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► **To cite this version:**

Michel Cabassud, Patrick Cognet, Valérie Garcia, Marie-Véronique Le Lann, Gilbert Casamatta, et al.. Modeling and Optimization of Lactic Acid Synthesis by the Alkaline Degradation of Fructose in a Batch Reactor. Chemical Engineering Communications, 2005, 192 (6), pp.758-786. 10.1080/009864490519852 . hal-03600408

HAL Id: hal-03600408

<https://hal.science/hal-03600408>

Submitted on 7 Mar 2022

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Modeling and Optimization of Lactic Acid Synthesis by the Alkaline Degradation of Fructose in a Batch Reactor

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The present work deals with the determination of the optimal operating conditions of lactic acid synthesis by the alkaline degradation of fructose. It is a complex transformation for which detailed knowledge is not available. It is carried out in a batch or semi-batch reactor. The "Tendency Modeling" approach, which consists of the development of an approximate stoichiometric and kinetic model, has been used. An experimental planning method has been utilized as the database for model development. The application of the experimental planning methodology allows comparison between the experimental and model response. The model is then used in an optimization procedure to compute the optimal process. The optimal control problem is converted into a nonlinear programming problem solved using the sequential quadratic programming procedure coupled with the golden search method. The strategy developed allows simultaneously optimizing the different variables, which may be constrained. The validity of the methodology is illustrated by the determination of the optimal operating conditions of lactic acid production.

Keywords Lactic acid; Fructose; Batch reactor; Stoichio-kinetic modeling; Optimization

Introduction

In the modern chemical industry, fine chemical activities have taken an increasingly important position. Generally, fine chemicals are high added-value, and high technology products with small production volumes. Due to competition and market fluctuations, their lifespan is relatively short. Commercial strategies have become as important as production strategies: the number of multiproduct or multipurpose plants and the organization of production by campaign have increased. Batch and flexible installations are used in growing proportion (Parakrama, 1985).

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The classical chemical engineering approach applied in the chemical industry, which consists of the development of the optimal installation for a given production according to an imposed volume, is not suitable for the fine chemical industry. The main concern of industrialists is to produce new products the most rapidly. However, due to high purity requirements, environmental regulation, and competitive pressure on the new products, the optimization of batch plants has become an important objective (Georgakis, 1990; Rippin, 1995).

The current practice in the chemical industry involves the use of optimal techniques based on experimental planning (Box et al., 1978). These methods do not attempt to determine a mechanistic interpretation of the transformation. They make use of an input-output model; although yielding good results in many cases, they do not allow one to incorporate any existing understanding of the transformation and thus all the information gained from the experience of chemists goes unused. Moreover, any change in the criterion or in the experimental factors induces one to repeat the whole procedure, resulting in an additional and expensive experimental effort. The numerical problem of batch reactor performance optimization has attracted a lot of attention (Bonvin, 1998); numerous numerical optimization techniques are available in the literature (Edgar and Himmelblau, 1988). The optimal temperature profile or the optimal feed rate profile has been determined for simple reaction networks and for several criteria such as the maximal concentration of a desired product (Rippin, 1983). Several types of objective functions can be readily studied at low cost, but these tools require an accurate model of the process under consideration. Since fine chemical reactions are usually complex, their kinetics are poorly known. Classical kinetic studies are not possible because they are time-consuming in comparison with the duration of the marketing campaigns and the economic objectives.

An alternative approach has been proposed by Filippi (Filippi-Bossy, 1987, Filippi et al., 1989). This strategy aims to conserve the numerical approach of optimization, based upon a structured nonlinear model. The model will not be a fundamental model but a "tendency model," i.e., an approximate stoichiometry and a pseudo-homogeneous kinetic model of the transformation. The tendency model does not attempt to represent correctly all the reaction mechanisms. It allows one to propose a mathematical support to integrate available knowledge on the transformation, thus providing better insight into the process than that offered by the approach based on a black box model. The aim of this tool is, first of all, to represent satisfactorily the influence of the most important operating parameters in order to elaborate an operating protocol leading to the improvement of a given criterion.

Filippi (Filippi-Bossy, 1987) proposed to use the data collected during an iterative procedure to update the model. The strategy was initiated by a few experiments and the data issued from the optimal protocol were added to the database at each step. The above cycle is repeated until no improvement in the criterion is observed. This strategy takes into consideration the uncertainties of the model by supposing that the model becomes increasingly accurate in the course of the iterations. The whole methodology was used again by Marchal-Brassely (Marchal-Brassely, 1990; Marchal-Brassely et al., 1992) for the optimization of technical economic criterion for industrial synthesis, by the computation of optimal temperature and feed rate trajectories. Rastogi et al. (1990, 1992) have used a slightly modified strategy to optimize the epoxidation of oleic acid. Cawthon and Knaebel (1989) have used

the “Tendency Modeling” approach for the acrylonitrile-styrene polymerization reaction. They assumed, however, that the initial model provides a good representation of the transformation and consequently computed the optimal temperature profile without repeating the procedure. Uhlemann (1992) has applied the same strategy for the optimization of 2-furyl oxirane synthesis. More recently, Abel et al. (2000) have studied the optimization of an industrial semi-batch reactor. In their work, they paid particular attention to the case of a cooling system failure.

With regard to optimization, the overwhelming majority of the studies in the literature deal with the determination of a temperature profile or a feed rate profile (Rippin, 1983). Jackson et al. (1971) have shown that for a parallel reaction scheme and for a criterion such as the maximal concentration of the desired product, optimality is never attained by varying both temperature and feed rate simultaneously. The optimal policy is always either to operate the reactor isothermally and to control the reaction by varying the feed rate of one of the reactants or to operate batch-wise and to use an optimal temperature profile. This seems to be true only for simple networks, since counter-examples are known in the domain of polymerization (Jang and Lin, 1991) and in industrial synthesis incorporating technical economical criterion (Marchal-Brassely et al., 1992).

Thus, the optimization tool used in this work needs to be general and flexible (i.e., to optimize one or more different variables: temperature and feed rate profiles, batch time, amount of reactant, etc.) and also to take into consideration the constraints on the different variables such as physical constraints on the process (in order to respect the heating and cooling capacities of the installation) or economic constraints (purity requirements). Nevertheless, such an optimization problem is a complex one, and its solution by the classical technique of the Maximum Principle of Pontryagin, used traditionally, leads to numerical difficulties (Cuthrell and Biegler, 1987). In this work, the optimization problem is treated as a nonlinear programming problem that can be solved by standard NLP codes. This technique was successfully used in batch processes: in batch distillation (Farhat et al., 1990), for a biochemical reactor (Cuthrell and Biegler, 1989), and for polymerization reactors (Jang and Lin, 1991).

In this work, the tools leading to the stoichiometric and kinetic model and the resolution of the optimization problem are described. The methodology will be illustrated through application to an example of a complex chemical transformation: the alkaline degradation of fructose. The database is provided by a still available experimental planning method that allows one to rigorously cover an experimental domain. The tendency model is developed in one step. The integration of experimental planning in the methodology allows the implementation of step assessing the accuracy of the model. It concerns the comparison between the experimental and model tendencies using the response surfaces. Then the optimal operating conditions will be determined and confirmed by an experimental study.

The Alkaline Degradation of Fructose—Background

With the realization of the progressive depletion of energy supplies of the planet, interest in alternatives for energy and chemical feed stock has been growing. Among the renewable resources, biomass ranks first. In this respect, the sugars (from cane,

beet, etc.) represent very important resources and are still used as a base material in the chemical industry.

Among the sugars, fructose has experienced growing interest, on the one hand due to its low price and on the other hand due to its reactivity potential. The economic attractiveness of processes based on fructose is increasing. Among them, we consider here lactic acid synthesis by the alkaline degradation of fructose.

Lactic acid is a very important commodity chemical (Lipinsky and Sinclair, 1986). Its market has not stopped growing and its world consumption has gone up from 35000 tons in 1982 to 50000 tons in 1989 (Greffeuille et al., 1989). It has functional groups (both hydroxyl group and carboxylic acid) that confer its interesting properties. It is used in numerous domains such as the pharmaceutical, cosmetics, and food industries, and new applications continue to appear. In particular, it is possible to make lactic acid copolymers whose biodegradation rate can be controlled. They present a benign environmental impact and can be used in packaging or consumer goods instead of the existing thermoplastics.

Lactic acid could be made from:

- Petroleum, thus obtaining the highest purity product but also the most expensive,
- Fermentation processes, requiring high quality process control and a very high purity of the culture used, which increases production costs,
- The alkaline degradation of sugars (for example, fructose), which allows one to obtain the least expensive product but with a limited yield.

Nowadays, fermentation processes are the most important part of the production of lactic acid. Yield improvement of lactic acid by the alkaline degradation of fructose may lead to an attractive method of production, competing with biochemical, processes and enabling one to avoid the shortcomings of the latter.

The alkaline degradation of fructose may be implemented in a simple way by introducing fructose in an alkaline solution. Nevertheless, the alkaline degradation of fructose is a nonselective transformation resulting, by means of a very complex reaction scheme, in numerous by products, such as:

- The isomers of fructose: glucose, mannose, sorbose, psicose, galactose, tagatose, gulose, etc.
- Formic, acetic, glycolic, glyceric, lactic, threonic, 2,4 and 3,4 dihydroxybutyric, 2-deoxypentonic, saccharinic acids, etc.
- Products of degradation such as cyclopentation, furanic compounds, phenolic compounds, volatile compounds, oligomers, polymers, colored products, etc.

For many years the degradation of fructose in alkaline medium attracted the attention of chemists who put forward several pathways to account for the products formed (Montgomery, 1953; Reintjes and Cooper, 1984; De Bruijn, 1986). All the reaction mechanisms will not be described here. For simplification, we can say that the transformation can be roughly decomposed in two kinds of reactions (Figure 1): isomerizations leading to the different isomers of fructose (reversible reactions) degradation leading to the different acids (irreversible reactions).

The first step of these two reactions is the formation of an intermediate called enediol. The enolization may be followed by numerous reactions: elimination, retroaldolization, rearrangements, etc. Through the enediols, the different acids may originate from fructose, glucose, mannose, or sorbose (Figure 2).

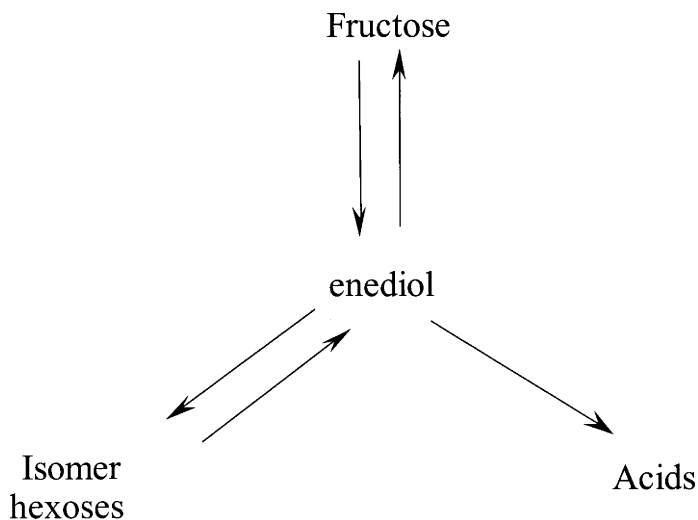


Figure 1. The two types of reactions involved in the alkaline degradation of fructose.

From a kinetic viewpoint, the isomerization reactions were studied in more detail (De Bruijn, 1986; MacLaurin and Green, 1969; El Khadem et al., 1987, 1989; Dubois, 1992); however, the results are not easy to compare and reuse due to the fact that the studies were performed under different conditions. Among the most recent studies, it is important to note the works of De Bruijn (1986) and Dubois (1992). De Bruijn (1986) has proposed a very complex scheme for the transformation. He has studied the transformation in a low alkaline medium under the following conditions: 0.01 mole of KOH, 0.025 mole of sugar, and a temperature of 78°C. He turned his attention to the isomerization reactions. All the acids were gathered into one constituent (Figure 3) in order to render the kinetic constants determination easier, especially for the isomerization reactions.

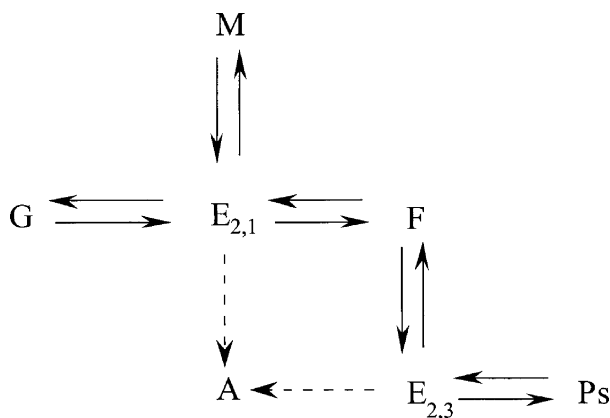


Figure 2. Isomerizations via enolizations; F, fructose; G, glucose; M, mannose, Ps, psicose; E, enediol; A, acids.

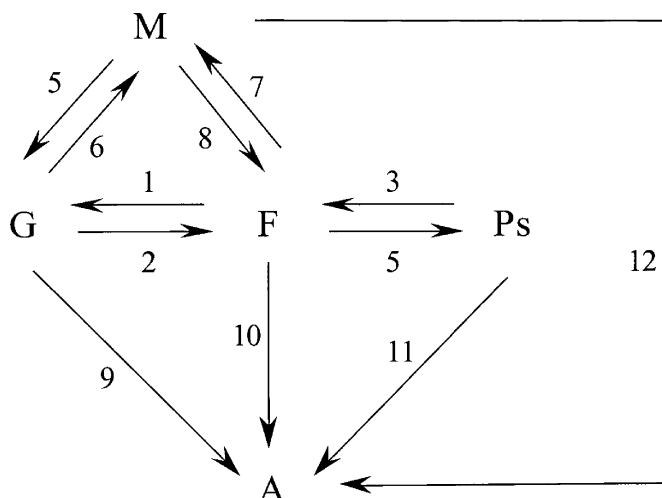


Figure 3. Simplified reaction scheme proposed by De Bruijn (1986).

Dubois (1992) has investigated the choice of the base (NaOH, KOH, etc.), the solvent (H₂, DMSO, etc.), and the eventual use of catalyst (resins). Good results were obtained with sodium hydroxide as a base and water as a solvent. In these conditions, the transformation is an homogeneous one and easy to carry out. The main difficulty remains the analysis of the reaction mixture and the separation and purification of the products.

Studies have been carried out by Dubois (1992) to improve the yield of lactic acid by the degradation of fructose. In order to tackle the difficulties in obtaining a model, the methodology of experimental planning was used. In order to study the influence of the main variables, the reaction temperature, the initial fructose, and sodium hydroxide concentrations, on the response of the system (such as yield in lactic acid), Dubois (1992) has implemented an experimental planning method. The operating levels are shown in Table I. The centered level is denoted “0,” the high level “+”, and the low level “-.”

The experiments have been run for a total batch time of nine hours. The amount of six sugars (fructose (F), glucose (G), mannose (M), sorbose (S), psicose (Ps), galatose (Gal)) and five acids (lactic acid (AL), acetic acid (AA), formic acid (AF), glycolic acid (AGlyco), and glyceric acid (AGlyce)), was determined by a high-performance liquid chromatography (HPLC) analysis (Dubois, 1992). Glucose, tagatose, and gulose could not be separated, and the glucose amount may have been

Table I. Experimental design

Factor	-	0	+
[NaOH] ^o (mole · L ⁻¹)	0.5	1.25	2
Temperature (°C)	40	70	100
[Fructose] ^o (g · L ⁻¹)	25	112.5	200

over-estimated. But, since tagatose and gulose are extremely rare sugars and produced in very small quantities, the error in the concentrations analysis is negligible. Essentially, the sugars produced from fructose are glucose, mannose, sorbose, and psicose. The experimental data are given Table II and are expressed in terms of mass yield:

$$R_X = \frac{\text{amount of X produced}}{\text{amount of fructose added}} \cdot 100$$

The mass yield of the remaining sugars with respect to the initial amount of fructose is given by:

$$R_{\text{sugar}} = \frac{\sum \text{sugars}}{\text{initial fructose}} \cdot 100$$

The lactic acid selectivity with respect to the transformed sugars is expressed by:

$$S_{AL} = \frac{\text{lactic acid}}{(\text{initial fructose} - \sum \text{sugars})} \cdot 100$$

R_{ND} is the mass yield in non-analyzed products.

The relation between the various responses and the different variables is given by a second-order polynomial model. The analysis of the results from the experimental planning indicates the following favorable conditions for lactic acid production: a high initial hydroxide sodium concentration, a low initial fructose concentration, and a low temperature, namely, $[\text{NaOH}]^0 = 2 \text{ mol} \cdot \text{L}^{-1}$, $[\text{F}]^0 = 25 \text{ g} \cdot \text{L}^{-1}$, and $T = 40^\circ\text{C}$.

In these optimal conditions, the lactic acid selectivity is 65.8% and its yield is 64.6% (Dubois, 1992). A time-dependent concentration profile for these optimal conditions (batch-isotherm 40°C) is given in Figure 4.

The work of Dubois (1992) on the alkaline degradation of fructose confirms the two main directions of the transformations assumed in previous studies (De Bruijn, 1986): the transformation in low alkaline medium favors the sugars' isomerization and the transformation in high alkaline medium favors the sugars' degradation leading to acids.

This plan provides a database that is going to be used for the development of the tendency model of the transformation.

Theoretical Development

The minimum necessary data for the development of the tendency model are:

- Total batch time,
- Reactor temperature,
- Initial compositions,
- Feed rate of the reactant (in the case of semi-batch operation),
- Final concentration of the different constituents.

In the case where material losses are observed due to unmeasured products, the definition of pseudo-constituents allows one to satisfy the molar component balances.

Table II. Data of the experimental planning: $X_1 = [\text{NaOH}]^\circ$, $X_2 = \text{temperature}$, $X_3 = [\text{Fructose}]^\circ$

Run	X_1	X_2	X_3	R_F	R_{AL}	R_G	R_M	R_S	R_{Ps}	R_{Gal}	R_{AGlyce}	R_{AGlyco}	R_{AF}	R_{AA}	R_{sucre}	S_{AL}	R_{ND}
1	-	-	-	4.3	32.0	6.9	5.0	0.5	0.6	0.1	8.0	5.2	7.4	2.4	17.4	38.8	27.6
2	+	-	-	0.1	64.6	0.7	1.0	0	0	0	6.3	1.3	4.6	1.1	1.8	65.8	20.3
3	-	+	-	0	28.8	0	0	0	0	0	3.6	5.0	5.5	4.9	0	28.8	52.2
4	+	+	-	0	62.0	0	0	0	0	0	3.3	0.8	2.8	1.8	0	62.0	29.3
5	-	-	+	22.5	0.8	31.0	10.4	5.8	0.5	0.8	0.9	1.5	1.8	1.3	71.0	2.8	22.7
6	+	-	+	3.2	28.1	5.3	3.6	0.6	0.6	0.2	3.6	2.7	3.2	1.5	13.5	32.5	47.4
7	-	+	+	9.6	1.4	12.2	5.6	1.3	1.2	0.6	1.3	2.9	2.7	4.8	30.5	2.1	56.4
8	+	+	+	0	18.4	0	0	0	0	0	3.3	5.4	5.2	3.7	0	18.4	64
9	-	0	0	4.0	1.0	6	3.1	1.6	0.6	0.4	1.6	2.3	2.5	4.9	15.7	1.2	72
10	+	0	0	0	38.2	0	0	0	0	0	3.0	1.2	2.8	2.1	0	38.2	52.7
11	0	-	0	2.5	25.2	6.4	3.7	0.2	0.4	0.2	3.2	2.6	2.9	1.6	13.4	29.1	51.1
12	0	+	0	0	24.1	0	0	0	0	0	3.6	4.4	4.8	3.9	0	24.1	59.2
13	0	0	-	0	51.8	0	0	0	0	0	3.6	2.2	2.4	2.6	0	51.8	37.4
14	0	0	+	1.0	4.2	0.8	0.1	0.4	0	0.1	2.9	4.0	4.9	7.0	2.4	4.3	74.6
15	0	0	0	0	20.6	0	0	0	0	0	4.0	4.4	5.1	3.8	0	20.6	62.1

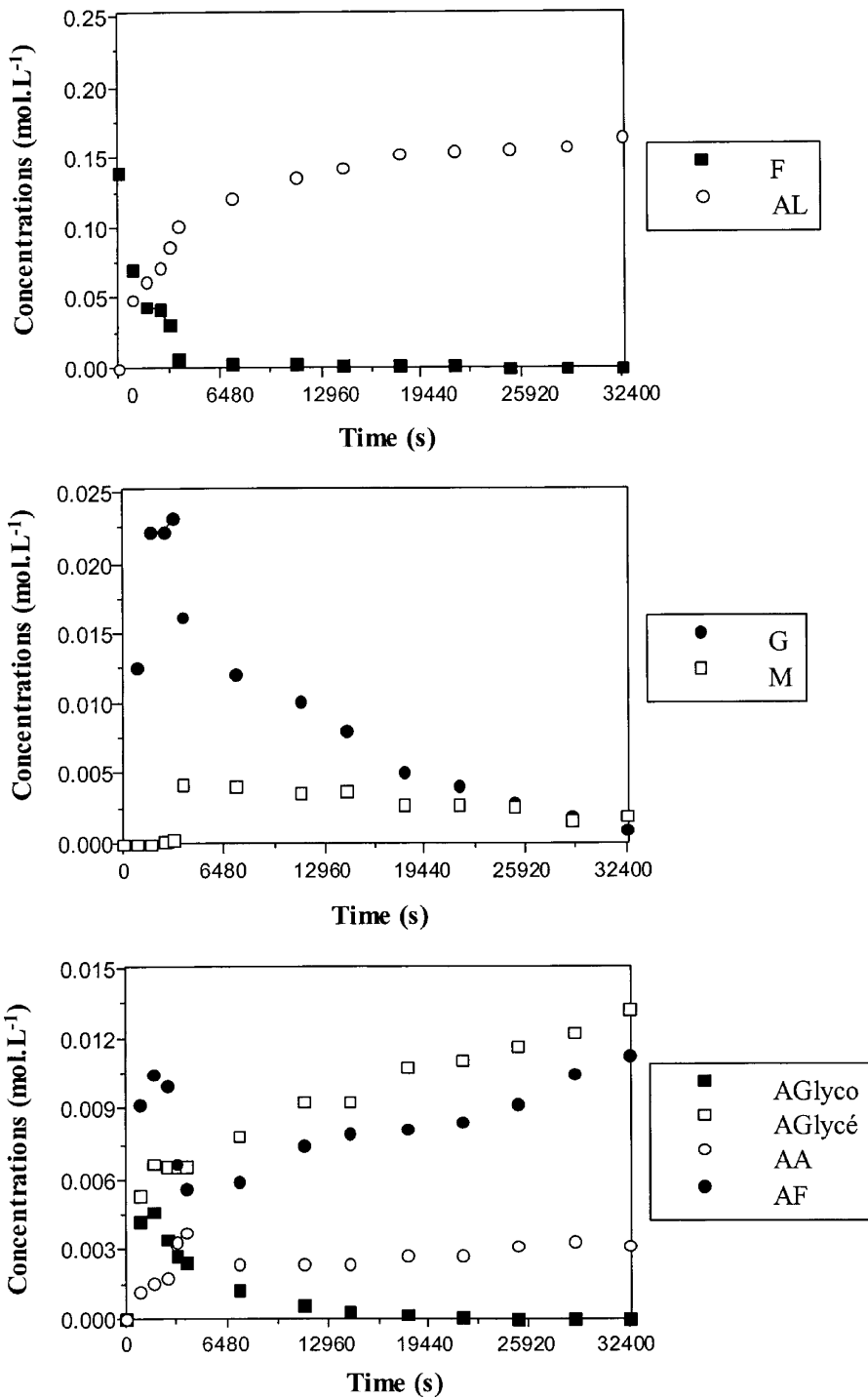


Figure 4. Time evolution of the concentrations for the optimal conditions determined by experimental planning ($[F]^{\circ} = 25 \text{ g} \cdot \text{L}^{-1}$; $[\text{NaOH}]^{\circ} = 2 \text{ mol} \cdot \text{L}^{-1}$; $T = 40^{\circ}\text{C}$).

Identification of a Stoichiometric Model

The first step is the identification of an approximate stoichiometric model of the transformation that correctly fits the batch data. The stoichiometry of a chemical transformation gives the proportions according to which the different constituents react or are produced. These proportions are generally integer or semi-integer.

The stoichiometry of a reaction system involving NC species A_j ($j = 1, NC$) and NR reactions R_i ($i = 1, NR$) can be written:

$$\sum_{j=1}^{NC} v_{ij} A_j = 0 \quad (1)$$

where v_{ij} is the stoichiometric coefficient of A_j in the reaction R_i .

if $v_{ij} > 0$ then A_j is a product in the reaction i

if $v_{ij} < 0$ then A_j is a reactant in the reaction i

if $v_{ij} = 0$ then A_j is not involved in the reaction i

For a batch reactor and a database of NE experiments ($1 = 1, NE$), the number of moles of the compound A_j in the chemical transformation, represented by several reactions R_i , is given by:

$$n_{jl} = n_{jl}^o + n^o \sum_{i=1}^{NR} v_{ij} X_{il} \quad (2)$$

where n_{jl} is the number of moles of A_j in experiment l , n_{jl}^o is the initial number of moles of A_j in experiment l , X_{il} is the extent of reaction R_i in experiment l , and n^o is a normalizing factor equal to the sum of the initial reactants' moles:

$$n^o \sum_{i=1}^{NC} n_{oijl} \quad l = 1, NE \quad (3)$$

Introducing the molar ratio:

$$Y_{jl} = y_{jl} - y_{jl}^o = \frac{n_{jl} - n_{jl}^o}{n^o} \quad (4)$$

Equation (2) leads to:

$$Y_{jl} = \sum_{i=1}^{NR} v_{ij} X_{il} \quad (5)$$

This system may be written in a matrix form as follows:

$$[Y_{jl}] = [v_{ij}]^T [X_{il}] \quad (6)$$

or in a simplified matrix notation:

$$Y = v^T X \quad (7)$$

The stoichiometric vectors of each reaction and the corresponding reaction extents have to be identified. Two algorithms have been proposed in the literature: the step-by-step method and singular value decomposition.

Step-by-Step Method

This method was developed by Filippi et al. (1986) and used for several industrial applications (Filippi-Bossy, 1987; Marchal-Brassely, 1990), organic synthesis (Uhlemann, 1992), and a polymerization system (Cawthon and Knaebel, 1989). It identifies the stoichiometric coefficients one reaction at a time. First, the algorithm assumes that only one reaction can fit the data. The extents are computed by the conjugate gradient technique and the stoichiometric coefficients by a least square method. The search is stopped if the representation is sufficiently good. Otherwise, a new reaction is added and its stoichiometric coefficients are identified, maintaining those of the previous reaction unchanged. The number of reactions is increased by one at each step. The procedure is stopped when the model accuracy, specified by the user, is obtained. The first reaction is a global representation of the transformation, and the others are added to complete the mass balances. The obtained stoichiometric matrix is always a linear combination of the real one (Garcia, 1993) and the difficulty lies in the recombination of the identified matrix. It is important to note that at each step, the operator can propose a stoichiometric vector that is either in agreement with the computed values (by rounding the real values proposed by the algorithm) or not. In this way, it is possible to incorporate available information on the transformation to assist the determination of the stoichiometric network. The flowchart of the procedure is presented in Figure 5.

Singular Value Decomposition Method

The second algorithm used factorial analysis techniques to separate stoichiometric vectors and extents of reaction from the data matrix \mathbb{Y} given by Equation (7). Hamer (1989) has applied this technique on fed-batch fermentation examples, and Tsobanakis et al. (1989) has presented an application with fermentation data. Bonvin and Rippin (1990) have proposed a more elaborate analysis of this technique for complex systems. Rastogi et al. (1990) determined the stoichiometry of the epoxydation of oleic acid. Harmon et al. (1994) have used this tool for the determination of bioprocess networks.

In this technique the number of required reactions, the stoichiometric vectors, and the extents are identified. The decomposition of the data matrix is carried out by a mathematical technique called singular value decomposition (SVD).

Since information about the transformation is often available from the chemist's experience, an approach called target factor analysis (TFA), which allows one to use this knowledge in a procedure deriving stoichiometric models, has been developed by Bonvin and Rippin (1990). This technique enables one to know whether a postulated stoichiometry from a priori information is compatible with the abstract factors.

In conclusion, with both methods, the main problem is the combination of the identified vectors so as to obtain physical meaningful vectors. In both cases, the problem may be solved by testing the proposed stoichiometries:

- In the iterative method, by forcing at each step one reaction of the postulated stoichiometry (by beginning with the principal reaction followed by the main side-reactions)
- In the factor analysis method by testing postulated stoichiometry using TFA.

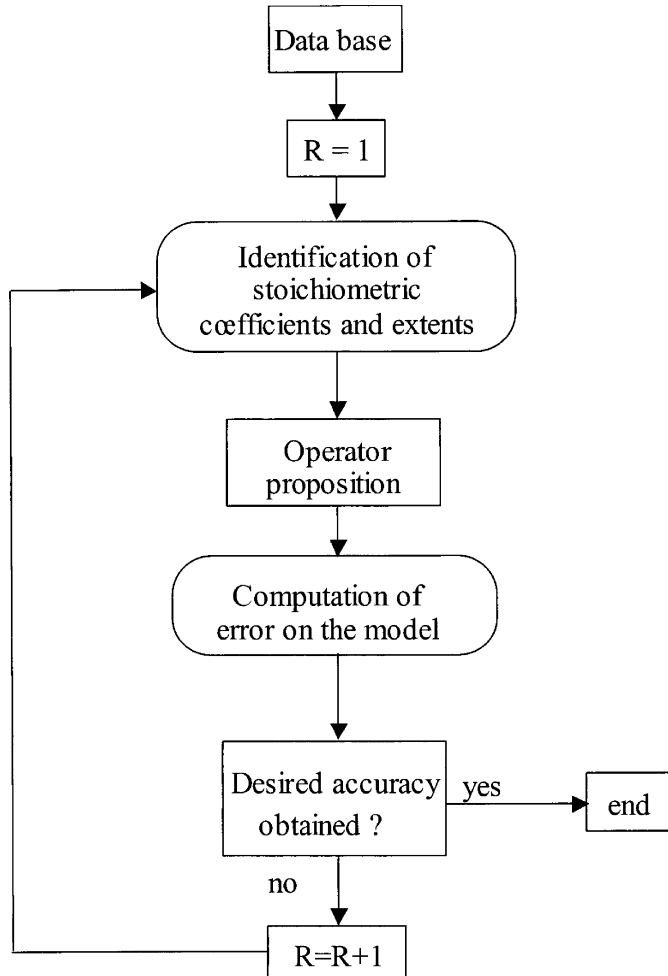


Figure 5. Step-by-step method for the stoichiometric model identification.

Identification of a Kinetic Model

If the reactor operates in batch or semi-batch mode, a molar balance gives:

$$\frac{dn_j}{dt} = Fe_j + R_j V \quad (8)$$

where n_j is the number of moles of A_j at instant t , Fe_j is the feed rate of the compound A_j ($j = 1, NC$), and V is the reactor volume.

And we have:

$$R_j = \sum_{i=1}^{NR} \nu_{ij} r_i \quad (9)$$

where r_i represents the rate of the reactions considered.

In this work, the transformation is supposed to be pseudo-homogeneous and the kinetic law is written as a classical Arrhenius's law. It is important to emphasize that the form of kinetic law and its degree of complexity depend on the user and the desired accuracy of the tendency model. So, we have:

$$r_i = k_i^0 e^{\frac{-E_i}{RT}} \prod_{j=1}^{NC} C_j^{a_{ij}} \quad (10)$$

The number of moles of a specie A_j in the reactor at instant t can be written:

$$n_j = n_j^0 + n^0 Z_j + n^0 \prod_{i=1}^{NR} v_{ij} X_i \quad (11)$$

where

$$Z_j = \frac{1}{n^0} \int_0^t F_{e_j} dt \quad \text{with } Z_j = 0 \text{ at } t = 0$$

We thus obtain:

$$n^0 \sum_{i=1}^{NR} v_{ij} \frac{dX_i}{dt} = V \sum_{i=1}^{NR} v_{ij} r_i = VR_j \quad (12)$$

$$\frac{dX_i}{dt} = \frac{V}{n^0} r_i \quad \text{for } i = 1, NR \quad (13)$$

According to Equation (10), Equation (13) may be written:

$$\frac{dX_i}{dt} = \frac{V}{n^0} k_i^0 \exp\left(\frac{-E_i}{RT}\right) \prod_{j=1}^{NC} C_j^{a_{ij}} \quad \text{for } i = 1, NR \quad (14)$$

where a_{ij} is the order of component j in reaction i , T is the reactor temperature, E_i is the activation energy of reaction i , k_i^0 is the preexponential factor of reaction i , and R is the perfect gas constant.

Preexponential factors (k_i^0), activation energies (E_i), and order (a_{ij}) with respect to each of the reactants for each reaction of the stoichiometric model and the form of the kinetic laws are unknown. The orders are assumed to be part of the data of the problem and are chosen a priori to be equal to the absolute value of the stoichiometric coefficients of every reactant. The problem is thus the determination of the preexponential factors and the activation energies for each reaction in order to minimize the difference between the experimental concentrations and those computed with the identified parameters for the different constituents, according to the following criterion:

$$J = \sum_{l=1}^{NE} \sum_{j=1}^{NC} \frac{C_{0j}^0}{C_{11}^0} \left(C_{jl}^{\text{fid}} - C_{jl}^{\text{exp}} \right)^2 \quad (15)$$

with

$$C_0^0 = \sum_{l=1}^{NE} C_{11}^0 \quad (16)$$

and C_{11}^0 is the concentration of a key reactant in experiment 1.

The criterion is weighted by the ratio C_0^0/C_{11}^0 , which allows weighting each experiment according to the initial concentration of the key reactant in order to avoid neglecting the experiments with small initial concentrations of the reactants. In order to improve the effectiveness of the method and reduce the high correlation between the activation energy and the preexponential factor in Arrhenius's law, a reparameterization is carried out. Only time and temperature are dimensioned parameters.

The different parameters are identified using the Rosenbrock algorithm. But classical parameter identification techniques can be used. The main difficulties are the initialization of the parameters and the significant difference between the orders of magnitude of the component concentrations. The method requires the integration of system (21). A Runge-Kutta-Merson fourth-order procedure with variable step integration size is used. The identification is carried out over the entire NE experiments.

Optimization Problem

A general and flexible tool allowing the optimization of different parameters (temperature, feed rate, amount of reactant, etc.) and respecting possible bounds and constraints was used. The optimal control problem is a complex one, and in order to avoid numerical difficulties arising with the use of Pontryagin's Maximum Principle, it was formulated as a nonlinear programming problem (Garcia et al., 1995; Toulouse et al., 1996).

For this purpose, the interval $[t_0, t_f]$ where t_0 is the initial time and t_f the final batch time is divided into a finite number of *nint* subintervals, and in each subinterval the control function is represented by a linear function versus time:

$$u(t) = z_{j-1} + (t - t_{j-1}) \left(\frac{z_j - z_{j-1}}{t_j - t_{j-1}} \right) \quad j = 1, n, \text{int} \quad (17)$$

The profiles (temperature or feed rate) are defined by parameters z_j and switching times t_j . One of the main advantages of the nonlinear programming approach is the opportunity to include different types of constraints, for example, physical constraints of the process such as constraints on the rate of heating and cooling with respect to plant capacities. If we denote b_{\max} and b_{\min} the upper and lower bounds of the temperature variations, the constraints can be expressed by:

$$(z_j - z_{j-1}) - b_{\max}(t_j - t_{j-1}) < 0 \quad (18)$$

$$(z_{j-1} - z_j) - b_{\min}(t_j - t_{j-1}) < 0 \quad (19)$$

A constraint can also be imposed to control M , the amount of introduced reactant. If the amount of reactant is fixed:

$$\sum_{j=1}^{nint} \int_{t_j}^{t_{j+1}} \phi_j(t, z_j) dt = M \quad (20)$$

or If the amount of reactant has to be optimized:

$$\sum_{j=1}^{n \text{ int}} \int_{t_j}^{t_{j+1}} \phi_j(t, z_j) dt \leq M \quad (21)$$

To respect high purity requirements often required in fine chemistry, constraints of purity restricting the formation of a by-product W under a threshold H_1 may be specified in the following manner:

$$C_W \leq H_1 \quad (22)$$

The problem is then to compute the variables z_j (for temperature and feed rate profile) at each bound of each subinterval so as to improve the objective function and simultaneously satisfy the bounds and the imposed constraints. The NLP problem is solved by means of the sequential quadratic programming (SQP) procedure described by Pibouleau et al. (1985 a,b). The optimal operation time is searched by the golden search method. The different states of the system are calculated by integration of the set of differential equations (21) on each subinterval by a Runge-Kutta-Merson fourth-order procedure with variable step integration size. The initial conditions for each period are the final state of the previous one. An example of temperature profile discretization is given in Figure 6. A more detailed description of the optimization approach is given by Garcia (Garcia, 1993; Garcia et al., 1995).

In this part, the theoretical framework of our global methodology for the optimization of batch chemical reactors has been presented. In the following section, this methodology will be applied to a very complex chemical synthesis: the production of lactic acid by the alkaline degradation of fructose. Actual industrial interest in this synthesis has motivated our choice.

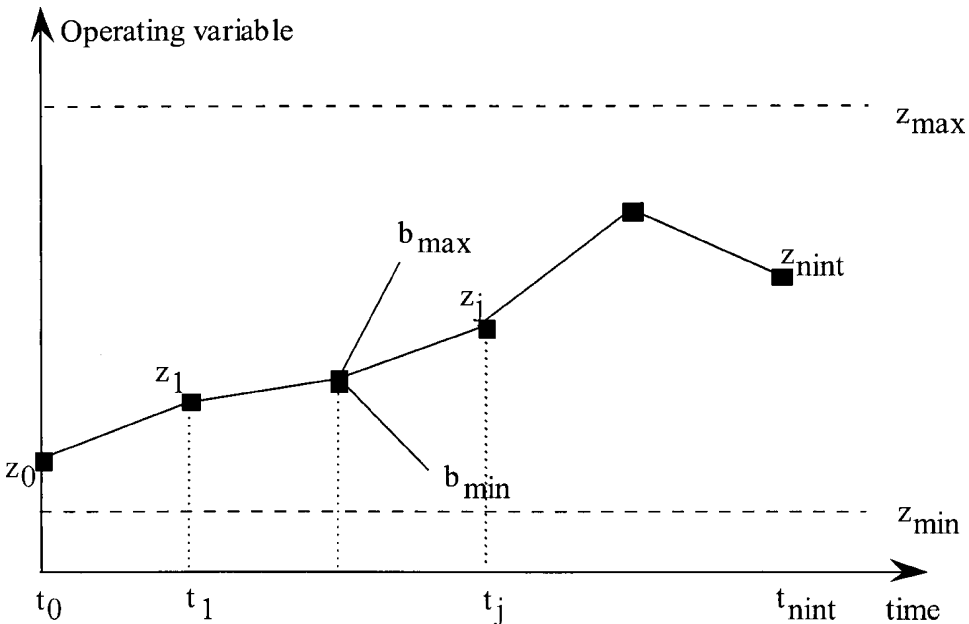


Figure 6. Example of profile discretization.

Development of the Stoichio-Kinetic Model

Assumptions: Forming of Pseudo-compounds

The amount of sodium hydroxide is estimated assuming that one mole of sodium hydroxide is used to produce one mole of acid. The consumption of the former in the non-analyzed products is assumed to be negligible. In the isomerizations, the sodium hydroxide is not consumed; it serves only as a catalyst.

The experimental data sometimes show a very important loss in raw materials due to the non-analyzed products. In order to take this parameter into account in the model, this quantity was expressed by means of a pseudo-constituent called P. Its molar concentration was roughly estimated assuming that the production of lactic, acetic, and formic acids is essentially achieved by means of triose and the production of glyceric and glycolic acids by means of pentose or hexose; thus one obtains:

$$C_P = C_F^{\circ} - [C_F + C_G + C_M + C_{So} + C_{Ps} + C_{Gal} + C_{AGlyce} + C_{AGlyco} + (C_{AL} + C_{AA} + C_{AF})/2]$$

Some assumptions were made in order to decrease the number of constituents present in the mixture. De Bruijn (1986) has gathered the different acids into one pseudo-acid in order to facilitate the determination of the kinetic constants of the isomerizations. In this work we have assumed that all the sugars, that lead to an enediol intermediate present similar sensitivities with respect to the operating variables. All the hexoses were gathered to form a pseudo-constituent FS:

$$FS = F + G + M + Ps + Gal$$

This assumption implies that the enediol formation reaction has to be very rapid in comparison with the degradation reactions or that the isomerization reactions are negligible.

The secondary acids were also grouped to obtain:

$$A = AGlyco + AGlyce + AA + AF$$

The sodium hydroxide and the lactic acid (product of interest) were kept unchanged.

We thus have now a system with only five components: NaOH, FS, AL, A, and P. The tendency model will have to establish as best as possible the influence of the operating variables (temperature, initial fructose and sodium hydroxide concentration) on the result of the transformation through the behavior of these five constituents or pseudo-constituents.

Stoichiometric Model Identification

For the identification of an approximate stoichiometric model of the transformation based on the five components described above, the two techniques previously presented were used (step-by-step and SVD methods).

Since the combination of the nonsensical reactions is a difficult problem we have chosen to test an a priori stoichiometry stemming from deductive reasoning based on the available knowledge about the transformation.

Table III. Postulated stoichiometric matrix

	NaOH	FS	AL	A	P
R ₁	-2	-1	2	0	0
R ₂	0	-1	0	0	1
R ₃	-3	-2	0	3	0

The determination of the singular value by singular value decomposition of the data matrix composed by the dimensionless mole fraction of each constituent gives:

$$(3.6478.7820.21540.0.0123)$$

The last two singular values are much smaller than the previous ones. This indicates that the data may be described adequately by three reactions.

According to the available knowledge about the transformation we have postulated a stoichiometry with three reactions:

- The first reaction represents the lactic acid formation from fructose and sodium hydroxide (one mole of fructose gives two moles of lactic acid).
- The Second reaction represents the unknown or non-measured by-product formation only from fructose, without hydroxide consumption sodium.
- In the third reaction the secondary acids are produced according to a particular molar ratio between fructose and sodium hydroxide. A ratio of two fructose moles for three sodium hydroxide moles to form three moles of acids allows a best fit of the experimental data.

The above postulated stoichiometry is given in Table III.

The matrix composed of the values proposed by the algorithm in the step-by-step method (without intervention of the user to round off the stoichiometric coefficients) is provided in Table IV. It corresponds to nonsensical reactions.

By proposing at each step one reaction of the postulated stoichiometry, a good representation of the data is obtained. The global error is $Er_2 = 1.75 \times 10^{-3}$ and the representation errors for each component over the whole experiments are:

$$Er_1(\text{NaOH}) = 2.03 \times 10^{-4}$$

$$Er_1(\text{FS}) = 8.39 \times 10^{-4}$$

$$Er_1(\text{AL}) = 2.22 \times 10^{-6}$$

$$Er_1(\text{A}) = 2.48 \times 10^{-4}$$

$$Er_1(\text{P}) = 4.63 \times 10^{-4}$$

By the singular value decomposition of the data matrix, the right singular

Table IV. Stoichiometric matrix from step-by-step method

	NaOH	FS	AL	A	P
R ₁	-0.94	-1.21	0.38	0.56	0.65
R ₂	-0.42	0.21	0.55	-0.13	-0.42
R ₃	0.076	-0.048	0.12	-0.20	0.12

Table V. Abstract stoichiometric matrix issued from SVD

	NaOH	FS	AL	A	P
R ₁	0.545	0.661	-0.249	-0.296	-0.339
R ₂	-0.394	0.238	0.174	-0.320	-0.417
R ₃	0.371	-0.217	0.293	-0.664	0.536

vectors associated with the three main singular vectors, called abstract factors, are given in Table V. The target stoichiometry of Table III was then postulated. Using the projection matrix, the stoichiometry of Table VI was obtained. As a measure of the closeness of the targeted and the transformed stoichiometries, the absolute norms of the vector difference between the target and the transformed stoichiometries were calculated. The residual vector between the target and the transformed stoichiometries was found to lie between 0.7 and 2% of the target stoichiometry. The results show that the postulated stoichiometry is compatible with the abstract factors, i.e., the former belongs to the stoichiometric space of the observed data.

In order to compare the results of the two methods, the matrix obtained with the step-by-step method (in Table IV) was postulated as target stoichiometry. The results are given in Table VII. It can be noted that the matrix issued from the step-by-step method belongs to the stoichiometric space of the observed data.

The stoichiometric matrices obtained by the iterative method (nonsensical matrix) and SVD decomposition are linearly dependent. The results observed for both methods are in good agreement. The approximate stoichiometric model with three reactions, based upon pseudo-constituents, results in a good fit with the experimental data.

Kinetic Model Identification

The identification of a kinetic model based upon the stoichiometry described above requires the determination of six parameters: three preexponential factors and three activation energies. The kinetic law is expressed as classical Arrhenius's law and the orders are assumed to be equal to the stoichiometric coefficients of reactants in absolute value.

Table VI. Transformed stoichiometric matrix with target matrix of table III

$$\begin{vmatrix} -2 & -1 & 2 & 0 & 0 \\ 0 & -1 & 0 & 0 & 1 \\ -3 & -2 & 0 & 3 & 0 \end{vmatrix}$$

Target matrix

↓

$$\begin{vmatrix} -1.987 & -1.030 & 1.996 & -0.0084 & -0.029 \\ 0.0071 & -0.98 & 0.0022 & 0.0049 & 1.017 \\ -2.991 & -2.022 & -0.0029 & 2.993 & -0.022 \end{vmatrix}$$

Transformed matrix

Table VII. Transformed stoichiometric matrix with target matrix of table IV

$$\begin{vmatrix} -0.94 & -1.21 & 0.38 & 0.56 & 0.65 \\ -0.42 & 0.21 & 0.55 & -0.13 & -0.42 \\ 0.076 & -0.048 & 0.12 & -0.20 & 0.12 \end{vmatrix}$$

Target matrix

⇓

$$\begin{vmatrix} -0.9399 & -1.2100 & 0.3799 & 0.5599 & 0.6499 \\ -0.4180 & 0.2051 & 0.5494 & -0.1313 & -0.4246 \\ 0.0766 & -0.0463 & 0.1215 & -0.1982 & 0.1216 \end{vmatrix}$$

Transformed matrix

The computed kinetic parameters are given in Table VIII. Figure 7 illustrates the comparison between the experimental and computed final concentrations. A good agreement between experimental and computed values can be observed.

The stoichio-kinetic model has been identified using data corresponding only to initial and final concentrations. Nevertheless, the structure of the model allows simulating time evolution of the concentrations.

A comparison between experimental time-dependent concentrations (from Figure 4) and time-dependent concentrations simulated with the identified model is given in Figure 8. The experimental conditions are the optimal conditions issued from the analysis of the experimental planning ($[\text{NaOH}]^{\circ} = 2 \text{ mol} \cdot \text{L}^{-1}$, $[\text{F}]^{\circ} = 25 \text{ g} \cdot \text{L}^{-1}$, $T = 40^{\circ}\text{C}$). Figure 8 shows a good representation of the time-evolution of the lactic acid concentration. The FS consumption is not always sufficient in the first instants of the reaction. The pseudo-compound A is over produced.

Optimal Operating Conditions Determination

Problem Statement

The main aim of this work is to improve lactic acid yield. With this intention in mind, some problems have to be taken into consideration. The maximum conversion of sugars is important (in order to consume all the raw material), but it is observed from the analysis of the experimental data that it is associated with an increase in the formation of the unknown products. Nevertheless, the presence of the sugars in the reaction mixture is not a severe problem (resulting only in the loss of yield through the unreacted raw material) because the sugar mixtures are easy to recycle.

Table VIII. Identified kinetic parameters

$$\begin{array}{lll} E_1 = 65960 \text{ J} \cdot \text{mole}^{-1} & E_2 = 64698 \text{ J} \cdot \text{mole}^{-1} & E_3 = 78156 \text{ J} \cdot \text{mole}^{-1} \\ k_1^{\circ} = 2.42 \times 10^6 \text{ l}^2 \cdot \text{mole}^{-2} \cdot \text{s}^{-1} & k_2^{\circ} = 2.00 \times 10^6 \cdot \text{s}^{-1} & k_3^{\circ} = 2.70 \times 10^8 \text{ l}^4 \cdot \text{mole}^{-4} \cdot \text{s}^{-1} \end{array}$$

Orders = absolute values of stoichiometric coefficients.

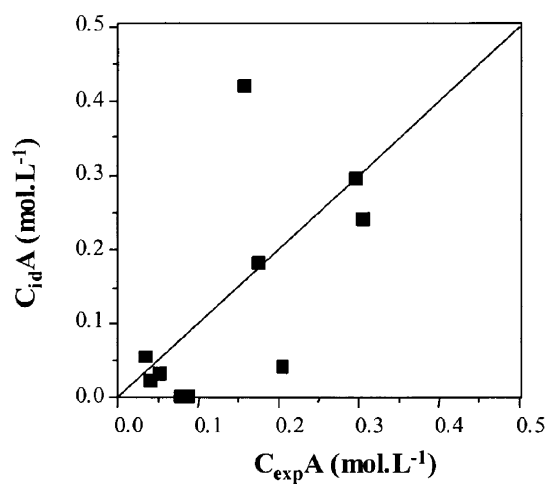
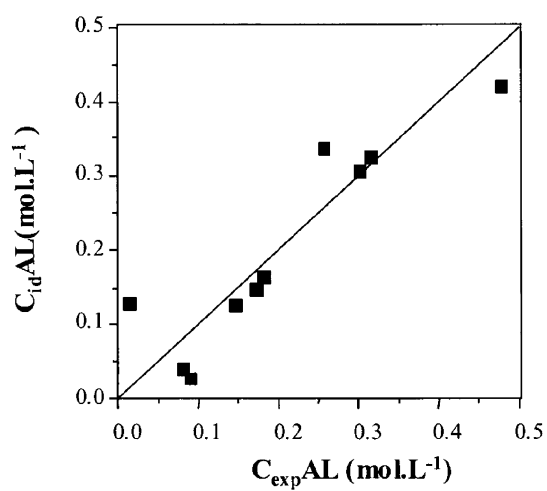
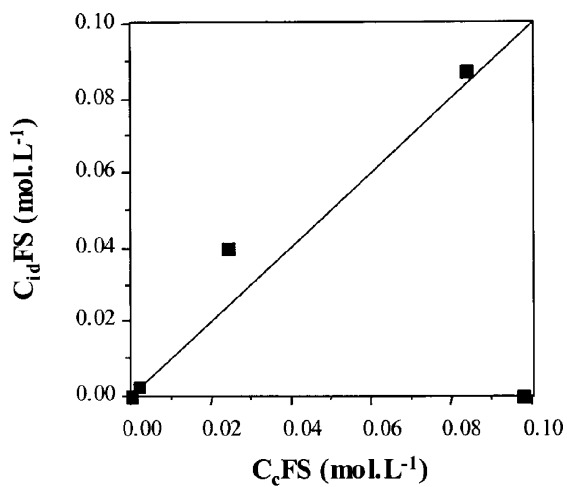


Figure 7. Comparison between the experimental final concentrations (C_{exp}) and final concentrations (C_{id}) computed with the kinetic models given in Table VIII.

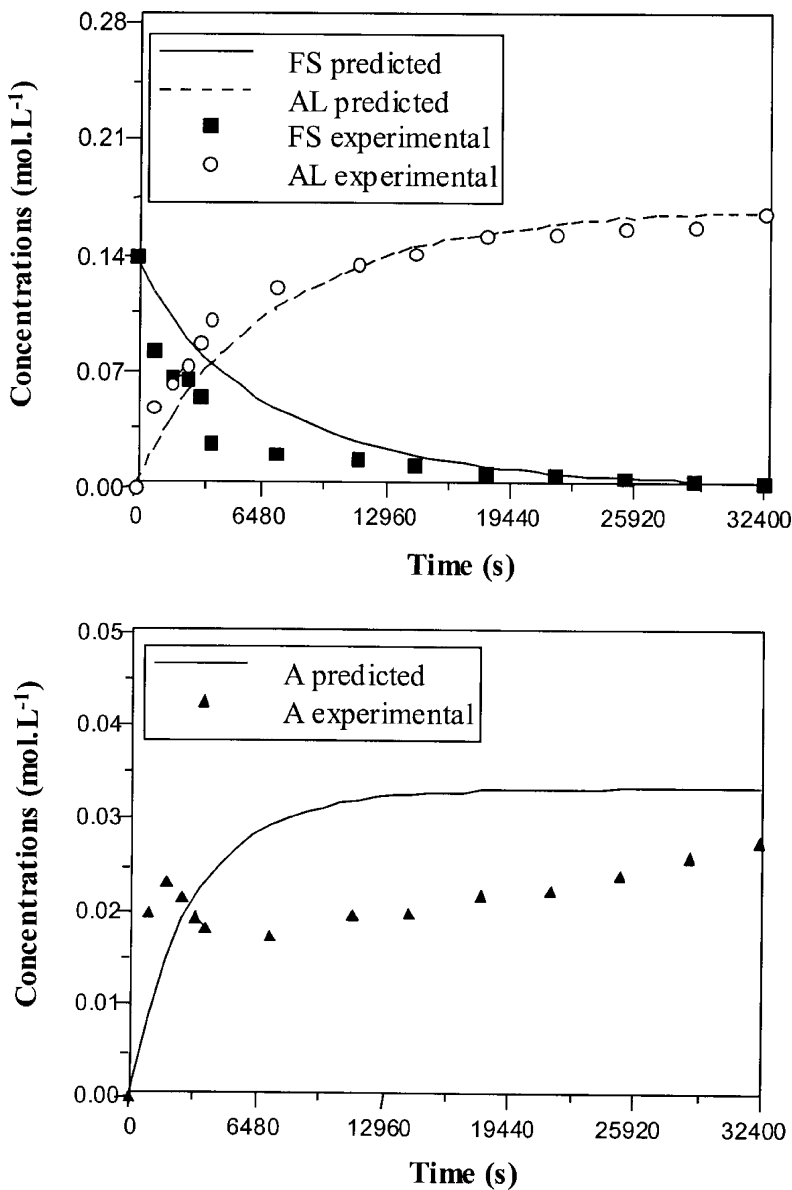


Figure 8. Comparison of time evolution of experimental concentrations and concentrations computed with the kinetic models given in Table VIII.

The presence of acids in the reaction mixture is a more difficult problem because the existing acid separation methods that are readily available are not optimal:

- Traditional methods that involve the precipitation of salts (generally calcium lactate) have several shortcomings: slow methods, numerous crystallizations needed, thus leading to a loss in acids,
- Liquid-liquid extraction is not selective,

- Distillation allows an easy elimination of the water and the formic and acetic acids. However, the recovery of lactic acid requires lower pressures thus entailing an eventual degradation of glycolic and glyceric acids. Distillation may be integrated with an esterification reaction to obtain a volatile lactate ester. The lactate ester could be purified further by redistillation or in some instances by crystallization. But numerous additional steps are need (esterification, saponification, alcohol recycling, etc.).

So it is particularly the presence of glycolic and glyceric acids that poses difficulties, and the limitation of their formation is thus important. Globally, the main objectives are the increase in lactic acid production and the minimization of unknown by-products and acids by-products formation. The objective function used is the following:

$$c = \frac{C_{AL}}{C_A + C_P}$$

As mentioned before, the analysis of the results of the experimental planning carried out by Dubois (1992) has provided the following optimal operating conditions: $[NaOH]^{\circ} = 2 \text{ mol}\cdot\text{L}^{-1}$, $[F]^{\circ} = 25 \text{ g}\cdot\text{L}^{-1}$, and $T = 40^{\circ}\text{C}$.

In these conditions (batch and isotherm at 40°C) the lactic acid yield and selectivity are:

$$R_{AL}^{\text{exp}} = 64.6\% \text{ and } S_{AL}^{\text{exp}} = 65.8\%$$

(and the value of the criterion described above is equal to 2.577).

One or more variables can be optimized using the optimization algorithm. The temperature and the feed rate of fructose will be computed in order to improve the previous criterion. The hydroxide sodium concentration is kept at its maximum value in the experimental range (i.e., $2 \text{ mol}\cdot\text{L}^{-1}$). The total batch time is nine hours. The reaction volume is 1 liter. The amount of fed fructose is fixed to 25 g. The following constraints and bounds on the variables were employed:

- Maximum temperature variations: $\pm 2^{\circ}\text{C}\cdot\text{min}^{-1}$
- Temperature bounds: $40^{\circ}\text{C} \leq T \leq 100^{\circ}\text{C}$
- Feed rate bounds: $0 \leq F \leq 10^{-4} \text{ kg}\cdot\text{s}^{-1}$

The results are given in Figure 9. It can be observed that the optimal conditions are: a fed-batch operation with feed rate of fructose and isothermal operation at the maximum temperature 100°C .

For these conditions one can note a very important improvement in the criterion, since it has gone from 2.577 to 5.785.

It is interesting to note that these results are in agreement with the information issued from the experimental planning. The positive effect of a low initial fructose concentration, predicted by the analysis of the experimental planning, suggests that the fructose may be introduced in semi-batch mode to favor the lactic acid production. The results of the optimization confirm this tendency.

Experimental Application

The reaction was performed in a 2 L glass-jacketed reactor. The solvent used was water, and, thus, the experiment was run at 98°C instead of 100°C to avoid boiling.

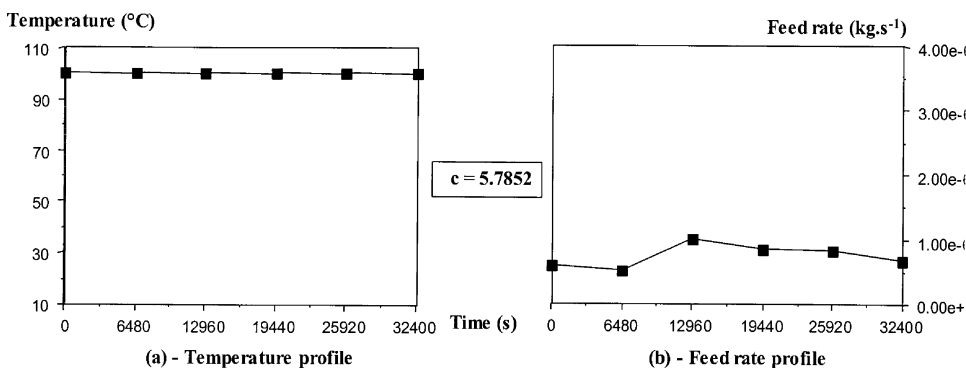


Figure 9. Optimal temperature and feed rate profiles.

However, since the transformation is not very temperature sensitive, the influence on the results is negligible. The optimal feed rate profile of fructose is nearly a constant profile. A simulation with a constant feeding of fructose over the total batch time has shown that there is not a significant difference in comparison with the results obtained with the optimal feed rate profile. The reaction was performed with a constant feeding of fructose. The problem is to introduce 25 g of fructose during a very long batch time (nine hours). In order to render the implementation of the fructose feeding easier, we have introduced a syrup of 75% fructose in water. The volume of the reaction mixture is 1.5 L. The volume increase due to the introduction of the water in the syrup is negligible (less than 2%). The syrup is introduced drop by drop with a pump during a batch time of 8 h 30 min. Some samples were analyzed every hour in order to obtain the concentrations of the different compounds: fructose, glucose, mannose, sorbose, psicose, galactose, lactic acid, acetic acid, formic acid, glycolic acid, and glyceric acid.

Figure 10 illustrates the time-dependent experimental concentrations. The theoretical and experimental yields and selectivities are given in Table IX. Rather better results were observed than those predicted by the tendency model. The comparison between the time-dependent concentrations obtained from the experiment and from the tendency model with five compounds is given in Figure 11. A good agreement was observed between the experimental and model representation of lactic acid. However, the evolution of the pseudo-compounds FS and A is not as good.

The amount of acids A predicted by the model is underestimated. The modeling problem associated with these constituents is due to the formation of the pseudo-constituents and can explain the experimental and model discrepancies in yield and selectivity.

Table IX. Yields and selectivities in lactic acid

	R_{AL}^{exp}	R_{AL}^{sim}	S_{AL}^{exp}	S_{AL}^{sim}
Best constant operating conditions (batch, 40°C)	64.6%	59.8%	65.8%	60.8%
Feeding of fructose (maximum isotherm)	76.3%	74.1%	83.0%	74.4%

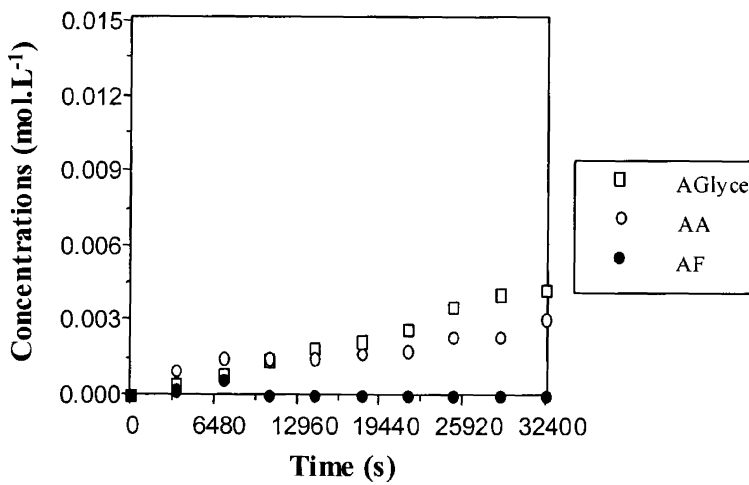
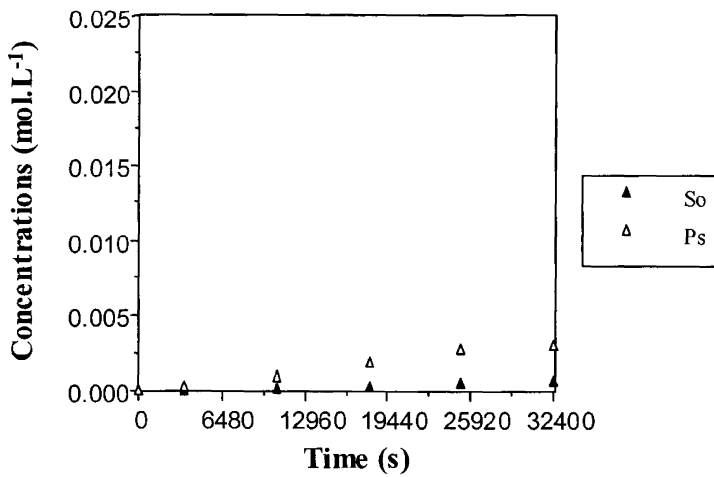
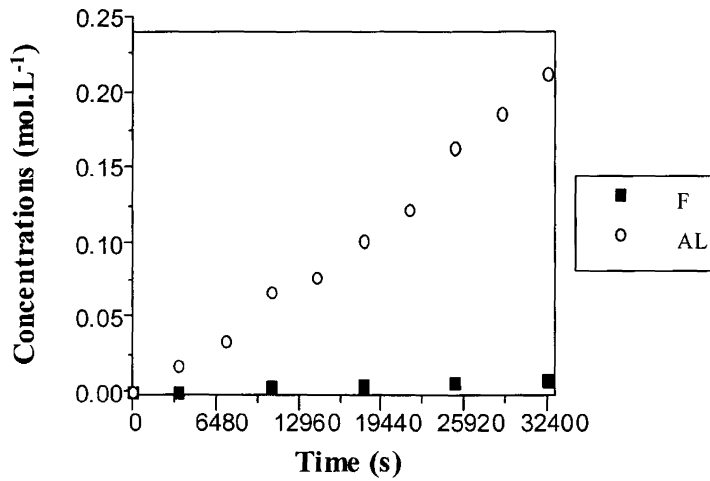


Figure 10. Time evolution of concentrations for the optimal conditions determined with the tendency model.

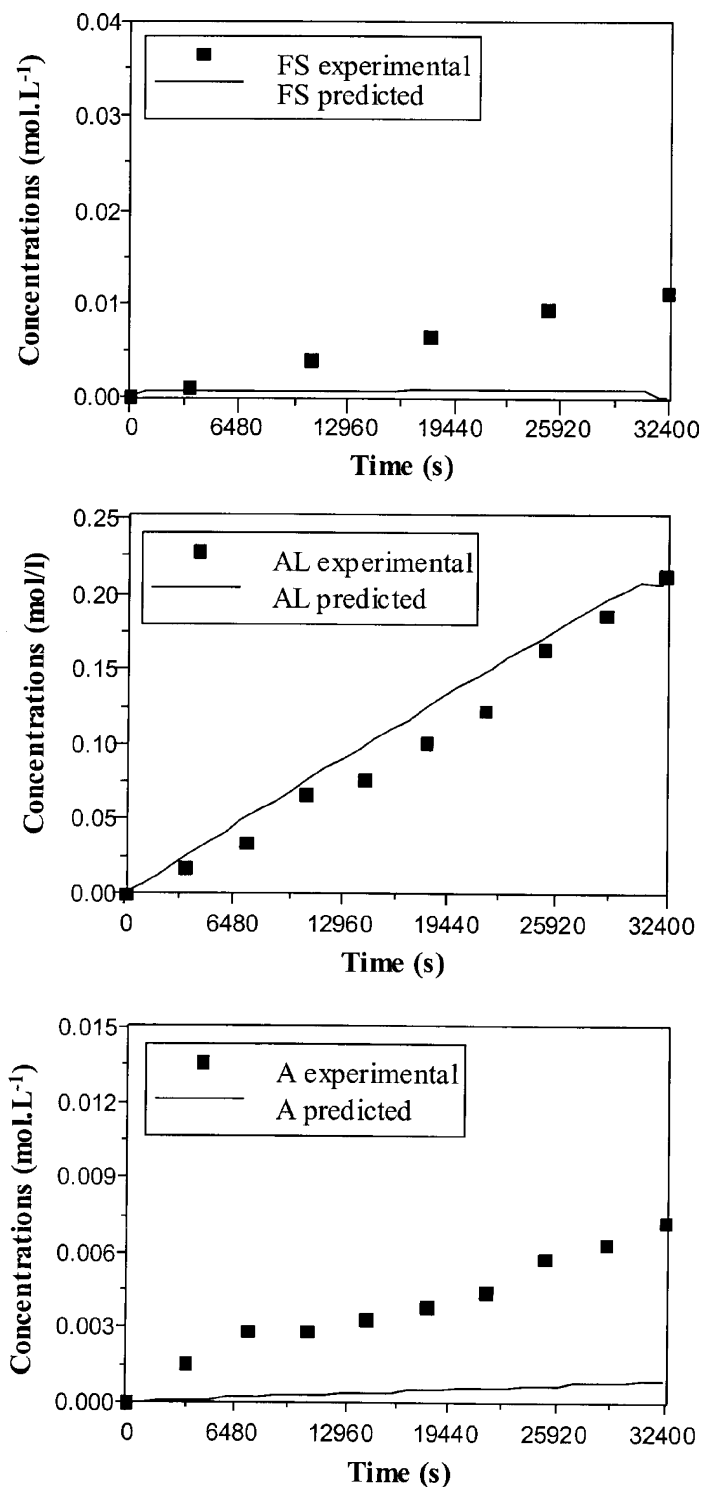


Figure 11. Comparison of time evolution of experimental concentrations and predicted concentrations of pseudo-compounds for the optimal conditions determined by experimental planning.

With respect to the results issued from the experimental planning conditions, a significant improvement in the yield (since it went up from 64.6% to 76.3%) and the selectivity (increased from 65.8% to 83%) in lactic acid is noted. Comparing the time evolution of the concentration in Figure 4 (with optimal experimental planning conditions) and Figure 10 (with optimal tendency model conditions), we can make these observations about fructose feeding:

- The production of lactic acid is slow, but at the final time the amount of lactic acid is more important.
- The feeding of fructose allows limiting the isomerization. Only sorbose and psicose are formed. Nevertheless, the amount of sugars remaining in the reaction mixture is more important than that in the batch mode.
- The amount of acids is decreased. Glycolic acid is not formed and the formic acid disappears during the reaction. These two acids are produced in more important amounts in batch mode. In fed-batch mode, the production of glyceric and acetic acids still remains, but in a more restricted volume than in the batch mode.

Conclusions

In fine chemistry, the development of a classical model incorporating detailed knowledge of the reaction mechanisms and kinetic processes is not readily feasible and the use of numerical optimization procedure is impossible. In this work, the “tendency modeling” approach was retained in order to solve the problem of lack of information concerning the transformation and to satisfy the constraint of rapid implementation required in fine chemistry. The tendency model was developed in one step.

In order to test the ability of the tendency model to represent correctly the influence of the different operating parameters, response surface methodology was used to compare experimental and model tendencies. In this case the initial database used is provided by an experimental planning method. This combined approach of tendency modeling and experimental planning allows the assessment of the accuracy of the tendency model behavior and thus avoids shortcomings during the optimization step.

In order to develop a tendency model that could be used with greater confidence, the main factors involved are user intervention and chemist experience during all the tendency model development steps: stoichiometry development in order to postulate a realistic model and kinetic model development, to determine an adequate form of the model (form of the kinetic laws, consideration of transfer limitations, mixing phenomena).

The entire success of the global methodology relies on the practical implementation of the optimal protocol, the main difficulty being the control of the temperature profile (the control of the feed rate does not represent a serious problem by itself). Robust algorithms based on generalized predictive control (GPC) have been developed in our laboratory and have demonstrated their ability to track different types of profiles (Rafalimanana et al., 1992; Jarupintusophon et al., 1993). Moreover, this step can be rendered easier to carry out if the heat exchange limitations of the plant can be integrated during the optimization procedure.

The global strategy for the optimization of batch reactors has been applied with success to improve the synthesis of lactic acid by alkaline degradation of

fructose. In spite of some crude assumptions concerning the pseudo-constituents and the number of reactions, it was feasible to determine an apparent stoichiometric and kinetic model. On the basis of this model, which correctly fits only the experimental data concerning AL, the optimal operating parameters computed were feeding profile of fructose and maximal isotherm. The experimental implementation of the optimal procedure has led to very positive results: the yield in lactic acid and the selectivity increased from 64.6 to 76.3% and from 65.8 to 83% respectively.

Nomenclature

a_{ij}	order of the constituent j in the reaction i
A_j	j th constituent
b_{\min}	minimum variation of temperature profile
b_{\max}	maximum variation of temperature profile
c	objective function
C_j	concentration of species j , $\text{mol} \cdot \text{L}^{-1}$
E_i	activation energy of reaction i , $\text{J} \cdot \text{mol}^{-1}$
$Er_1(j)$	error of representation of constituent j over the whole experiments
Er_2	global error of representation
F	feed rate, $\text{kg} \cdot \text{s}^{-1}$
Fe_j	feed rate of constituent j , $\text{kg} \cdot \text{s}^{-1}$
H_1	threshold for purity constraint
J	optimization criterion
k_i°	preexponential factor of reaction i , $\text{L}^{\text{si}-1}/(\text{mol}^{\text{si}-1} \cdot \text{s})$
M	amount of introduced reactant, kg
n	number of moles, mol
n°	normalizing factor, mol
n_{int}	number of intervals of the discretization
NC	number of constituents
NE	number of experiments
NR	number of reactions involved in the stoichiometric matrix
r_i	rate of reaction i , $\text{mol} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$
R_i	i th reaction of the stoichiometric matrix
R_j	overall rate of production of species j , $\text{mol} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$
R_{il}	normalized reaction rate of the i th reaction for the l th experiment, s^{-1}
R_X	mass yield of species X
s_i	global order of the i th reaction
S_X	selectivity of species X
t	time, s
t_i	subinterval, s
t_0	initial batch time, s
t_f	final batch time, s
T	reactor temperature, K
u	control function
V	reactor volume, L
$[X]$	concentration of species X , $\text{mol} \cdot \text{L}^{-1}$
X_i	experimental factor

X_i	extent of reaction i
y	dimensionless mole fraction
Y	difference between dimensionless mole fractions at instant t and initial instant
\bar{Y}	composition data matrix
\mathbf{Y}	studied response (in response surface technique)
z_j	parameter of control law relative to the j th subinterval
Z_j	production term relative to feeding of species j

Greek Letters

ν	matrix of stoichiometric coefficients
ν	stoichiometric coefficient
ϕ	feed rate

Superscripts

o	initial
exp	experimental
f	final
T	transposed matrix
th	theoretical

Subscripts

exp	measured
i	i th reaction
id	calculated
j	j th constituent
k	k th factor (response surface technique)
l	l th to experiment

Abbreviations

SQP	Sequential Quadratic Programming
NLP	Non Linear Programming
SVD	Singular Value Decomposition
TFA	Target Factor Analysis

Constants

$R = 8.314$	universal gas constant, $\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$
$T_R = 274$	reference temperature, K

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