Ternary Diffusivities by Model-Based Analysis of Raman Spectroscopy Measurements

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Even though multicomponent mixtures are ubiquitous in mass transfer processes, mutual diffusion data in these systems are scarce. This is due to the fact that established diffusion measurements are laborious. In particular, several experiments are required to determine multicomponent diffusion coefficients at a single composition. In order to overcome these deficiencies, a diffusion experiment employing one-dimensional Raman spectroscopy is presented. Concentrations of the individual species are resolved with high spatial and temporal resolution during the diffusion process. In this work, it is shown that these data allow determining the ternary Fick diffusion matrix from a single isothermal diffusion experiment. The experimental procedure is further optimized using model-based experimental design techniques, where general design guidelines for diffusion experiments are derived. Thereby, precision of the diffusion measurements can be improved by an order of magnitude. The theoretical calculations are validated by experimental results for the system n-*propanol + 1-chlorobutane +* n-*heptane*. © 2006 American Institute of Chemical Engineers *AIChE J,* 52: 4004–4015, 2006
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Introduction

Today, mutual diffusion coefficients in multicomponent liquids cannot be predicted with sufficient accuracy.[1] Experimental data are rare and often of questionable quality.[2] Established diffusion experiments (for a review, see Woolf et al.[3]) require rather high effort with respect to measurement time and/or specialized equipment. For example, the diaphragm cell offers on the one hand a simple, versatile design and low cost for diffusion measurements. Since concentration measurements can be performed off-line, for example, by gas chromatography, it has been the first technique to study multicomponent systems. On the other hand, diaphragm cells are rarely employed today due to the reliance on calibration, long measurement times (12–18 days for one ternary data point[4]), modest accuracy,[3] and occasional unreliability.[5] Today, Gouy and Rayleigh interferometry is considered to give the most accurate diffusion data,[3] while Taylor dispersion is becoming more popular since it allows for faster but still reliable measurements.[6] These techniques typically rely on refractive index measurements, which cannot be unambiguously related to the concentration information on the indi-

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vidual species. Therefore, at least two experiments are required to determine the diffusion coefficients in a ternary mixture. In practice, four and more diffusion experiments are performed.[7] In addition, the underlying assumption of a linear relationship between the component specific refraction index and the molar concentration might have to be tested in a nonlinear calibration procedure.[8]

Due to these disadvantages the use of other measurement techniques not relying on the refractive index has been repeatedly suggested.[6,8] Spectroscopic measurement techniques have, therefore, been tested for their ability to measure ternary diffusion coefficients. Today, spectroscopic measurements are still expected to be less precise than those with established methods. But spectroscopic methods will allow faster measurements in multicomponent mixtures. Tanigaki et al.[9] used a position-scanning spectrophotometer in a vertical column setup, and Rutten[10] employed UV-Vis measurements along with Taylor dispersion. Reliable data of moderate precision were obtained, but the determination of the ternary Fick matrix from a single experiment was still "far beyond the limit."[9]

In the last few years, Raman spectroscopy has matured to an efficient, reliable, and versatile technique for quantitative analysis.[11] Still, there have been only very few attempts to employ the Raman technique for diffusion measurements. The idea was first proposed in a patent[12] and later implemented in combination with microscope techniques for binary aqueous[13] and hydrogel-stabilized systems.[14] In order to accommodate the poor temporal and spatial resolution in the order of hours and millimeters, very long experiments, up to 25 days, were performed. Still, the precision of the measured diffusion coefficients was comparatively low.

Recently, the authors have developed a new Raman diffusion experiment overcoming these deficiencies. Experiments are performed in a vertical column. One-dimensional Raman spectroscopy is used to obtain concentration data with high spatial resolution along the diffusion path. The new setup has been validated for binary mixtures[15] and shown to allow for the direct determination of concentration dependent binary diffusion coefficients from one short single experiment.[16]

In this work, the technique is extended to ternary systems. Here, the benefit of a spectroscopic technique, allowing for the quantification of all diffusing species directly from the spectra, becomes significant. Experimental results are presented for the system *n*-propanol + 1-chlorobutane + *n*-heptane and used to validate the new approach by comparison to literature data. In order to make the best use of the data provided from the experiment, the investigation is carried out within the framework of model-based experimental analysis (MEXA),[17] which is presented next. Here, optimal experimental design provides general guidelines for diffusion measurements applicable beyond the Raman setup considered here. In particular, restricted diffusion experiments are strongly favored over the free diffusion setup commonly used.

Work Process for the Measurement of Multicomponent Diffusivities

Even though Raman spectroscopy enables simultaneous concentration measurements of all diffusing species, the estimation of multicomponent diffusivities remains a demanding problem. In ternary mixtures, four diffusivities have to be determined from only twice as much independent concentration information (such as molar fractions x_1, x_2) compared to the binary case. It seems, therefore, mandatory to follow a rational strategy for the design and analysis of the experiments.

Systematic approaches to the experimental analysis of kinetic phenomena have been discussed in the literature for more than three decades.[18] Most approaches include a basic working cycle consisting of experimental design, data collection, and analysis, which is iteratively repeated.[19] More recently, the use of model-based methods for the individual steps has been emphasized.[20] Research in this area was traditionally stimulated from the investigation of reaction kinetics, while applications of model-based methods to diffusion problems have been rare and limited to the design of diaphragm cell experiments.[4,21,22]

In this work, the general methodology for model-based experimental analysis[17] of kinetic phenomena currently developed in Collaborative Research Center 540 at RWTH Aachen University is implemented for ternary Raman diffusion experiments (Figure 1). In very early stages of the investigation, a mathematical model of the Raman experiment to describe the diffusion process is developed based on a priori knowledge about the studied system, knowledge transfer from similar problems, and intuition. This model can be used in numerical simulation studies to explore the expected behavior of the experiment. Here, it is also employed for rigorous model-based qualitative and quantitative experimental design. In qualitative design, it is analyzed under which measurement conditions the diffusivities are uniquely identifiable from the data. The free design variables of the experiment are then further optimized in quantitative design to maximize the information content of the data while satisfying the stability requirements for vertical column diffusion experiments.

The designed diffusion experiment is then performed, and the variables of interest are observed using appropriate measurement techniques. In this work, Raman spectra are detected with both high spatial and temporal resolution. In a data preprocessing step, these mixture spectra are transformed into the desired concentration information using the indirect spectral hard modeling[23,24] approach. For this purpose, a calibration model is derived from the analysis of a few samples with known composition preceding the diffusion experiment. The concentration data, including information about the measurement error, are finally used along with the initially proposed model in the formulation and solution of inverse problems. In this work, constant diffusion coefficients are assumed to be applicable. Thus, the inverse problem reduces to the estimation of the unknown parameter set D complemented by information on its uncertainty.

The additional knowledge gained on the diffusion process may be used to refine the model and the design of the experiment. If necessary, subsequent iterations of the work process are performed until the diffusivities are determined with sufficient precision. The application of this approach to the new Raman diffusion experiment is exemplified in the following.

Diffusion Process Model

Raman diffusion experiments are performed in a vertical column setup as commonly used, for example, in interferometry.[3] During the diffusive concentration equilibration pro-

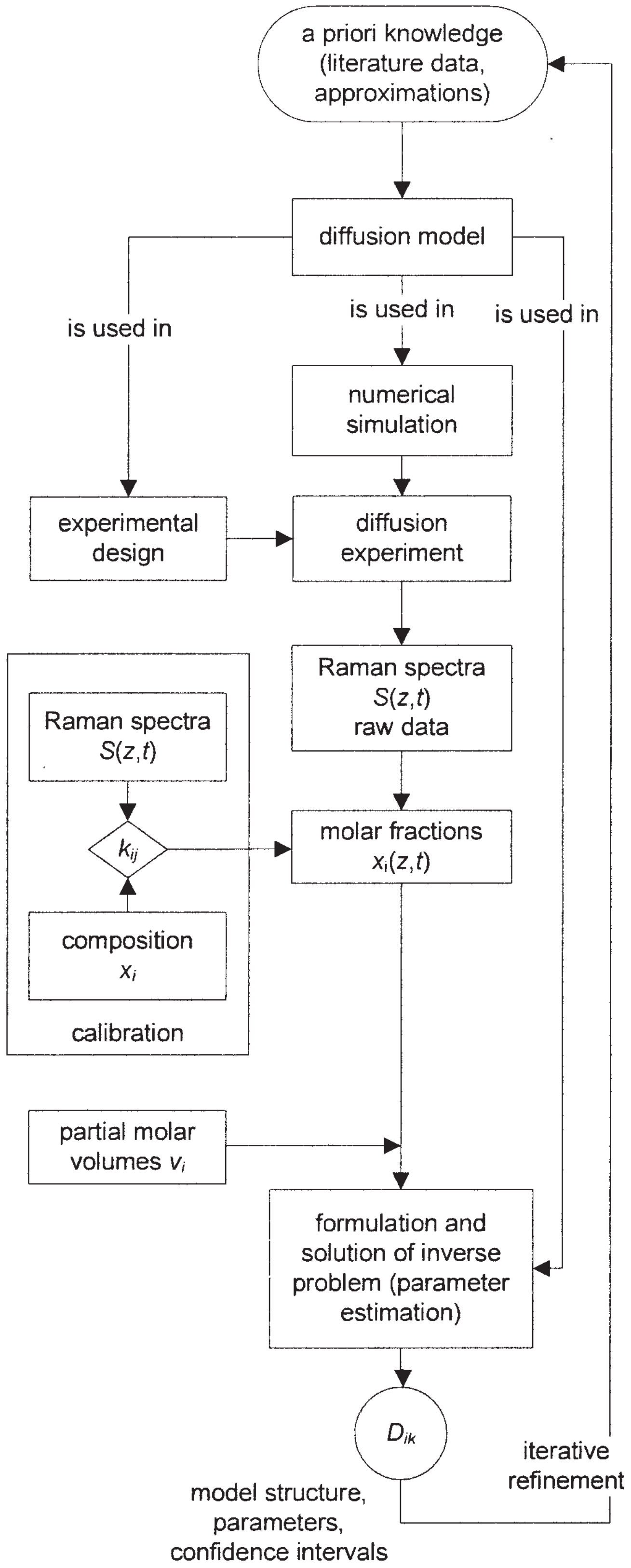

Figure 1. MEXA work process for the model-based design and analysis of ternary Raman diffusion experiments.

cess, the mole fractions $x_i(z,t)$ are measured by Raman spectroscopy. These measurements are treated as input data to the parameter estimation problem. A model is, therefore, required to relate these measurements to the unknown diffusion coefficients. If only small concentration ranges are covered, as typical for diffusion experiments, the volume average velocity is zero.[3] Furthermore, diffusion coefficients and partial molar volumes can be assumed constant. Assuming generalized Fick's law to describe the diffusive fluxes, the model for the one-dimensional diffusion process in a mixture of n_c components can be given in the volume average velocity reference frame as:

$$\begin{aligned}
\frac{\partial c_i}{\partial t} &= \sum_{k=1}^{n_c-1} D_{ik}^{v} \frac{\partial^2 c_k}{\partial z^2}, \quad i = 1,\ldots,n_c-1,\\
x_i &= \frac{c_i}{c_t}, \quad i = 1,\ldots,n_c,\\
0 &= c_t - \sum_{i=1}^{n_c} c_i,\\
\frac{1}{c_t} &= \sum_{i=1}^{n_c} x_i \bar{v}_i,\\
\frac{\partial c_i(0,t)}{\partial z} &= \frac{\partial c_i(L,t)}{\partial z} = 0, \quad i = 1,\ldots,n_c-1,\\
c_i(z,0) &= c_{i0}(z). \qquad (1)
\end{aligned}$$

Here, c_i, x_i, $\bar{v}_i$ denote the molar concentration, the mole fraction, and the partial molar volume of species i, respectively. The Fick diffusion coefficients D_{ij}^{v} are determined in the volume reference frame. Noteworthy, as mole fractions are considered that add up to one, the approach is quite insensitive to component numbering.

Model-Based Experimental Design

Qualitative design—local identifiability

In qualitative experimental design,[25] it is analyzed which minimal set of measurements would allow for the unique determination of the diffusivities. The general advantage of spectroscopic measurements is that all mixture components are resolved. It is shown below that a single Raman diffusion experiment allows for the determination of a constant ternary diffusion matrix D. For this purpose, the local identifiability of the diffusion coefficients is established. Identifiability is given if the mapping from parameters to measurements is injective[26] (one-to-one), that is, if there exists a unique correspondence between parameters and the measurements obtained. If this condition holds only in a neighborhood of the parameters, one speaks of local identifiability.

Local identifiability can be tested by computation of the determinant of the so-called Fisher information matrix F, which is the inverse of the estimated covariance matrix of the parameter estimates. The Fisher information matrix F can usually be calculated as:[25]

$$F(\Theta) = \sum_{\mu=1}^{N} \frac{1}{\sigma_\mu^2} \frac{\partial x_\mu(\Theta)}{\partial \Theta} \frac{\partial x_\mu(\Theta)}{\partial \Theta^T}, \qquad (2)$$

where x are the mole fractions predicted by the model and the index μ runs over all measurements, σ_μ^2 is the measure-

Table 1. Results of Local Identifiability Study

Sample times	1	1	1	2	1	2	2
Sample positions	1	1	2	1	2	1	2
Resolved species	1	2	1	1	2	2	1
Rank of F	1	2	2	2	**4**	**4**	**4**

Rank of the Fisher information matrix is given depending on the number of measurements in time and space and the individual species resolved within a single Raman experiment.

ment variance, and the vector Θ collects all unknown parameters, here the diffusion coefficients. The sensitivities ($\partial x_\mu / \partial\Theta$) are computed from partial differentiation of the model equations (Eq. 1). The Fisher information matrix quantifies how sensitive the measurements are in the parameter values. If the rank of the Fisher information matrix is equal to the number of unknown parameters, there is independent information on each parameter and local identifiability is ensured.[26]

This concept has been used to analyze ternary Raman diffusion experiments. Diffusion and partial molar volume data for the ternary mixture *n*-propanol + 1-chlorobutane + *n*-heptane at $\vartheta = 25$ °C and equimolar composition have been taken from the literature.[4] The initial condition is set to an infinitely sharp boundary at $z = z_0$. The rank of the Fisher information matrix is determined for different sets of experimental data available. The results in Table1 show that a very minimalist setup would be sufficient to guarantee local identifiability (in this work rank $(F) = 4$): if all independent diffusing species can be resolved, as in Raman experiments, it is sufficient to measure at one time instance at two locations in the diffusion cell or at one location at two different times. If any further measurement information is dropped, the rank decreases. In this sense, the given measurement setup is minimal. In a mathematically strict sense, this analysis still depends on the actual values of the diffusion coefficient matrix. However, further numerical experiments with randomly generated Fick diffusion matrices indicate that this result holds for arbitrary mixtures. The analysis given here provides support for earlier more qualitative arguments.[27] Hence, it can be concluded that Raman spectroscopy allows for the measurement of ternary diffusion coefficients in a single experiment.

In contrast, the Fisher matrix F is rank-deficient if data from a single ternary Taylor or Rayleigh diffusion experiment using refractive index measurements are analyzed.[19] The measurements principles are, therefore, fundamentally different from Raman spectroscopy with respect to the potential of reducing the number of multicomponent diffusion experiments. They necessarily require a second experiment to fulfill the criterion, which is independent of the number of measurement points within one experiment.[19] The given results further imply that the current Raman setup with 400 spatial points and many sample times should provide excessive information to determine the Fick matrix from a single experiment.

Quantitative design of ternary Raman experiments

The new Raman diffusion experiment allows for a fundamental reduction of experimental effort, as shown above. Still, the experiments should be optimized in order to make the best use of this potential. The optimal design of ternary Raman diffusion experiments is, therefore, considered. The system *n*-Propanol (1) + 1-Chlorobutane (2) + *n*-Heptane (3) at equimolar composition is again used as an example. The diffusion coefficients are:[4]

$$D^v = \begin{bmatrix} 1.033 & -0.174 \\ 0.255 & 2.463 \end{bmatrix} \cdot 10^{-9}\,\frac{m^2}{s}. \tag{3}$$

Thus, the goal of the optimal experimental design is to find the best conditions for the Raman experiment to recover these diffusion coefficients D^v as if they were unknown.

Design Variables. In Raman diffusion experiments, a number of degrees of freedom can be chosen by the experimenter. These free settings should be chosen such that maximum information on the desired coefficients is retrieved. This problem can be approached using optimal experimental design theory.[25]

A sketch of the Raman diffusion experiment is shown in Figure 2. The design variables d of a ternary Raman diffusion are: the total cell height, L; the initial height of the lower mixture, z_o; the position of the measurement zone, z_{sensor}; and the duration of the experiment, t_{max}. In addition to these variables, the composition of the solutions initially placed in the upper and lower part of the cell, x_u and x_L, can be chosen. The initial composition will be parameterized by an angle ϕ as introduced in Figure 2. This angle gives the relative position of the upper and lower mixture to the average experiment composition x_c in a clock-like diagram. The maximum difference Δx between the initial compositions is chosen such that mixing effects can be neglected and constant diffusion coefficients can be expected. The length of the measurement line is $z_{measurement} = 0.4\,L$, with a resolution of 400 spatial points as in the setup currently used. It is assumed that samples are taken at 60 times equidistributed in $[0, t_{max}]$.

It is beneficial to express the model equations (Eq. 1) in dimensionless form in order to identify the true underlying influence parameters. In the given scenario, the balance equations for a ternary diffusion experiment may thus be given as:

$$\begin{bmatrix} \frac{\partial \bar{c}_1}{\partial \tau} \\ \frac{\partial \bar{c}_2}{\partial \tau} \end{bmatrix} = \mathrm{Fo} \begin{bmatrix} \overline{D^v_{11}} & \overline{D^v_{12}} \\ \overline{D^v_{21}} & \overline{D^v_{22}} \end{bmatrix} \begin{bmatrix} \frac{\partial^2 \bar{c}_1}{\partial \bar{z}^2} \\ \frac{\partial^2 \bar{c}_2}{\partial \bar{z}^2} \end{bmatrix}, \tag{4}$$

with $\bar{c}_i = \frac{c_i - c_{iL}}{c_{iU} - c_{iL}}, \quad \tau = \frac{t}{t_{max}}, \quad \bar{z} = \frac{z}{L}, \quad \overline{D^v_{ij}} = \frac{D^v_{ij}}{\sqrt{D_1^\dagger D_2^\dagger}},$

$\mathrm{Fo} = \frac{\sqrt{D_1^\dagger D_2^\dagger}\, t_{max}}{L^2}.$

The eigenvalues $D_1^\dagger$, $D_2^\dagger$ of the Fick matrix have been used to scale the diffusivities. The dimensionless notation emphasizes the aspect that the design variables mentioned above do not influence the process independently; the process is rather characterized by a smaller number of dimensionless settings. Thus, the design variables d to be considered in the optimal experimental design study are:

- the dimensionless position of the measurement zone, $d_1 = \bar{z}_{sensor}$;
- the dimensionless height of the lower phase, $d_2 = \bar{z}_0$;
- the experiment duration expressed by the Fourier number, $d_3 = \mathrm{Fo}$; and

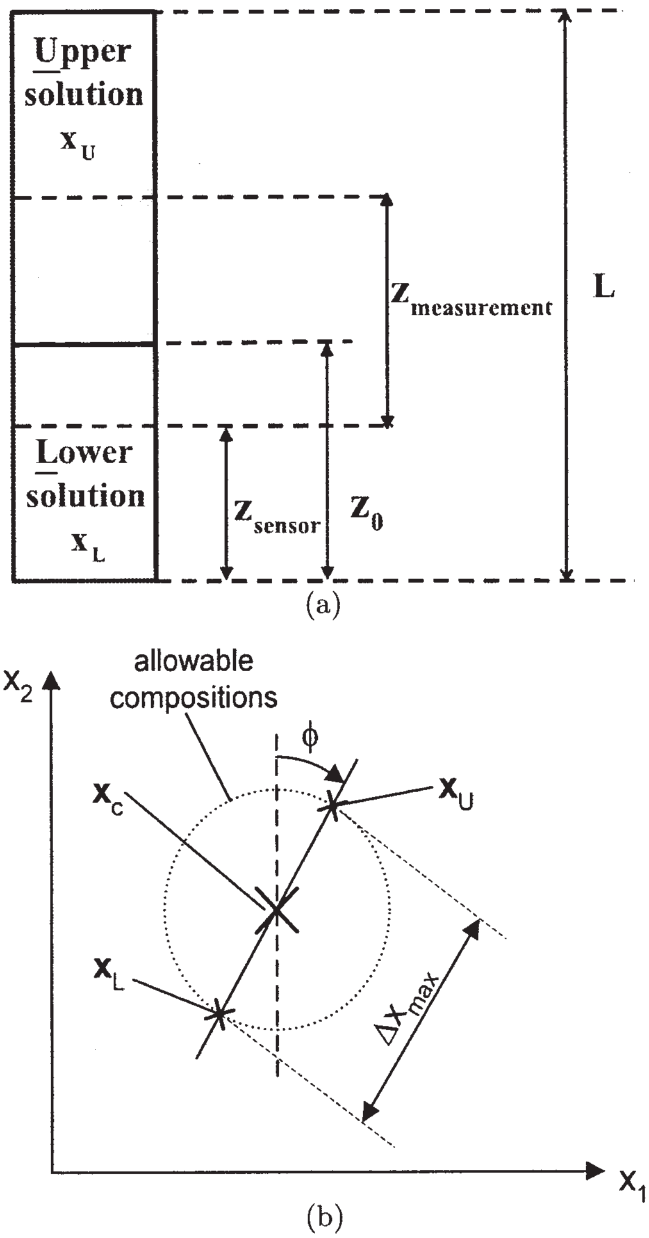

Figure 2. Design variables for a ternary experiment: (a) sketch of the diffusion cell; (b) parameterization of the initial composition.

- the initial conditions x_u and x_L parameterized by the angle ϕ, $d_4 = \phi$.

Stability Requirements. In practice, the design space for ternary Raman experiments is limited by stability requirements. Mass transport should only occur due to diffusion, but convection may occur in multicomponent diffusion experiments performed in vertical cells.[3] It is no longer sufficient to guarantee that the experiment is statically stable at the start, that is, density decreases with column height, $(\partial\rho/\partial z)_{t=0} < 0$. Design criteria to avoid the onset of convective instabilities have, therefore, been derived.[28–30] Miller and Vitagliano[31] summarized the results and gave the following conditions to ensure stability in the course of ternary diffusion experiments:

$$\frac{\partial\rho}{\partial z} = H_1\frac{\partial c_1}{\partial z} + H_2\frac{\partial c_2}{\partial z} < 0,$$
$$(H_1D^v_{22} - H_2D^v_{21})\frac{\partial c_1}{\partial z} + (H_2D^v_{11} - H_1D^v_{12})\frac{\partial c_2}{\partial z} < 0, \qquad (5)$$

where H_i denotes the coefficient of the linearized density equation

$$H_i = \frac{\partial\rho(c_1, c_2)}{\partial c_i} = M_i - \frac{\bar{V}_i}{\bar{V}_3}M_3, \quad i = 1, 2. \qquad (6)$$

The first condition (5a) ensures that density decreases with height throughout the experiment; the second condition (5b) prevents the so-called fingering instability.[28,29]

These constraints have to be added to the design problem. In principle, the constraints have to be fulfilled at all times t and locations z, which renders the problem semi-infinite. Since the constraints follow a smooth time evolution, they are enforced here on a grid only. The remaining design space for the chosen example is shown in Figure 3. It can be concluded that the requirement of stable conditions limits the design variable ϕ only. The allowable range is reduced to roughly a third of the full circle in the studied example ($\phi \in [140°, 268°]$).

Design Problem Formulation. The design variables should be chosen to increase parameter precision, which can be measured by the variance. The inverse of the Fisher information matrix F (Eq. 2) provides an estimate for the covariance matrix of the measured diffusion coefficients. In order to minimize the variance, the Fisher information matrix should, therefore, be maximized. A scalar measure of the matrix has to be introduced to formulate an optimization problem. The most popular

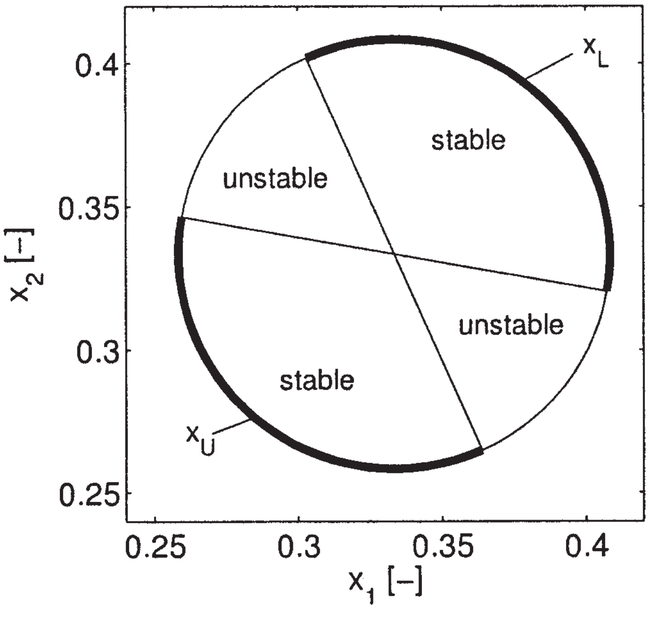

Figure 3. Allowable initial conditions for a Raman diffusion experiment within the mixture *n*-propanol + 1-chlorobutane + *n*-heptane.

Stable conditions are indicated by thick lines.

Table 2. ζ-Efficiency Computed for Ternary Raman Diffusion Experiments

N	1	2	3	4	5	6	7	8	10	50	100
ζ [%]	12.3	99.3	94.1	99.1	97.5	99.3	98.5	99.4	99.6	100.0	100

The Fisher matrix is scaled by the number of experiments N.

method is the so-called D-optimal design:[25]

$$\max_{d} \det(F(D^v, d)). \tag{7}$$

It will be assumed that the errors in the measured mole fractions $\bar{x}_1$, $\bar{x}_2$ are independent with constant variance σ_x^2, which is a good approximation for small initial concentration differences. Thus, the Fisher information matrix (Eq. 2) can be specified here as:

$$F(D^v, d) = \sum_{\mu=1}^{N} \begin{bmatrix} \frac{\partial x_{1,\mu}}{\partial D^v_{11}} & \frac{\partial x_{2,\mu}}{\partial D^v_{11}} \\ \frac{\partial x_{1,\mu}}{\partial D^v_{12}} & \frac{\partial x_{2,\mu}}{\partial D^v_{12}} \\ \frac{\partial x_{1,\mu}}{\partial D^v_{21}} & \frac{\partial x_{2,\mu}}{\partial D^v_{21}} \\ \frac{\partial x_{1,\mu}}{\partial D^v_{22}} & \frac{\partial x_{2,\mu}}{\partial D^v_{22}} \end{bmatrix} \begin{bmatrix} \frac{1}{\sigma_x^2} & 0 \\ 0 & \frac{1}{\sigma_x^2} \end{bmatrix} \begin{bmatrix} \frac{\partial x_{1,\mu}}{\partial D^v_{11}} & \frac{\partial x_{1,\mu}}{\partial D^v_{12}} & \frac{\partial x_{1,\mu}}{\partial D^v_{21}} & \frac{\partial x_{1,\mu}}{\partial D^v_{22}} \\ \frac{\partial x_{2,\mu}}{\partial D^v_{11}} & \frac{\partial x_{2,\mu}}{\partial D^v_{12}} & \frac{\partial x_{2,\mu}}{\partial D^v_{21}} & \frac{\partial x_{2,\mu}}{\partial D^v_{22}} \end{bmatrix}. \tag{8}$$

The ternary diffusion model (Eq. 1) along with the appropriate sensitivity equations ($\partial x_i / \partial D_{ij}$) have been implemented using the analytical solution.[32]

The D-optimal design (Eq. 7) tries to minimize the volume of the parameter confidence ellipsoids. In order to assess the performance of a particular design, the so-called D-efficiency is introduced:

$$\zeta(D^v, d) = \left[\frac{\det(F(D^v, d))}{\det(F(D^v, d^*))}\right]^{1/4}, \tag{9}$$

where d^* is the optimal design. The ζ-efficiency measures the average precision loss per parameter for a design d; for example, for an experiment with $\zeta = 1/5$, the parameter variance is expected to increase by a factor of five on average compared to the optimal design.

Optimization Study. Above, it is shown that the full ternary Fick matrix is locally identifiable from a single Raman diffusion experiment. However, the question arises whether it may be significantly better to perform more experiments and, finally, what the optimal number of ternary Raman diffusion experiments is. For this purpose, the experimental design calculation is performed for up to 100 Raman diffusion experiments. Since every new experiment will yield additional information, the objective function (Eq. 7) would favor as many experiments as possible. In order to evaluate if an increase of the objective is significant, the Fisher information matrix is normalized by the number of experiments N. Thus, the information density retrieved per experiment is measured.[25] The ζ-efficiency, which compares the expected accuracy per parameter with the best design, is shown in Table2. A significant increase in precision is expected from the addition of a second experiment ($N = 2$). After that, the ζ-efficiency stays roughly constant. Thus, the greatest gain in diffusion coefficient precision is expected from the use of a second experiment. Whether further experiments are then still required, depends on the accuracy obtained from the two runs. Any even number of experiments yields efficiencies higher than 99%, while odd numbers of experiments give lower efficiencies, increasing with the total number of runs. This behavior is ascribed to the fact that one run per diffusion mode is favored. Based on these results, it is therefore assumed in the following that two Raman diffusion experiments are performed to estimate the ternary Fick diffusion coefficient matrix. For ease of computation, the sensor location, the initial height of the boundary, and the experiment duration will be chosen identical in both experimental runs.*

The optimal design found from the solution of Eq. 7 places the sensor at the lower wall, $\bar{z}_{sensor} = 0$. The initial boundary is at $\bar{z}_0 = 0.433$. The cell is not equally filled due to the difference in molar volumes of the components. Only if all components have equal molar volume should the initial boundary be in the center of the cell. The duration expressed by the Fourier number is Fo $= 0.157$. Remarkably, restricted diffusion experiments are favored over the free diffusion design commonly used. The ζ-efficiency of a typical free diffusion experiment ($L = 300$ mm, $t_{max} = 4$ h) is $\zeta = 2.5 \cdot 10^{-7}$, that is, the standard deviation of the parameters is expected to increase by a factor of 2,000 in comparison to the optimal design.

It should be noted that the dimensionless design variables discussed above practically retain their values from the binary case.[15,19] Thus, it may be conjectured that these values are characteristic for the chosen setup and sampling policy—independent of the number of components studied.

The optimal initial conditions are given by $\phi^{(1)} = 153.0°$, $\phi^{(2)} = 242.2°$. Thus, the angles $\phi^{(i)}$ characterizing the initial conditions are almost perpendicular to one another. This implies that the measured molar fractions should be as distinct as possible (compare Figure 2).

In order to assess the sensitivity of the optimal design with respect to the experimental settings d, the D-efficiency is computed for a variety of parameter choices. Figure 4a shows that it is the relative choice of the initial compositions $\phi^{(1)}$, $\phi^{(2)}$ rather than the actual values that determines the quality of the experiment. Good experiments should be performed with $\phi^{(2)} = \phi^{(1)} + 90°$. The actual value of $\phi^{(1)}$, $\phi^{(2)}$ has a minor influence. For this reason, the hydrodynamic stability constraints also have only minor influence on the attainable precision. The ζ-efficiency is decreased by 5% in comparison to a hypothetical zero-gravity experiment. In addition, Figure 4a visualizes also that the use of only one Raman experiment would come at the cost of substantial loss of precision (compare Table 2). Since the Fisher information matrix is additive (compare Eq. 8), a single experiment would contain half of the information obtained by the combination $\phi^{(1)} = \phi^{(2)}$, yielding extremely small ζ-efficiencies ($\zeta \approx 0.07$). In particular, the correlation between the main and cross diffusion coefficients is higher than 0.999, indicating large uncertainty in this case.

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* This assumption does not impair the general conclusions derived in the following.[33]

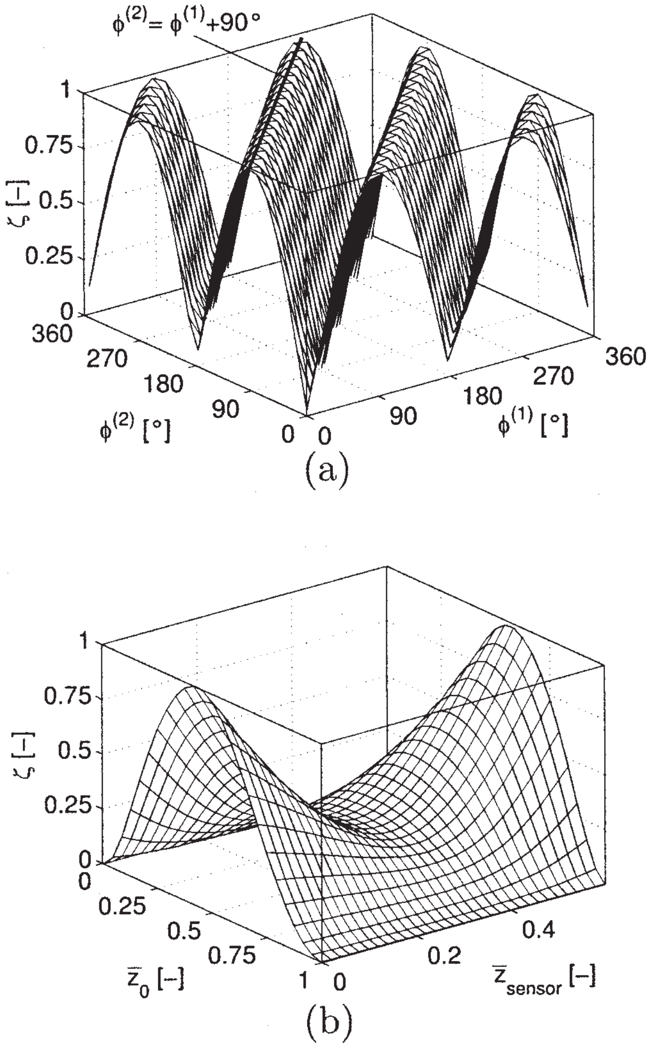

Figure 4. *D*-efficiency ζ: (a) as function of initial composition and (b) as function of sensor location $\overline{Z}_{sensor}$ and initial height of bottom mixture $\overline{Z}_0$.

For the considered example, the diffusion coefficients D_{ij}^{v} obtained from the optimal experiment are expected with standard deviations from $0.8 \cdot 10^{-12}$ to $1.9 \cdot 10^{-12} m^2/s$. This corresponds to 0.08% for the main term and up to 0.71% for the cross diffusion coefficients. Larger uncertainties are found in practice due to unavoidable systematic errors.

As the relationship between measurements and diffusion coefficients is nonlinear, the whole design procedure does depend on an initial guess for the diffusivities that are actually sought. This is the standard dilemma of optimal experimental design theory.[25] Robust formulations could be used to minimize the dependence on this initial guess.[25] For the diffusion problem considered, this dependence is, however, very weak: measurements at the wall are always favored. The cell should be filled roughly equally with both solutions. Only experiment duration depends on the actual value of the diffusion constants. Thus, a conservative design would employ a long experiment to initiate the iterative procedure. Raman experiments then allow determining a first estimate of the diffusivities from a single run based on which the second experiment can already be optimized. The density requirements are more severe as they might destroy the whole measurement. Here, an initial experiment along the direction of the highest density gradient is recommended.

Experimental Section

Raman diffusion experiment

For a diffusion experiment, two solutions with slightly differing composition are prepared (all chemicals from FLUKA in *spectroscopic grade*, purity $> 99.8\%$). Raman diffusion experiments are then performed in a vertical column (Figure 2). Before each experiment, the diffusion cell is filled first with the lighter solution up to four-fifths of its inner height. Then, the denser solution is added carefully from below with the help of a syringe pump (ABG). The filling is stopped when the denser solution has reached a level of about 8 mm, measured from the bottom of the cell. The premixed liquid is slowly withdrawn from the cell via a capillary borehole in one side wall at $z = 6$ mm. In this way, the boundary is sharpened and lowered to the borehole level set at the center of the CCD-chip in the optical setup. The position of the borehole has been chosen based on preceding design calculations. Optimal experiments last about 4 h in this case. In order to minimize evaporation effects, the total height of the liquid column reaches up to the top of the diffusion cell ($L = 30$ mm), which also adds to the information content of the measurements. High repetition rate 1-D-Raman spectroscopy allows the online control of the experimental preparation.

After the cell has been closed, the first picture is recorded. In the cell, mixing occurs due to diffusion. The mole fractions of all species are simultaneously measured in a section of the diffusion cell by Raman spectroscopy. For concentration determination with Raman spectroscopy, the components must be nonfluorescent and Raman-active. This is in general a minor limitation, but dissociating species of single ions, such as NaCl and $MgCl_2$, cannot be studied. In this work, organic mixtures are, therefore, considered.

In order to induce Raman scattering, the beam of an Argon Ion Laser (SPECTRA PHYSICS, excitation wavelength 514.5 nm, power 1.5 W) is focused and directed vertically through the diffusion cell made of quartz-glass. Molecules in the sample get excited and emit Raman signals with shifted frequencies depending on their structure. The scattered light is collected along the 10 mm long measuring line in a 90°-angle to the cell (Figure 5). The dominating, disturbing Rayleigh scattering is removed by filtering. An imaging spectrograph (ARC, Spectra Pro 500 i) then resolves the spectral information of the Raman signal. In this way, a two-dimensional image with one spatial and a spectral coordinate is obtained. The image is detected by a thermal-electrically cooled, back-illuminated CCD camera (PI, SPEC-10:400) and stored sequentially on a PC. One image contains the information about the concentration of all species at 400 equidistant local positions along the measurement line. The exposure time is 20 s in all runs. Delays between two images increased from 45 s at the start up to 400 s for the last exposures at 2.5 to 4 h. The temperature is constant within 0.2 K.

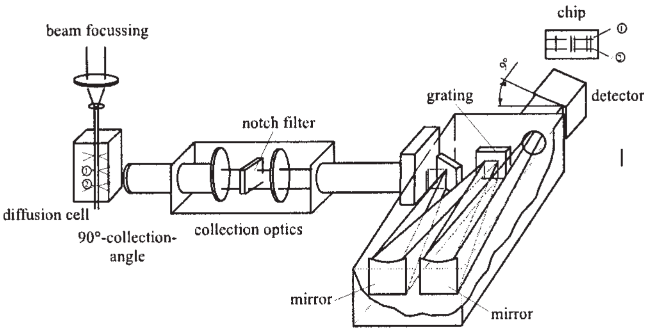

Figure 5. Experimental setup of one-dimensional Raman spectroscopy for diffusivity measurements.

Spectra analysis

At every measurement instance, 400 Raman spectra are simultaneously collected along the one-dimensional measurement line. A typical spectrum for the mixture 1-chlorobutane–*n*-heptane–*n*-propanol is shown in Figure 6. From these mixture spectra, the concentrations of the individual components are extracted. This deconvolution step is performed here using the *indirect spectral hard modeling* (ISHM) method developed by some of the authors and co-workers.[23,24] In the calibration phase of the ISHM method, the pure component spectra of a mixture are approximated by hard modeling using overlapping Voigt profiles. A mixture spectrum is then modeled by the weighted superposition of all pure component spectra models and a model to account for the background intensity level. In this procedure, the pure component spectra models are allowed to adapt to the systematic modifications of vibration bands due to molecular interactions in the mixture. For this purpose, some Voigt profile parameters in the hard models are set as free variables in the mixture spectrum fitting problem.

The basic assumption of quantitative Raman spectroscopy is a linear relationship between the partial signal intensity and the concentration c_i of each species i.[11] This holds for a variety of nonideal systems over a wide concentration range with good precision.[34] In ISHM, the weight w_i of the pure component spectrum of species i in the mixture model is, therefore, proportional to the concentration of this analyte in the scattering volume. In order to utilize this relationship independently of drifts in laser power or other exterior influences, the method of an internal standard is employed.[35] In a mixture with n_c components, a species j is, therefore, chosen as a reference component. Dividing the scaling factor w_i of the individual spectrum by that of the reference component, the following relationship can be obtained:[23]

$$\frac{w_i}{w_j} = \frac{c_i}{c_j} k_{ij}, \tag{10}$$

where the proportionality factor k_{ij} between the ratios of molar concentration and the individual scaling factors has to be determined by calibration. For this purpose, mixtures of known composition are analyzed. In a ternary mixture, two independent proportionality factors k_{13} and k_{23} have to be determined. In principle, a single calibration sample would be sufficient. In practice, these factors k_{ij} might, however, depend on spatial position and mixture composition.[16] Such effects might be caused by systematic errors in the optical parts and their adjustment, lack of the spectral model, or the nonideal behavior of the system due to intermolecular forces. For high-precision measurements, it is therefore recommended to test and identify spatial and concentration dependencies by using additional test samples of known composition. In this work, the dependence on position z is represented by a 5-row-average-value, while no concentration dependence has to be considered due to the small concentration differences used.

With the knowledge of the proportionality factors $k_{ij}(z)$ from calibration, mixtures of unknown composition can be analyzed. The weighting factors w_i of the individual species are determined for the mixture spectrum. The mole fraction of each component can then be calculated from:

$$x_i = \frac{c_i}{\sum_{k=1}^{n_c} c_k} = \frac{c_i/c_j}{\sum_{k=1}^{n_c} c_k/c_j} = \left(\sum_{k=1}^{n_c} \frac{w_k}{w_i} \frac{k_{ij}}{k_{kj}} \right)^{-1}. \tag{11}$$

In this work, Raman mixture spectra from 1-chlorobutane, *n*-heptane, and *n*-propanol are analyzed in the region from [580…1200] cm^{-1} (Figure 6). An inclusion of bands beyond the chosen region leads to poorer results since the correlation of the pure component spectra is increased. At Raman shifts of $\nu = 1250$ or 1410 cm^{-1}, for example, the three species show no separated characteristic spectral bands.

The mixture spectrum model consists of 29 Voigt profiles for 1-chlorobutane, 30 for *n*-heptane, and 19 for *n*-propanol. For an efficient representation of the vibration bands shifts in the mixture, peaks showing nearly identical behavior are grouped. Thereby, only two peak position plus six parameters for the background signal have to be fitted for each mixture spectrum, taking about 3 s on a standard PC (Intel P4, 1.5 GHz). The concentration profiles obtained by this procedure are shown for ternary diffusion experiments in Figure 7. The concentration equilibration is much faster for 1-chlorobutane than for the other two species. For this species, moderate diffusive cross-effects are visible at the center of the measuring line ($z = 5$ mm), leading to a temporal local maximum of its molar fraction.

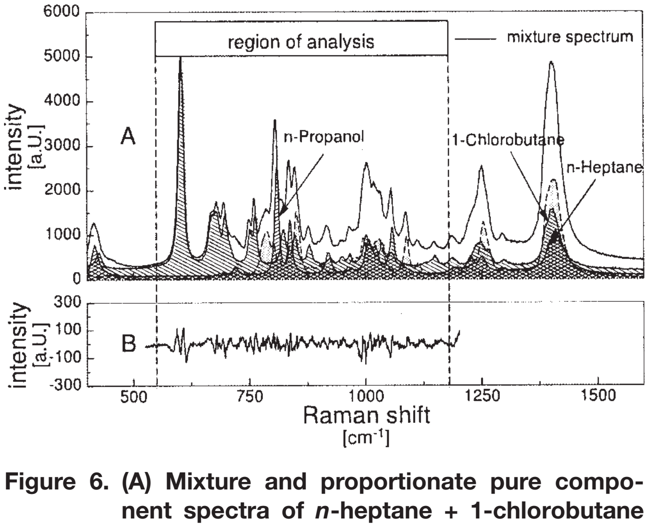

Figure 6. (A) Mixture and proportionate pure component spectra of *n*-heptane + 1-chlorobutane + *n*-propanol within and next to the region of spectral analyses; (B) lack of fit.

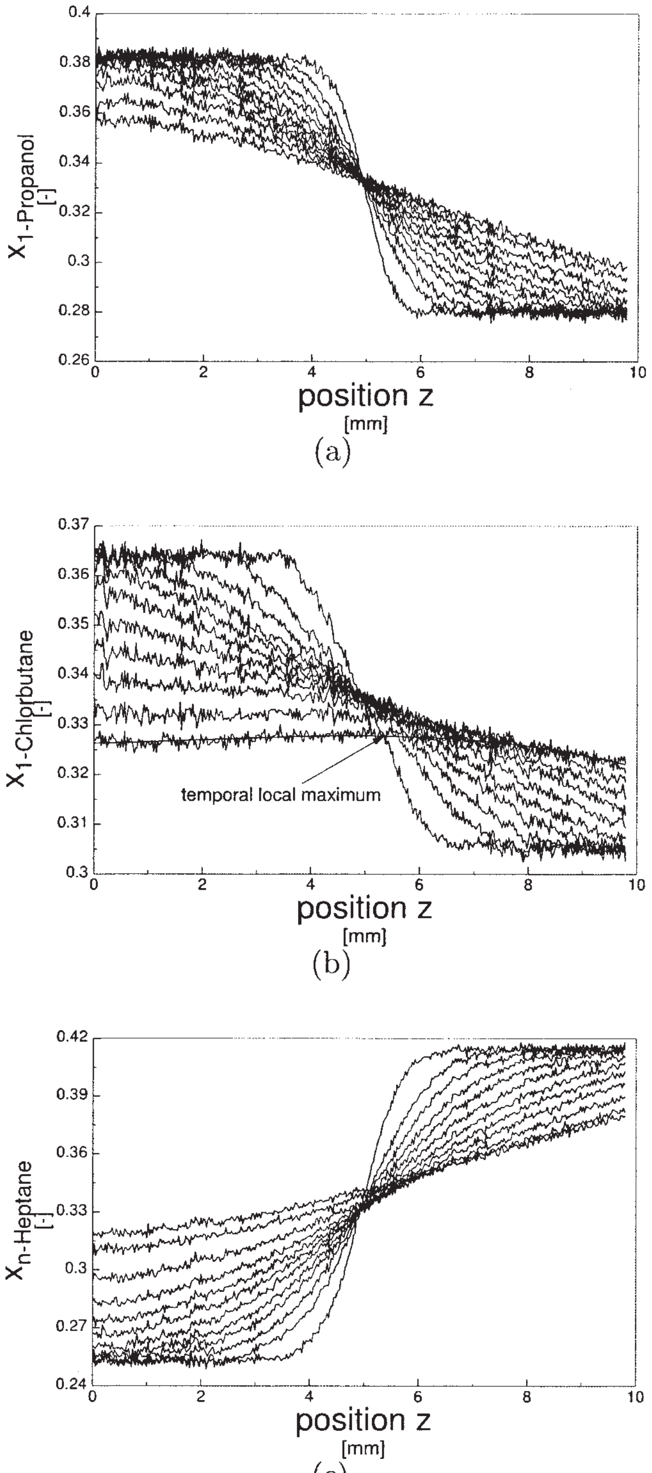

Figure 7. Concentration profiles determined by Raman spectroscopy over 4 h in a ternary diffusion experiment of (from top to bottom) *n*-propanol, 1-chlorobutane, and *n*-heptane for $\overline{X}_i$ = 0.333 at 25°C.

In this mixture, Raman spectroscopy allows for the determination of the molar fractions of the three species with an accuracy of ±0.27 mol%.[34] This error estimate was obtained by measurement of samples with known composition that were not used during calibration. In general, accuracy of concentration measurements by Raman spectroscopy deteriorates for diluted systems ($x < 0.05$ mol%). Noteworthy, the accuracy depends mostly on how well the individual species can be resolved in the Raman spectrum, while the actual number of components has only a minor influence. This indicates the possibility to study truly multicomponent mixtures in the Raman diffusion experiment.

Estimation Problems for Ternary Diffusion Data

The data analysis procedure for ternary diffusion experiments is a straightforward extension of the binary case.[15] Since the goal is the determination of constant Fick diffusion matrices, only small concentrations regions are covered in one experiment. Thus, the concentration dependence of the measurement error variance σ_x^2 may be neglected, and the errors can be expected to be independent with a constant covariance matrix. In this case, a maximum likelihood formulation reduces to weighted least squares estimation.[19] Preliminary experiments have shown that the measurement errors differ for varying mixture ratios, but are usually similar for all components within one mixture. It may, therefore, be assumed in a first approximation that the measurement variance σ_x^2 is the same for all components i. This allows for a further simplification of the weighted least squares objective to the following least-squares problem, where $\tilde{x}_{i\mu}$ denotes the measured and $x_{i\mu}$ the calculated molar fractions:

$$\min_{D^v} \sum_{i=1}^{2} \sum_{\mu=1}^{N} (\tilde{x}_{i\mu} - x_{i\mu})^2, \tag{12}$$

where the model equations (Eq. 1) serve as constraints. In order to solve Eq. 12 by a sequential optimization strategy, the model equations have to be solved first. This is only possible if the Fick matrix D^v is positive definite. This constraint is derived from the thermodynamics of irreversible processes.[36] For ternary mixtures, positive definiteness may be imposed by the following constraints:[36]

$$\begin{aligned} D_{11}^v + D_{22}^v &> 0, \\ D_{11}^v D_{22}^v - D_{12}^v D_{21}^v &> 0, \\ (D_{11}^v - D_{22}^v)^2 + 4 D_{12}^v D_{21}^v &> 0. \end{aligned} \tag{13}$$

These equations have to be added to the optimization problem.[12] In practice, many optimizers employ so-called infeasible path strategies, that is, the constraints may be violated during the iterations. A solution of the diffusion equations is then no longer possible, and the whole optimization procedure may fail. It, therefore, seems to be beneficial to employ a re-parameterization to avoid these difficulties: The diffusion matrix D^v is positive definite if its eigenvalues $D_1^\dagger$, $D_2^\dagger$ are positive. This condition may be enforced using bound constraints, which are much easier imposed and usually always satisfied. Therefore, the following re-parameterization is proposed:

$$\theta_1 = D_1^\dagger, \quad \theta_2 = D_2^\dagger, \quad \theta_3 = D_{11}^v - D_{22}^v, \quad \theta_4 = D_{12}^v. \tag{14}$$

If the eigenvalues are greater than zero, the constraints (Eq. 13) are trivially satisfied. Now, with the new set of variables

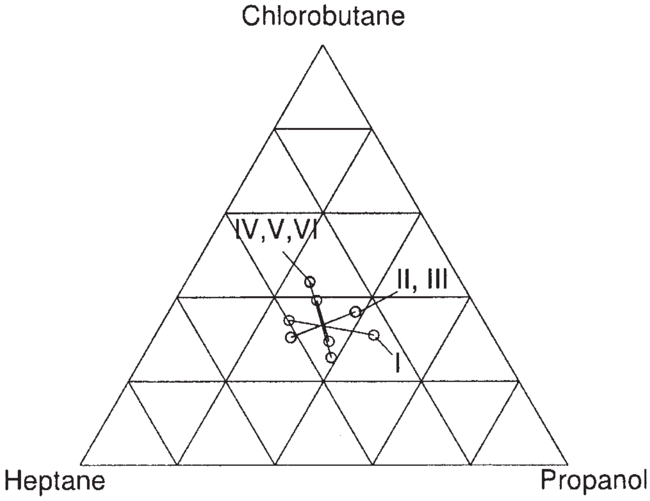

Figure 8. Initial compositions of ternary Raman diffusion experiments.

Different experiments are labeled by Roman numbers. Experiments II and III as well as IV, V, and VI are practically repeated runs using almost identical initial conditions and, therefore, are difficult to distinguish in the diagram.

θ, only the entry D^v_{12} of the Fick matrix is determined directly. The other entries may be recovered from:

$$D^v_{11} = \frac{\theta_1 + \theta_2 + \theta_3}{2}, \quad D^v_{22} = \frac{\theta_1 + \theta_2 - \theta_3}{2},$$
$$D^v_{21} = \frac{(\theta_1 - \theta_2)^2 - \theta_3^2}{4\theta_4}. \qquad (15)$$

The diffusion coefficients D^v estimated in this way are still optimal due to the invariance principle of maximum likelihood estimation.[37] However, the procedure requires the division by the unknown parameter θ_4 to compute D^v_{21}. One would expect that this might cause difficulties in the numerical solution, but an exact value of zero for a variable is rarely encountered in numerical computations. No difficulties have been found so far employing the proposed approach for the analysis of ternary diffusion experiments.

Results

Ternary Fick diffusion coefficients are now determined from Raman diffusion experiments. The local identifiability study has shown that Raman experiments allow the determination of the Fick diffusion matrix from a single run. However, the quantitative assessment using optimal experimental design methods suggests that the employment of a second experiment is expected to lead to a dramatic improvement in the precision of the diffusion coefficients. The following presentation is intended to validate these design predictions as well as the suggested parameter estimation formulation (Eqs. 12–15).

For this purpose, the mixture *n*-propanol + 1-chlorobutane + *n*-heptane is studied. Reference data were measured at $\vartheta = 25°C$ by Käshammer et al.[4] A total number of six Raman diffusion experiments are conducted. The initial compositions are shown in Figure 8. Note that the temperature setpoint was $\vartheta = 23.5°C$ for runs I, V, and VI. The overall consistencies of the results from these runs with remaining runs conducted at $\vartheta = 25°C$, however, suggests that the influence is minor and all runs are, therefore, included in the analysis.

Fick diffusion coefficients D^v are computed using the parameter estimation problem (Eq. 12) with data from a single experiment and data from arbitrary combinations of two and three experiments. The first concentration profile measured is smoothed and taken as the initial condition. In contrast to earlier work,[15] no further corrections are necessary. After parameter estimation, the difference between simulation and data is less than 0.2 mol-%, corresponding well to the expected measurement uncertainty. The estimated diffusion coefficients are plotted in Figure 9.

Three groups are separated by vertical lines. The first group shows diffusion coefficients determined from a single experiment; in the second set two experiments are analyzed together, and in the last group three experiments are jointly used in parameter estimation.

It can be seen that a single Raman experiment suffices to determine the Fick diffusion matrix D^v. Though there is substantial scatter in the estimates, data sets V and VI already yield very good values for the *D*-matrix. These runs possessed a significant initial concentration difference for all three diffusing species, which is favorable for the spectral analysis. From these results, it seems possible to obtain reliable multicomponent diffusion coefficients from a single Raman diffusion experiment if the initial conditions are chosen properly.

The scatter found for the analysis of single runs is significantly reduced if a second experiment is included in the analysis. This confirms the optimal design prediction. Still, occasional outliers are observed in this case. They can be removed by the addition of another experiment, as can be seen from the third group. This observation might lead to the conclusion that three Raman experiments are required in practice today to measure ternary Fick diffusion coefficients. However, the preceding analysis neglected the results of the optimal design

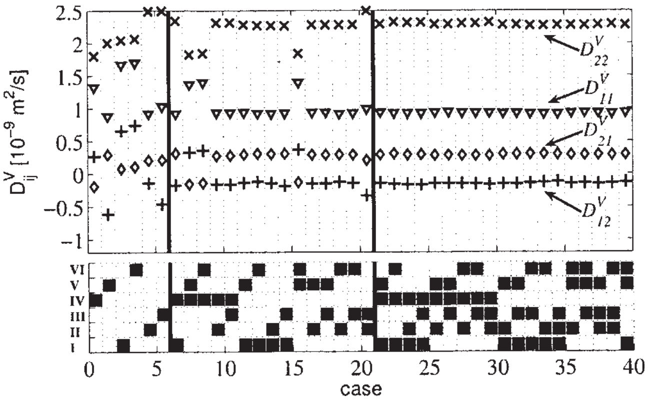

Figure 9. Ternary Fick diffusion coefficients D^v_{ij} at $\vartheta = 25°C$ determined by Raman diffusion experiments for different combinations of the six experiments (=cases) indicated by the black boxes in the lower plot.

The vertical lines separate cases employing one, two, and three experiments for parameter estimation.

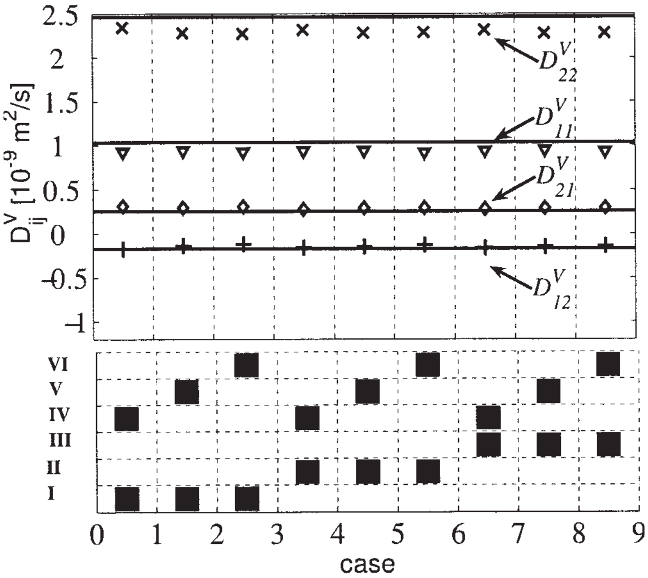

Figure 10. Ternary Fick diffusion coefficients D^v_{ij} at ϑ = = 25°C determined by two optimal designed Raman diffusion experiments in comparison to data from Käshammer et al.[4] (full lines).

The black boxes in the lower plot indicate the experiments used for parameter estimation.

study: *All* possible combinations of the experiments have been used for parameter estimation. The optimal experimental design calculations predicted that the uncertainty will be minimal if the experiments are as distinct as possible. If only combinations are used that satisfy this condition, consistent estimates are obtained from only two experiments (Figure 10). Thus, the results validate the theoretical design predictions.

The numerical value of the Fick matrix determined from the optimized experiments is:

$$D^v = \begin{bmatrix} 0.9308 & -0.1568 \\ 0.2969 & 2.2669 \end{bmatrix} \cdot 10^{-9} \frac{m^2}{s}. \qquad (16)$$

In general, measurement errors in multicomponent mixtures are larger for all diffusion measurement methods.[3] Still, the values are in good agreement with the reference data (Eq. 3). The consistency of the two methods is much better than the accuracy of predictive correlations for multicomponent diffusion today.[38] The main diagonal coefficients measured in this work have values 8–10% lower, whereas agreement in the off-diagonal elements (−9% and +16%) is already within the level of statistical errors (16% and 5%) reported by Käshammer et al. for their measurements. Smaller main diagonal diffusion coefficients might have been found from the Raman data since three runs were conducted at temperatures 1.5 K lower than 25°C, as noted above. This effect can be expected to account for 1.6–4.9% difference based on the temperature correction equation by Tyn.[38,39] Still, the overall consistency of the diffusion coefficient values found from these runs with the values found at the regular temperature suggests that this effect should be minor. A further reason for the deviation is expected to stem from the averaging over the concentration intervals in the experiment, which have been chosen conservative in these validation experiments. On the other hand, Käshammer et al.[4] used diaphragm cell measurements which are known to be difficult to calibrate for multicomponent organic mixtures.[3] They report statistical errors from non-linear regression for the main diagonal elements of 1.5% and 0.7%. Since these error estimates neglect systematic errors, they may be regarded as the lower bound for the true error. The deviation for the main diagonal elements may, therefore, be assumed to be within the joint experimental error of both methods. Recently, even better consistency between the Raman diffusion experiment and an established technique, Taylor dispersion, could be obtained.[40]

For the diffusion coefficients D^v_{ij} determined by the Raman experiments, the standard deviations are 0.89% and 1.99% for D^v_{11} and D^v_{22}, respectively. The scatter in the off-diagonal components D^v_{12} and D^v_{21} are 12.2% and 4.4%, respectively. This corresponds to 1.32% and 0.90% of the geometric mean of the main diagonal diffusivities, which is usually chosen as the reference.[41] The standard deviations were determined from the analysis of different experiments. The overall uncertainty of optimal single, double, and triple runs decreases from 10% to 1.8% to 1.3%. Remarkably, this corresponds very well to the predicted increase in ζ-efficiency presented in Table 2.

The reproducibility of the results over several experiments is compatible with the values reported for other diffusion measurement techniques.[3] The excellent precision in the estimation of the cross diffusion coefficients is especially striking. Errors of 50% and more are usually regarded as common and sufficiently accurate.[38] It seems that the fundamental advantage of the Raman technique to resolve all species in the measurements allows the estimation of all diffusivities with similar quality.

Conclusions

The 1-D Raman spectroscopy technique presented in this work is a powerful and versatile tool for spatially resolved quantitative analysis in liquid systems. In combination with model-based methods for optimal experimental design and parameter estimation, it allows for fast and efficient diffusion measurements in multicomponent mixtures.

A single Raman diffusion experiment provides sufficient information to determine the ternary Fick diffusion matrix uniquely. This result could be established by theoretical analysis and validated in experiments. Raman diffusion experiments, therefore, allow for a substantial reduction of experimental effort for multicomponent diffusion measurements.

General design rules for diffusion experiments in vertical columns could be established using quantitative methods for model-based experimental design. Restricted diffusion experiments are beneficial. If one experiment per diffusion mode is performed, the largest gain in information content is obtained. All further runs add proportional information only. The composition of the mixtures should be as distinct as possible while obeying hydrodynamic stability constraints. These design rules could be confirmed quantitatively in experiments.

Precision and performance of established methods can also be improved by model-based design, as recently shown,[19] for interferometry and Taylor dispersion. Still, only measurement techniques that resolve all individual species, as does the new Raman diffusion experiment, allow for a fundamental reduction in experimental effort due to the reduced number and duration of the experiments. A detailed comparison of the new Raman diffusion experiment with the classical Taylor dispersion method is available.[40]

Currently, quaternary and quinternary mixtures are analyzed using the presented Raman diffusion experiment. It is expected the advantages of the combination of spectroscopic measurements with model-based methods will become even more important as more components are added.

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