$ and $C_{B_0}$ (see, for example, Fig. 5*c*, curves I and II, and Figs. 6*c* and 7*c*).

Thus the reliability of the results depends both on the reliability of the method of calculation and on the correct formulation of the experiment. Mathematical experimental design methods [223-226] make it possible, in principle, to select the optimum conditions for the experiment. In problems of the determination of the stoichiometric scheme and of the physicochemical parameters of complexes, a successive design is most suitable. It can be achieved in two ways: (1) design for refining the values of the required parameters for a known stoichiometry; (2) design for refining and selecting stoichiometric reaction schemes [224]. It is noteworthy that in problems of the type under consideration mathematical experimental design has not yet found sufficiently extensive applications [224,226].

In the study of two-component systems mathematical treatment of the first series of titration curves and analysis of equilibrium concentration distribution diagrams as a rule make it possible to select the concentration conditions for yet another one or two series of experiments and to obtain fairly reliable results by treating all the experimental data together [43,169,170,221,225].

An effective criterion of the reliability of the physicochemical parameters determined is a satisfactory agreement between the stoichiometric schemes for complex-formation reactions and equilibrium constants for individual stages obtained in the mathematical treatment of the results of studies of the same reactions by several physical methods [6,13,43,155,169,170].

In conclusion it must be emphasised that the development of methods for the mathematical and statistical treatment of experimental results greatly extends the scope of physicochemical studies of complex-formation reactions. In particular the study of multistage reactions and multicomponent systems became possible only after the development of the corresponding computational methods.

## REFERENCES


1. F.J.C.Rossotti and H.S.Rossotti, "Determination of Stability Constants and Other Equilibrium Constants in Solution" (Translated into Russian), Izd. Mir, Moscow, 1965.
2. M.T.Beck, "Chemistry of Complex Equilibria" (Translated into Russian), Izd. Mir, Moscow, 1973.
3. G.L.Shlefer, "Kompleksoobrazovanie v Rastvorakh" (Complex Formation in Solutions), Izd. Khimiya, Moscow-Leningrad, 1964.
4. J.Rose, "Molecular Complexes", Pergamon Press, Oxford, 1967.
5. R.Foster, "Organic Charge-Transfer Complexes", Acad. Press, London-New York, 1969.
6. E.N.Gur'yanova, I.P.Gol'dshtein, and I.P.Romm, "Donorno Aktseptornaya Svyaz'" (The Donor-Acceptor Bond), Izd.Khimiya, Moscow, 1973.
7. F.J.Rossotti, M.S.Rossotti, and R.J.Whewell, J.Inorg.Nuclear Chem., 33, 2051 (1971).
8. L.Lamberts, Ind.Chim.Belg., 36, 347 (1971).
9. D.V.Fenby and L.G.Hepler, Chem.Soc.Rev., 3, 193 (1974).
10. J.J.Christensen, J.Ruckman, D.J.Eatough, and R.M.Izatt, Thermochim.Acta, 3, 203 (1972).
11. A.I.Brodskii, V.D.Pokhodenko, and V.S.Kuts, Uspekhi Khim., 39, 753 (1970) [Russ.Chem.Rev., No.5 (1970)].
12. I.P.Gol'dshtein, E.S.Shcherbakova, E.N.Gur'yanova, and L.A.Muzychenko, Teor.Eksper.Khim., 6, 634 (1970).
13. E.S.Shcherbakova, I.P.Gol'dshtein, E.N.Gur'yanova, and K.A.Kocheshkov, Izv.Akad.Nauk SSSR, Ser.Khim., 6, 1262 (1975).
14. B.Warngist and E.Hogfeldt, Chemica Scripta, 7, 196 (1975).
15. M.I.Temkin, Dokl.Akad.Nauk SSSR, 152, 156 (1963).
16. R.Aris, "The Optimal Design of Chemical Reactors: A Study in Dynamic Programming" (Translated into Russian), Izd.Khimiya, Leningrad, 1967.
17. L.S.Polak (Editor), "Primenenie Vychislitel'noi Matematiki v Khimicheskoi i Fizicheskoi Kinetike" (Application of Computational Mathematics to Chemical and Physical Kinetics), Izd. Nauka, Moscow, 1969.
18. Yu.S.Snagovskii, G.M.Ostrovskii, and I.I.Malkin, Symposium, "Modelirovanie Khimicheskikh Protsessov i Reaktorov" (Modelling of Chemical Processes and Reactors), Novosibirsk, 1969, Vol.5, No.2, p.97.
19. A.A.Bezdenezhnykh, "Inzhenernye Metody Sostavleniya Uravnenii Skorostei Reaktsii i Rascheta Kineticheskikh Konstant" (Engineering Methods for the Derivation of Reaction Rate Equations and the Calculation of Kinetic Constants), Izd.Khimiya, Leningrad, 1973.
20. R.S.Tobias and N.Jasuda, Inorg.Chem., 2, 1307 (1963).
21. N.Ingri and L.G.Sillén, Arkiv Kemi, 23, 97 (1965).
22. L.G.Sillén and B.Warnquist, Arkiv Kemi, 31, 315 (1969).
23. N.Ingri, W.Kakotowich, L.G.Sillén, and B.Warnquist, Talanta, 14, 1261 (1967).
24. B.Warnquist, Chemica Scripta, 1, 49 (1971).
25. R.Arnek, Arkiv Kemi, 32, 81 (1970).
26. D.D.Perrin, Nature, 206, 107 (1965).
27. D.D.Perrin and I.G.Sayce, J.Chem.Soc.A, 1086, 1755 (1966).
28. V.N.Kumok, Zhur.Neorg.Khim., 17, 3098, 3230 (1972) [Russ.J.Inorg.Chem., No.11, No.12 (1972)].
29. Th.Kadem and A.Zuberbühler, Talanta, 18, 61 (1971).
30. D.D.Perrin and I.G.Sayce, Talanta, 14, 833 (1967).

31. D. D. Perrin, I. G. Sayce, and V. S. Sharma, J. Chem. Soc., 53, 446 (1968).
32. I. G. Sayce, Talanta, 15, 1397 (1968).
33. V. N. Kumok, Zhur. Neorg. Khim., 16, 1186 (1971) [Russ. J. Inorg. Chem., No. 5 (1971)].
34. A. V. Nikolaev and V. N. Kumok (Editors), "Issledovanie Khimicheskikh Ravnovesii (Metody Rascheta, Algoritmy i Programmy)" [Investigation of Chemical Equilibria (Methods of Calculation, Algorithms, and Program)], Izd. Nauka, Novosibirsk, 1974.
35. A. A. Bugaevskii and B. A. Dunai, Zhur. Anal. Khim., 26, 205 (1971).
36. V. O. Kruglov and A. A. Bugaevskii, Dokl. Akad. Nauk SSSR, 215, 105 (1974).
37. P. Paoletti, A. Vacca, and D. Arenare, J. Phys. Chem., 70, 193 (1966).
38. P. Paoletti, A. Vacca, and D. Arenare, J. Chem. Soc. A, 2202 (1970).
39. D. Arenare, P. Paoletti, and A. Vacca, J. Chem. Soc., Dalton Trans., 736 (1972).
40. A. Sabatini and A. Vacca, J. Chem. Soc., Dalton Trans., 1693 (1972).
41. P. Gans and A. Vacca, Talanta, 21, 45 (1974).
42. A. Sabatini, A. Vacca, and P. Gans, Talanta, 21, 53 (1974).
43. E. S. Shcherbakova, Candidate's Thesis, Karpov Physicochemical Institute, Moscow, 1974.
44. J. Grundnes, S. D. Christian, V. Cheam, and S. B. Farnham, J. Amer. Chem. Soc., 93, 20 (1971).
45. E. M. Arnett, E. J. Mitchell, and T. S. S. Murty, J. Amer. Chem. Soc., 96, 3875 (1974).
46. Ya. Kh. Grinberg, Dokl. Akad. Nauk SSSR, 221, 117 (1975).
47. E. S. Shcherbakova, I. P. Gol'dshtein, I. P. Romm, K. A. Kocheshkov, A. V. Suvorov, and V. I. Trusov, Izv. Akad. Nauk SSSR, Ser. Khim., 704 (1976).
48. A. Schepp and S. H. Bauer, J. Amer. Chem. Soc., 76, 265 (1954).
49. K. B. Yatsimirskii, V. P. Vasil'ev, N. A. Kostromina, and V. V. Korableva, Teor. Eksper. Khim., 7, 460 (1971).
50. V. I. Skomorokhov and S. V. Dmitriev, Zhur. Fiz. Khim., 48, 831 (1974) [Russ. J. Phys. Chem., No. 4 (1974)].
51. A. V. Suvorov, "Termodinamicheskaya Khimiya Paroobraznogo Sostoyaniya" (Thermodynamic Chemistry of the Vapour State), Izd. Khimiya, Leningrad, 1970.
52. A. V. Suvorov and V. I. Trusov, Zhur. Neorg. Khim., 18, 1953 (1973) [Russ. J. Inorg. Chem., No. 7 (1973)].
53. V. I. Trusov and A. V. Suvorov, Zhur. Neorg. Khim., 19, 3253 (1974) [Russ. J. Inorg. Chem., No. 12 (1974)].
54. N. A. Benesi and J. H. Hildebrand, J. Amer. Chem. Soc., 71, 2703 (1949).
55. R. L. Scott, Rec. Trav. chim., 75, 787 (1956).
56. R. Foster, L. E. Hammich, and A. A. Vardley, J. Chem. Soc., 3817 (1953).
57. R. Foster and I. Horman, J. Chem. Soc. B, 171 (1966).
58. W. B. Person, J. Amer. Chem. Soc., 87, 167 (1965).
59. R. L. Scott, Phys. Chem., 75, 3843 (1971).
60. E. L. Heric, Phys. Chem., 73, 3496 (1969).
61. L. M. Julien, W. E. Bennet, and W. B. Person, J. Amer. Chem. Soc., 91, 6915 (1969).
62. L. M. Julien and W. B. Person, J. Phys. Chem., 72, 3059 (1968).
63. D. A. Bahnick, W. E. Bennet, and W. B. Person, J. Phys. Chem., 73, 2309 (1969).
64. W. Litay, Z. Elektrochem., 65, 375 (1961).
65. C. C. Thompson and P. A. D. de Maine, J. Amer. Chem. Soc., 85, 3096 (1963).
66. P. R. Hammond, J. Chem. Soc., 479 (1964).
67. P. H. Emslie, R. Foster, C. A. Tyle, and J. Horman, Tetrahedron, 21, 2843 (1965).
68. P. J. Trotter and M. W. Hanna, J. Amer. Chem. Soc., 88, 3724 (1966).
69. D. W. Tammer and T. C. Bruice, J. Phys. Chem., 70, 3816 (1966).
70. J. Moriguchi and N. Kaneniwa, Chem. Pharm. Bull. (Tokyo), 17, 2173 (1969).
71. E. M. Lane, S. D. Christian, and J. D. Childs, J. Amer. Chem. Soc., 96, 38 (1974).
72. R. Mathur, E. D. Becker, R. B. Bradley, and N. C. Li, J. Phys. Chem., 67, 2190 (1963)
73. D. A. Deranleau, J. Amer. Chem. Soc., 91, 4044 (1969).
74. V. K. Pogorenyi and I. I. Kukhtenko, Teor. Eksper. Khim., 8, 684 (1972).
75. M. W. Hanna and D. G. Rose, J. Amer. Chem. Soc., 94, 2601 (1972).
76. L. K. Vasyanina, Yu. S. Bogachev, N. N. Shapet'ko, F. S. Yakushin, and Z. Z. Gurevich, Zhur. Obshch. Khim., 42, 2256 (1972).
77. L. K. Skrunts and B. A. Geller, Teor. Eksper. Khim., 9, 219, 556 (1973).
78. J. Homer and R. R. Jadova, J. Chem. Soc., Faraday Trans., 70, 609 (1974).
79. V. V. Pokhodenko, T. S. Slipenyuk, and V. S. Kuts, Teor. Eksper. Khim., 11, 50 (1975).
80. R. K. Chan and S. C. Liao, Canad. J. Chem., 48, 299 (1970).
81. J. Cantacuzene, Bull. Soc. chim. France, 4, 747 (1962).
82. R. A. la Budde and M. Tamres, J. Phys. Chem., 74, 4009 (1970).
83. N. N. Polle, V. N. Nagareva, and E. G. Polle, Zhur. Fiz. Khim., 47, 2662, 2711 (1973) [Russ. J. Phys. Chem., No. 10 (1973)].
84. G. D. Johnson and R. E. Bowen, J. Amer. Chem. Soc., 87, 5015 (1965).
85. R. Foster, Ind. chim. Belge, 37, 547 (1972).
86. C. W. H. Cumper, Talanta, 20, 775 (1973).
87. I. P. Gol'dshtein, E. N. Gur'yanova, and I. R. Karpovich, Zhur. Fiz. Khim., 39, 932 (1965) [Russ. J. Phys. Chem., No. 4 (1965)].
88. W. Carr Peter, Thermochim. Acta, 3, 427 (1972).
89. K. B. Yatsimirskii and L. I. Budarin, Zhur. Neorg. Khim., 7, 1090 (1962) [Russ. J. Inorg. Chem., No. 5 (1962)].
90. "Spektroskopicheskie Metody v Khimii Kompleksnykh Soedinenii" (Spectroscopic Methods in the Chemistry of Complex Compounds), Izd. Khimiya, Moscow–Leningrad, 1964.
91. F. Holemes and D. R. Williams, J. Chem. Soc. A, 729 (1967).
92. I. P. Gol'dshtein, E. N. Gur'yanova, T. I. Perepelkova, N. I. Sheverdina, V. A. Chernoplekova, V. S. Yakovleva, and K. A. Kocheshkov, Izv. Akad. Nauk SSSR, Ser. Khim., 251 (1971).
93. Ya. B. Yatsimirskii, V. A. Bidzilya, N. K. Davidenko, and L. P. Golovkova, Teor. Eksper. Khim., 10, 115 (1974).

94. V. I. Dulova and T. A. Zhuravel', Zhur. Fiz. Khim., 47, 2685 (1973) [Russ. J. Phys. Chem., No. 10 (1973)].
95. W. A. E. McBryde, Talanta, 21, 979 (1974).
96. E. Lippert, Ber. Bunsenges. phys. Chem., 67, 267 (1963).
97. O. P. Yablonskii, L. F. Lapuka, E. G. Chekalova, and V. A. Belyaev, Teor. Eksper. Khim., 7, 122 (1971).
98. Yu. S. Bogachev, L. K. Vasyanina, N. N. Shapet'ko, V. M. Egorov, and T. L. Alekseeva, Izv. Akad. Nauk SSSR, Ser. Khim., 1021 (1972).
99. G. L. Birman, M. E. Elyashberg, N. P. Makoveeva, Yu. Z. Karasev, and N. N. Shapet'ko, Dokl. Akad. Nauk SSSR, 208, 631 (1973).
100. J. J. Christensen, R. M. Izatt, L. D. Hansen, and J. A. Partidge, J. Phys. Chem., 70, 2003 (1966).
101. R. M. Izatt, J. H. Rutting, L. D. Hansen, and J. J. Christensen, J. Amer. Chem. Soc., 83, 2641 (1966).
102. J. J. Christensen, D. P. Wrathall, R. M. Izatt, and D. O. Tolman, J. Phys. Chem., 71, 2700, 3001 (1967).
103. J. J. Christensen, D. P. Wrathall, and R. M. Izatt, Anal. Chem., 40, 175 (1968).
104. J. J. Christensen, M. D. Slade, D. E. Smith, R. M. Izatt, and J. Tzang, J. Amer. Chem. Soc., 92, 4164 (1970).
105. R. M. Izatt, D. P. Nelson, J. H. Rytting, R. L. Haymore, and J. J. Christensen, J. Amer. Chem. Soc., 93, 1619 (1971).
106. N. I. Rose and R. S. Drago, J. Amer. Chem. Soc., 81, 6138 (1959).
107. R. S. Drago, R. L. Carlson, R. J. Rose, and D. Wenz, J. Amer. Chem. Soc., 83, 3572 (1961).
108. T. F. Bolles and R. S. Drago, J. Amer. Chem. Soc., 87, 5015 (1965).
109. R. S. Drago and T. D. Epley, J. Amer. Chem. Soc., 91, 2883 (1969).
110. F. L. Slejko and R. S. Drago, J. Amer. Chem. Soc., 94, 6546, 9210 (1972).
111. F. L. Slejko and R. S. Drago, J. Amer. Chem. Soc., 95, 6935 (1973).
112. S. D. Christian and E. E. Tucker, J. Phys. Chem., 74, 216 (1970).
113. G. B. Sergeev, V. A. Batyuk, V. V. Romanov, and N. V. Rostovshchikova, Zhur. Fiz. Khim., 48, 2662 (1974) [Russ. J. Phys. Chem., No. 11 (1974)].
114. L. Lambert and Th. Zeegers-Huyskens, J. Chim. Phys., 60, 435 (1963).
115. D. P. Graddon and K. B. Heng, Austral. J. Chem., 24, 1781 (1971).
116. D. R. Dakternieks and D. P. Graddon, Austral. J. Chem., 27, 1351 (1974).
117. G. Oloffson, Acta Chem. Scand., 21, 1892 (1967).
118. G. Oloffson and J. Wirbrant, Acta Chem. Scand., 25, 1408 (1971).
119. I. P. Gol'dshtein and E. N. Gur'yanova, Teor. Eksper. Khim., 7, 410, 542 (1971).
120. T. I. Perepelkova, E. S. Shcherbakova, I. P. Goldshtein, and E. N. Gur'yanova, Zhur. Obshch. Khim., 45, 656 (1975).
121. B. J. Thamer, J. Phys. Chem., 59, 450 (1955).
122. B. Both and J. F. Bunnett, J. Amer. Chem. Soc., 87, 334 (1965).
123. J. K. Romary, D. L. Donnelly, and A. C. Andrews, J. Inorg. Nuclear Chem., **29**, 1805 (1967).
124. P. Gans and H. M. N. H. Irving, J. Inorg. Nuclear Chem., 34, 1885 (1972).
125. M. C. Chattopadnyaya and R. S. Singh, Anal. Chem. Acta, 70, 49 (1974).
126. H. Cramèr, "Mathematical Methods of Statistics" (Princeton Univ. Press, 1946) (Translated into Russian), Inostr. Lit., Moscow, 1948.
127. E. S. Shcherbakova, Zhur. Fiz. Khim., 50, 716 (1976) [Russ. J. Phys. Chem., No. 3 (1976)].
128. D. Dyrssen, N. Ingri, and L. G. Sillén, Acta Chem. Scand., 15, 694 (1961).
129. L. G. Sillén, Acta Chem. Scand., 16, 159 (1962).
130. N. Ingri and L. G. Sillén, Acta Chem. Scand., 16, 173 (1962).
131. L. G. Sillén, Acta Chem. Scand., 18, 1085 (1964).
132. N. Ingri, Acta Chem. Scand., 16, 439 (1962); 17, 573, 597 (1963).
133. R. S. Tobias and Z. Z. Hugus, J. Phys. Chem., 65, 2165 (1961).
134. V. P. Vasil'ev and E. V. Kozlovskii, Zhur. Fiz. Khim., 47, 2582 (1973) [Russ. J. Phys. Chem., No. 10 (1973)].
135. V. V. Tsibanov, I. O. Bogatyrev, and K. B. Zaborenko, Zhur. Fiz. Khim., 48, 1613 (1974) [Russ. J. Phys. Chem., No. 6 (1974)].
136. V. N. Kumok and N. A. Skorik, Zhur. Neorg. Khim., 15, 291 (1970) [Russ. J. Inorg. Chem., No. 2 (1970)].
137. P. Ulmgren and O. Wahlberg, Chemica Scripta, 3, 193, 153, 158 (1973).
138. G. S. Tereshin, K. S. Astakhov, and N. I. Vdovenko, Zhur. Neorg. Khim., 16, 3237 (1971) [Russ. J. Inorg. Chem., No. 12 (1971)].
139. V. I. Bolevantsev, V. A. Fedorov, L. P. Shishin, I. M. Bol'shakov, and A. M. Ryabov, Teor. Eksper. Khim., 10, 245 (1974).
140. L. Pettersson, Chemica Scripta, 7, 145 (1975).
141. K. Conrow, G. Johnson, and R. E. Bowen, J. Amer. Chem. Soc., 86, 1025 (1964).
142. G. D. Johnson and R. E. Bowen, J. Amer. Chem. Soc., 87, 1655 (1965).
143. K. Schaarschmidt, Z. phys. Chem., 235, 17 (1967).
144. W. E. Wentworth, W. Wipsch, and R. Chen, J. Phys. Chem., 71, 218 (1967).
145. J. Grundness and S. D. Christian, J. Amer. Chem. Soc., 90, 2239 (1968).
146. H. Boudevske, Macromol. Chem. (Bulgaria), 143, 11 (1971).
147. K. Nagano and D. E. Metzler, J. Amer. Chem. Soc., 89, 2891 (1967).
148. L. P. Varga and F. C. Veatch, Anal. Chem., 39, 1101 (1967).
149. D. R. Rosseinsky and H. Kellawi, J. Chem. Soc. A, 1207 (1969).
150. R. J. Grabenstetter and W. A. Cilley, J. Phys. Chem., 75, 676 (1970).
151. P. J. Lingane and Z. Z. Hugus, Inorg. Chem., 9, 757 (1970).
152. J. Prasad and N. C. Peterson, Inorg. Chem., 8, 1622 (1969).
153. C. C. Thompson, Canad. J. Chem., 47, 2605 (1969).
154. J. M. Daisey and A. J. Sonnessa, J. Phys. Chem., 76, 1895 (1972).
155. T. O. Maier and R. S. Drago, Inorg. Chem., 11, 1801 (1972).
156. S. Feldberg, P. Klotz, and L. Newman, Inorg. Chem., 11, 2860 (1972).
157. N. P. Bazhulin, A. Ya. Lomakin, Yu. V. Morozov, and F. A. Savin, Zhur. Prikl. Spektrosk., 14, 682 (1971).
158. L.-N. Lin, S. D. Christian, and J. D. Childs, J. Amer. Chem. Soc., 96, 2727 (1974).

159. T.R.Griffiths and P.J.Potts, J.Chem.Soc., Dalton Trans., 344 (1975).
160. D.J.Leggett and W.A.E.McBryde, Anal.Chem., 47, 1065 (1975).
161. B.Nelander, Acta Chem.Scand., 20, 2289 (1966).
162. E.Gore and S.S.Danyluk, J.Phys.Chem., 69, 89 (1965).
163. S.Cabani and P.Giani, J.Chem.Soc.A, 547 (1968).
164. E.Coburn and W.C.Grunwald, J.Amer.Chem.Soc., 80, 1318, 1322 (1958).
165. R.M.Izatt, D.Eatough, R.L.Snow, and J.J.Christensen, J.Phys.Chem., 72, 1208 (1968).
166. J.J.Christensen, J.H.Rytting, R.M.Izatt, J.Chem.Soc.A, 861 (1969).
167. D.J.Eatough, Anal.Chem., 42, 635 (1970).
168. I.P.Gol'dshtein, E.N.Gur'yanova, and E.S.Shcherbakova, Zhur.Obshch.Khim., 40, 183 (1970).
169. M.E.Peisakhova, I.P.Gol'dshtein, E.N.Gur'yanova, and E.S.Shcherbakova, 43, 159 (1973).
170. V.V.Puchkova, E.N.Gur'yanova, E.S.Shcherbakova, and I.P.Gol'dshtein, Zhur.Obshch.Khim., 46, 892 (1976).
171. P.Gravelle, R.D.Joly, and J.L.Petit, Rev.General Thermochim., 12, No.138, 513, 515, 517, 545 (1973).
172. B.Danielsson, O.Grinstrup, and N.Ingri, Chemica Scripta, 3, 81, 101 (1973).
173. R.Oliver and P.Clechet, Thermochim.Acta, 8, 249 (1974).
174. R.W.Taft and J.W.Carten, J.Amer.Chem.Soc., 86, 4199 (1964).
175. R.W.Taft, G.B.Klingensmith, and S.Ehrenson, J.Amer.Chem.Soc., 87, 3620 (1965).
176. D.Gurka and R.W.Taft, J.Amer.Chem.Soc., 91, 4794 (1969).
177. C.J.Creswell and A.L.Allred, Phys.Chem., 66, 1469 (1962).
178. L.Lussan, B.Lananceau, and N.Souty, Compt. rend., 254, 1980 (1962).
179. C.Lussan, J.Chim.phys.et phys.chim.biol., 60, 1100 (1963).
180. B.Lemanceau, C.Lussan, N.Sonty, and J.Biais, J.Chim.phys.et phys.chim.biol., 61, 195 (1964).
181. L.A.Laplanche, H.B.Thompson, and M.T.Rogers, J.Phys.Chem., 69, 1482 (1965).
182. L.L.Graham and G.J.Chang, J.Phys.Chem., 75, 776, 784 (1971).
183. J.Homer and P.J.Huck, J.Chem.Soc.A, 277 (1968).
184. Yu.A.Kruglyak, G.G.Dyadyusha, V.A.Kuprievich, L.M.Podol'skaya, and G.I.Kagan, "Metody Rascheta Elektronnoi Struktury i Spektrov Molekul" (Methods for the Calculation of the Electronic Structure and Spectra of Molecules), Izd.Naukova Dumka, Kiev, 1969.
185. B.L.Shapiro and M.D.Johnston, J.Amer.Chem. Soc., 94, 8185 (1972).
186. S.V.Zenin, D.L.Pinskii, and G.V.Sergeev, Zhur. Fiz.Khim., 46, 1974 (1972) [Russ.J.Phys.Chem., No.8 (1972)].
187. V.L.Antonovskii, A.S.Gukovskaya, B.I.Sukhorukov, and I.P.Chervin, Zhur.Fiz.Khim., 46, 2902 (1972) [Russ.J.Phys.Chem., No.11 (1972)].
188. S.Shimokawa, H.Fukui, J.Sohma, and K.Hotta, J.Amer.Chem.Soc., 95, 1777 (1973).
189. K.W.Jolley, L.M.Hughes, and I.D.Watson, Austral.J.Chem., 27, 287 (1974).
190. N.Muller, J.Phys.Chem., 79, 287 (1975).
191. M.I.Varkhin and E.S.Shcherbakova, Zhur.Fiz. Khim., 49, 2742 (1975)[Russ.J.Phys.Chem., No.10 (1975)].
192. C.Treiner, J.F.Skinner, and R.M.Fuoss, J.Phys. Chem., 68, 3406 (1964).
193. J.H.House, R.S.Reiter, and D.W.Hopkins, Trans. US Acad.Sci., 64, 3 (1971).
194. G.N.Kartsev, V.I.Aleinikov, N.V.Smirnova, Yu.M.Glubokov, and E.S.Shcherbakova, Izv.Akad. Nauk SSSR, Ser.Khim., 1972 (1973).
195. P.Bordewijk, M.Kunst, and A.Rip, J.Phys.Chem., 77, 548 (1973).
196. C.Campbell, G.Brink, and L.Glasser, J.Phys. Chem., 79, 660 (1975).
197. G.Eriksson, Acta Chem.Scand., 25, 2651 (1971); 27, 193 (1973).
198. V.G.Gontar', A.M.Evseev, and R.U.Arifov, Zhur. Fiz.Khim., 51, 1673 (1977) [Russ.J.Phys.Chem., No.7 (1977)].
199. H.G.Mendelbaum, F.Madaule, and M.Desgranges, Bull.Soc.chim.France, 1619 (1973).
200. A.D.Rusin and O.P.Yakovlev, Vestnik Moskov.Gos. Univ., Khim., 15, 427 (1974).
201. Yu.I.Krasnokutskii, V.I.Fedorov, S.N.Ganz, V.D.Parkhomenko, and A.M.Alekseev, Zhur. Prikl.Khim., 47, 1972 (1974).
202. J.Kenttamaa, Acta Chem.Scand., 12, 1323 (1958).
203. S.R.Tobias, Inorg.Nuclear Chem., 19, 348 (1961).
204. D.J.Wilde, "Optimum Seeking Methods" (Translated into Russian), Izd.Nauka, Moscow, 1967.
205. B.T.Polyak, Ekonomika i Matematicheskie Metody, 3, No.6, 881 (1967).
206. H.H.Rosenbrock and C.Storey, "Computational Techniques for Chemical Engineers" (Translated into Russian), Izd.Mir, Moscow, 1968.
207. G.M.Ostrovskii and Yu.M.Volin, "Metody Optimizatsii Khimicheskikh Reaktorov" (Methods for the Optimisation of Chemical Reactors), Izd. Khimiya, Moscow, 1967.
208. D.Himmelblau, "Applied Non-linear Programming" (Translated into Russian), Izd.Mir, Moscow, 1975.
209. B.P.Pshenichnyi and Yu.M.Danilin, "Chislennye Metody v Ekstremal'nykh Zadachakh" (Numerical Methods in Extremum Problems), Izd.Nauka, Moscow, 1975.
210. I.M.Gel'fand and M.L.Tsetlin, Dokl.Akad.Nauk SSSR, 137, 2 (1961).
211. I.M.Gel'fand, E.B.Vul, S.L.Ginzburg, and Yu.G.Fedorov, "Metod Ovragov v Zadachakh Rentgenostrukturnogo Analiza" (The Pit Mapping Method in X-Ray Diffraction Problems), Izd.Nauka, Moscow, 1966.
212. E.S.Shcherbakov and L.A.Muzychenko, Zavod. Lab., 295 (1974).
213. Yu.V.Linnik, "Metod Naimen'shikh Kvadratov i Osnovy Matematiko-Statisticheskoi Obrabotki Nablyudenii" (The Method of Least Squares and Principles of the Mathematical Statistical Treatment of Observations), Fizmatgiz, Moscow, 1962.
214. D.K.Fadeev and V.N.Fadeeva, "Vychislitel'nye Metody Lineinoi Algebry" (Computational Methods in Linear Algebra), Fizmatgiz, Moscow, 1960.
215. D.D.McCracken and W.S.Dorn, "Numerical Methods and FORTRAN Programming" ["Numerical Methods with Fortran IV Case Studies"] (Translated into Russian), Izd.Mir, Moscow, 1967.

216. J. M. Ortega and W. C. Rheinboldt, "Iterative Solution of Non-linear Equations in Several Variables" (Translated into Russian), Izd. Mir, Moscow, 1975.
217. V. V. Nalimov, "Teoriya Eksperimenta" (Theory of Experimentation), Izd. Nauka, Moscow, 1971.
218. B. L. van der Waerden, "Mathematical Statistics" (Translated into Russian), Inostr. Lit., Moscow, 1960.
219. D. J. Hudson, "Statistics for Physicists" (Translated into Russian), Izd. Mir, Moscow, 1970. [We are unable to trace this reference, it may be Hudson, D. J., "Statistics Lectures", Vols. 1 and 2, CERN, Geneva, 1963 (Ed. of Translation)].
220. D. M. Himmelblau, "Process Analysis by Statistical Methods" (Translated into Russian), Izd. Mir, Moscow, 1973.
221. E. S. Shcherbakova, I. P. Gol'dshtein, M. E. Peisakhova, E. N. Gur'yanova, V. I. Aleinikov, and A. I. Gorbanev, Symposium, "Fiziko-Khimicheskie Issledovaniya v Metallurgii i Metallovedenii s Primeneniem EVM" (Physicochemical Studies in Metallurgy and Metallography Using Computers), Izd. Nauka, Moscow, 1974, p. 82.
222. V. I. Bolevantsev and V. I. Malkova, Izv. Sibir. Otd. Akad. Nauk SSSR, Ser. Khim., No. 3, 46 (1975).
223. V. V. Nalimov and N. A. Chernova, "Statisticheskie Metody Planirovaniya Eksperimentov" (Statistical Experimental Design Methods), Izd. Nauka, Moscow, 1965.
224. V. V. Fedorov, "Teoriya Optimal'nogo Eksperimenta" (Optimum Experiment Theory), Izd. Nauka, Moscow, 1971.
225. E. E. Matskin and V. N. Kumok, Zavod. Lab., 845 (1973).
226. H. S. Rossotti, Talanta, 21, 809 (1974).

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