Design of Reactive Extraction Systems for Bioproduct Recovery

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Liquid-liquid extraction, combined with chemical reaction, can improve overall yields of product. Reactive extraction is an alternative for separations in bioprocessing, for example, for the production of carboxylic acids such as lactic or citric acid, alcohols such as ethanol, or antibiotics such as penicillin, cephalosporin or streptomycin. A method for the design of reactive extraction cascades was used for the recovery of Penicillin G and for lactic acid from aqueous mixtures using mixtures of organic solvents with reactive amines as extractants. Effects of such variables as residence time, flow rates, pH, number of stages and amine concentration are quantified. Designs capable of essentially complete recovery are reported.

Introduction

Process systems combining reaction with separation have been studied extensively for reactive distillation and to a lesser extent for reactive extraction, reactive crystallization, and reactive adsorption. Along with product recovery, simultaneous reaction and liquid extraction can improve yields, and can overcome limitations of reaction equilibrium and product inhibition, especially in bioprocessing when conventional separation methods like distillation cannot be used.

An important application of reactive extraction is for the recovery of products from fermentations, often used for the production of a large number of compounds, including carboxylic acids (such as lactic and citric acids), antibiotics (such as Penicillin and streptomycin), and alcohols (such as ethanol). The products can be recovered from the fermentation broth by precipitation, adsorption, membrane processes, or extraction. Precipitation is often not selective enough, and may lead to the production of a waste product which is not desirable, such as, in traditional methods of recovery of lactic and citric acids (Van Ness, 1981). Membrane processes often have relatively of low selectivity and fouling, (Jaquet et al., 1999). Physical extraction is sometimes not selective enough and has low yields (Yang et al., 1991). However, the introduction of a reversible complexation reaction with a suitable extractant can greatly increase the selectivity, as well as the fractional recovery. Various extractants such as high molecular weight aliphatic amines or phosphorus-bound oxygen containing extractants have been used for the recovery of alcohols, aliphatic carboxylic acids, amino acids, as well as for complex molecules like antibiotics (Yang et al., 1991).

Many bioconversions, including fermentations, are highly inhibited by the product. A means to overcome this inhibition is *In-Situ* Product Recovery (ISPR) (Chauhan and Woodley, 1997; Freeman et al., 1993). Among alternative processes for the simultaneous removal of the product, extraction is often the most suitable (Freeman et al., 1993; Jaquet et al., 1996, 1999). The combination of reaction with this extraction step may also be useful, but is not studied here.

Closely boiling organic acids and bases, which are difficult to separate by methods like distillation or solvent extraction, can be separated by taking advantage of the difference in their dissociation constants, via "dissociation extraction." For example, a mixture of two bases can be separated by contacting the mixture with an aqueous solution of an acid in less than the stoichiometric amount. The stronger of the two bases reacts with the acid to give a dissociated salt in the aqueous phase, while the other base remains undissociated. The undissociated base can subsequently be extracted into a separate organic phase, thereby giving a partial separation of the bases. Various studies have been done on the possibility of separation of industrially important mixtures by dissociation extraction. For example, Anwar et al. (1995a, 1998) examined the multistage separation of quinoline and iso-quinoline by dissociation extraction and found conditions for obtaining high purity quinoline and iso-quinoline. Sharma and co-

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workers (Jagirdar and Sharma, 1981; Wadekar and Sharma, 1981; Gaikar and Sharma, 1984a, b) discuss the use of dissociation extraction for separation of a number of mixtures, as well as regeneration methods for recycle of the aqueous phase to make the process economically attractive. The method developed here can also be applied for dissociation extraction, although we do not consider examples.

Design methods for simultaneous reaction and liquid-liquid extraction have been developed for both dilute (Piret et al., 1960) and concentrated (Trambouze and Piret, 1960) systems. The studies made a number of simplifying assumptions, such as constant phase ratios, perfectly immiscible solvents, and constant partition coefficients. Minotti et al., (1996) developed a geometric method for design of liquid-liquid extractors, which was later extended for the design of simultaneous reaction and liquid-liquid extraction systems (Minotti et al., 1998; Minotti, 1998). This geometric method accommodates the variation of flows along the cascade of reactor-extractors, when the thermodynamic parameters needed to model the liquid-phase nonidealities are available.

In this article, a new method is developed for the design of cascades of liquid-liquid reactor-extractors. The problem is decomposed into a phase equilibrium problem for the carrier-water mixture and then the reaction of the other species is superimposed. The phase equilibrium problem describes the nonreactive liquid-liquid equilibrium between the water in the aqueous feed and the organic carrier in the solvent. The model is solved by the geometric method of Minotti et al., (1996). The reaction is superimposed by accounting for the distribution of components between the two liquid phases using partition coefficients. It is assumed that the reactive components partition between the organic and the aqueous phases without altering the carrier-water liquid-liquid equilibrium. This decomposition is especially accurate for small amounts of the reactive components. It is also a good approximation if a significant amount of the reacting component is present, but resides primarily in only one of the liquid phases. This is often the case for reactive extraction in biological systems.

The design procedure is developed using two examples for recovery of organic compounds from fermentation broths. The first example is the recovery of Penicillin G from an aqueous stream using amine extractants in an organic carrier. The second example considers the recovery of lactic acid, for which several complexes are formed with the amine, unlike the case of Penicillin G.

Recovery of Penicillin G

Penicillin is an important β-lactam antibiotic and a raw material for many semi-synthetic Penicillin antibiotics. It is produced commercially by submerged aerobic fermentation using strains of *Penicillium chrysogenum*. Two kinds of Penicillin are widely produced: Penicillin G (benzyl penicillin), which we study here, and Penicillin V (phenoxymethylpenicillin).

Penicillin G is a weak acid ($pK_A^{\text{pen}G} = 2.75$) with a molecular weight of 334.3, which is slightly soluble in water. The traditional method for recovery involves the physical extraction into organic solvents like amyl acetate, butyl acetate, or a mixture of butyl acetate and kerosene. Since only undissociated Penicillin can be extracted into the organic solvent, the *pH* of the aqueous phase is adjusted in the range 2.0 to 2.5 using mineral acids, so that most of the Penicillin is in the undissociated state. The medium is cooled to 3–5°C and Penicillin G is then recovered in a series of extractors (Reschke and Schügerl, 1984a). A subsequent back extraction of Penicillin from the organic solvent is done using potassium phosphate or carbonate buffers at a *pH* of 6 to 8, and the resulting salt of Penicillin G is crystallized.

This process has a disadvantage in that the Penicillin G is unstable at low *pH*, and some of the product decomposes irreversibly into undesired byproducts. For example, at $pH = 2.0$ and 25°C, 1% of the aqueous phase Penicillin G decomposes in 10s. To partially counter this effect, the extraction can be carried out in centrifugal extractors to reduce the contact time, although these are more expensive, but there is still a 10 to 15% loss of the Penicillin G (Reschke and Schügerl, 1984a), which is significant. It would be advantageous to carry out the extraction at a higher *pH*, such as 6.0 to 8.0, where it is more stable. However, in this higher *pH* range, physical extraction gives a low recovery since Penicillin G exists mostly in the dissociated form which has low solubility.

Reactive extraction of Penicillin G using amine extractants dissolved in an organic carrier provides an alternative to carry out the recovery at a higher *pH*. Schügerl and co-workers (Reschke and Schügerl, 1984a,b,c; Likidis and Schügerl, 1987; Schügerl et al., 1988; Schügerl and Deneger, 1992) made an extensive experimental study of this process. Reschke and Schügerl (1984a) found that the stability of Penicillin G is not adversely affected by the various amine extractants and certain extractants like Amberlite LA-2 or dioctylamine may even inhibit the decomposition of Penicillin G. Yang and Cussler (2000) studied the use of hollow fibers for the reactive extraction and back extraction of Penicillin G. They found that hollow fibers are suitable for Penicillin G recovery, and they suggested other potential candidates for hollow-fiber extraction. However, the design of reactive extraction systems for recovery of Penicillin G has not been studied.

We consider the recovery of Penicillin G by the formation of a complex via the interfacial reaction

$$H^+ + \text{pen}G^- + \overline{\text{Amine}} \rightleftharpoons \overline{\text{pen}G} - \overline{\text{Amine}} \qquad (1)$$

where overbars indicate that the component is present only in the organic phase and otherwise indicates that the component is present only in the aqueous phase. The pen$G$ – Amine complex is rapidly extracted into the organic phase as it is formed (see Figure 1).

Primary amines are unsuitable extractants because of their fairly high solubility in water and a tendency to form stable emulsions. Secondary amines are more suitable and give higher reaction equilibrium constants for the complexation reaction than primary or tertiary amines, although they do have the disadvantage of higher reactivity with the solvents than the tertiary amines. Quaternary salts suffer the disadvantage that back extraction of the penicillin is difficult and requires large amounts of anion (Reschke and Schügerl, 1984b). In this example, we consider a secondary amine, N-lauryl-N-trialkylmethylamine (Amberlite LA-2) as the extractant. The value of the reaction equilibrium constant depends

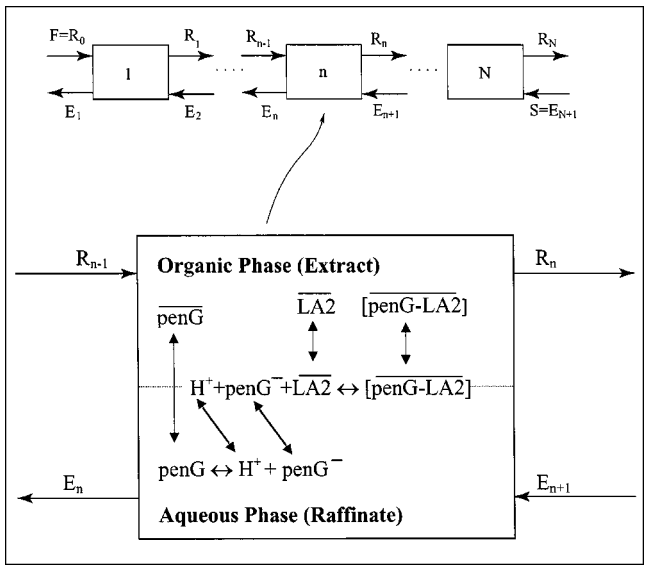

Figure 1. Countercurrent cascade.

on the stability of the complex, and depends largely on the nature of the organic carrier used. Of the various carriers studied in the literature, butyl acetate gives a fairly high reaction equilibrium constant (Schügerl and Degener, 1992) and a rapid rate of mass transfer. The equilibrium constant with a few solvents, most notably decanol, is higher (Lee et al., 1993; Yang and Cussler, 2000), but mass transfer is slower (Yang and Cussler, 2000). Butyl acetate is also a solvent used in the traditional process, which makes it a good candidate in the light of product quality and materials handling.

There are many other combinations of extractant and solvent, each with their unique advantages and disadvantages. Comparison of the various options according to performance and cost is possible with a quantitative model, which is developed below.

Kinetics of Penicillin G reactive extraction

Reschke and Schügerl (1984c) studied the kinetics of Penicillin G extraction using a stirred Lewis cell. They found that the rates of extraction can be described using a two-film theory with an instantaneous reaction at the interface. More recent work (Lee and Wang, 1995; Wang and Lee, 1995; Juang and Lin, 1998) shows that the overall rate of extraction can depend not only on the diffusion of components to the interface, but also on the rate of the interfacial reaction. For this example, we consider the limiting case, where the rate of the interfacial reaction controls the process. That is, the mass-transfer rate of the components to the interface is much faster than the rate of the interfacial reaction.

The kinetics of the interfacial reaction of Penicillin G was studied by Juang and Lin (1998) using a stirred membrane cell. They found that the forward reaction step is first-order in the concentrations of H^+, Penicillin G anion, and Amberlite LA-2. Previous studies by Juang and Lin (1996) indicate the presence of only the (1,1) complex Penicillin G and Amberlite LA-2. The rate of the interfacial complexation reaction is (Juang and Lin, 1998)

$$R_F = k'_F\left([H^+][\text{pen}G^-][\overline{LA2}] - \frac{[\overline{\text{pen}G - LA2}]}{k'_{\text{eq}}}\right) \quad (2)$$

where k'_F and K'_{eq} are the concentration-based forward rate and reaction equilibrium constants for the complexation reaction. Values of these parameters are reported as $k_F = 9.0 \times 10^{-5} m^7/(mol^2 - s)$ and $K_{eq} = 1.25 \times 10^2 m^6/(mol^2)$ at 298 K. The rate expression 2 in terms of mol fractions (Venimadhavan et al., 1995) is

$$R_F = k_F\left(x_{\text{penG}^-} y_{LA2} - \frac{y_{\text{penG}-LA2}}{K_{eq}}\right) \quad (3)$$

where k_F is the mol fraction-based forward rate constant and K_{eq} is the mol fraction-based reaction equilibrium constant, which are both functions of the pH. The x_i and y_i are the mol fractions of species i in the aqueous and the organic phases, respectively.

The amount of Penicillin G in the dissociated form is related to the total amount of Penicillin G by the expression (Reschke and Schügerl, 1984a)

$$x_{\text{penG}-} = \frac{x_{\text{penG}}}{1 + 10^{(pK_A^{\text{penG}} - pH)}} \quad (4)$$

Cascade model

We develop steady-state models for cascades consisting of a series of reactor-extractors (Figure 1 shows a countercurrent cascade), with the following assumptions:

(1) Each of the reactor-extractors are at the same constant temperature and pressure. We neglect the effects of heat of the complexation reaction.

(2) The output streams from each reactor-extractor are in phase equilibrium. This implies that the rate of mass transfer is significantly faster than the rate of the reaction. For a final design, the efficiencies of mass transfer should also be studied.

(3) The complexation reaction between the product (Penicillin G) and the amine extractant (Amberlite LA-2) occurs at the interface between the aqueous and the organic phase in each of the reactor-extractors.

(4) Regarding the partitioning of the reactive components and the product complex, we assume that:

(a) The amine extractant is essentially insoluble in the aqueous phase. (The solubility of Amberlite LA-2 is ca. 2.4×10^{-6} vol/vol, Juang and Lin (1998).)

(b) The product-amine complex is insoluble in the aqueous phase.

(c) Undissociated product can be extracted physically, as well as by reaction into the organic phase.

(5) The dissociation of product is unaffected by the presence of other components.

(6) The feed consists of product in pure water and the organic solvent enters as a mixture of an organic carrier and the amine. No product-amine complex is present in the entering solvent.

Assumptions 4 and 5 enable solution of the phase equilibrium problem for the carrier-water system independently of the complexation reaction.

Countercurrent cascades do not always give a better performance than cocurrent cascades (Minotti et al., 1998a) and it can be useful to examine both cocurrent and countercurrent cascades. The effect of the number of reactor-extractors on the fractional recovery of Penicillin G at a *pH* of 6 was studied for cocurrent and countercurrent cascades. However, the countercurrent cascade was found to give a higher fractional recovery than the cocurrent cascade for the examples studied here, and we focus on the countercurrent arrangement. The model and results for the cocurrent cascade have been developed similarly and are reported elsewhere (Pai, 2001). The steady-state model for the countercurrent cascade is obtained as follows.

First, we solve the phase equilibrium problem for the carrier-water system. For the nth reactor-extractor of the cascade, the component material balances and the phase equilibrium relations are

$$E_{n+1}\tilde{\mathbf{y}}_{n+1} + R_{n-1}\tilde{\mathbf{x}}_{n-1} = E_n\tilde{\mathbf{y}}_n + R_n\tilde{\mathbf{x}}_n \tag{5}$$

$$\tilde{\mathbf{y}}_n = f_{eqm}(\tilde{\mathbf{x}}_n) \tag{6}$$

for $n = 1, 2, \ldots, N$. The composition vectors $\tilde{\boldsymbol{y}}_n$ and $\tilde{\boldsymbol{x}}_n$ describe the two components of the carrier-water system; the model also extends to multiple organic carriers. E_n and R_n are the molar flow rates of the extract and raffinate streams, respectively. These compositions and flow rates consider only the species of the carrier-water system. No reactive species are yet accounted for, so the compositions and flow rates determined in this step will change when the reactive species are introduced.

In addition to Eqs. 5 and 6 the mol fractions of the c components in each phase sum to unity.

$$\sum_{i=1}^{c} \tilde{y}_{i,n} = 1 \tag{7}$$

$$\sum_{i=1}^{c} \tilde{x}_{i,n} = 1 \tag{8}$$

The second step in modeling superimposes the complexation reaction on the phase equilibrium problem. That is, the reactive components are introduced assuming that they do not affect the liquid-liquid equilibrium of the carrier-water system.

The complexation reaction is shown in Figure 1 for the nth reactor-extractor. For Amberlite LA-2, Penicillin G, and the Penicillin G-amine complex, the balances for this unit are

$$E_{n+1,\,LA2} - H_n k_F \underline{a}\left(\frac{x_{n,\text{penG}}}{1+10^{(pK_A^{\text{penG}}-pH)}} y_{n,\,LA2} - \frac{y_{n,\text{penG}-LA2}}{K_{\text{eq}}}\right) = E_{n,\,LA2} \tag{9}$$

$$R_{n-1,\text{penG}} + E_{n+1,\text{penG}} - H_n k_F \underline{a} \times \left(\frac{x_{n,\text{penG}}}{1+10^{(pK_A^{\text{penG}}-pH)}} y_{n,\,LA2} - \frac{y_{n,\text{penG}-LA2}}{K_{\text{eq}}}\right) = R_{n,\text{penG}} + E_{n,\text{penG}} \tag{10}$$

$$E_{n,\text{penG}-LA2} + H_n k_F \underline{a}\left(\frac{x_{n,\text{penG}}}{1+10^{(pK_A^{\text{penG}}-pH)}} y_{n,\,LA2} - \frac{y_{n,\text{penG}-LA2}}{K_{\text{eq}}}\right) = E_{n,\text{penG}-LA2} \tag{11}$$

H_n is the molar holdup of the nth reactor-extractor, $\underline{a}$ is the interfacial area per mol of holdup (which depends on the hydrodynamics), and $E_{n,j}$ is the component flow rates of species j in the extract (organic) phase. $R_{\text{n,penG}}$ is the component flow of Penicillin G in the raffinate (aqueous) phase leaving.

It is convenient to use dimensionless extract (e_n) and raffinate (r_n) flow rates

$$e_n = \frac{\hat{E}_n}{S} = \frac{E_n + E_{n,\,LA2} + E_{n,\text{penG}-LA2} + E_{n,\text{penG}}}{S_C + S_{LA2}} \tag{12}$$

$$r_n = \frac{\hat{R}_n}{F} = \frac{R_n + R_{n,\,\text{penG}}}{F_W + F_{\text{penG}}} \tag{13}$$

where S_C and F_W are the molar flow rates of the organic carrier and water feed, excluding Penicillin G. Equations 9 to 11 become

$$\left(\frac{S}{F}\right)e_{n+1}y_{n+1,\,LA2} - Da\kappa w_n\left(\frac{x_{n,\text{penG}}}{1+10^{(pK_A^{\text{penG}}-pH)}} y_{n,\,LA2} - \frac{y_{n,\text{penG}-LA2}}{K_{\text{eq}}}\right) = \left(\frac{S}{F}\right)e_n y_{n,\,LA2} \tag{14}$$

$$r_{n-1}x_{n-1,\text{penG}} + \left(\frac{S}{F}\right)e_{n+1}y_{n+1,\text{penG}} - Da\kappa w_n\left(\frac{x_{n,\text{penG}}}{1+10^{(pK_A^{\text{penG}}-pH)}} y_{n,\,LA2} - \frac{y_{n,\text{penG}-LA2}}{K_{\text{eq}}}\right) = r_n x_{n,\text{penG}} + \left(\frac{S}{F}\right)e_n y_{n,\text{penG}} \tag{15}$$

$$\left(\frac{S}{F}\right)e_{n+1}y_{n+1,\,\text{penG}-LA2} - Da\kappa w_n\left(\frac{x_{n,\,\text{penG}}}{1+10^{(pK_A^{\text{penG}}-pH)}} y_{n,\,LA2} - \frac{y_{n,\,\text{penG}-LA2}}{K_{\text{eq}}}\right) = \left(\frac{S}{F}\right)e_n y_{n,\,\text{penG}-LA2} \tag{16}$$

for $n = 1, 2, \ldots, N$. The Damköhler number is a key parameter, and gives the ratio of two characteristic times, H_T/F for the process and $1/k_{F,ref}\underline{a}$ for the reaction. Additional parameters are $\kappa = k_F/k_{F,\text{ref}}$ and $w_n = H_n/H_T$, the fraction of the

total holdup in the nth reactor-extractor. The component mol fractions of interest in the extract phase are $y_{n,LA2} = E_{n,LA2}/\hat{E}_n$, $y_{n,\text{penG}} = E_{n,\text{penG}}/\hat{E}_n$ and $y_{n,penG-LA2} = E_{n,\text{penG}-LA2}/\hat{E}_n$; the mol fraction of unrecovered Penicillin G in the raffinate phase is $x_{n,\text{penG}} = R_{n,\text{penG}}/\hat{R}_n$.

The Damköhler number can be varied by changing the residence time (H_T/F) or the specific interfacial area. The interfacial area $\underline{a}$ is related to the Sauter mean diameter (d_{32}) for droplets of the dispersed phase by

$$\underline{a} = \frac{6\phi_{\text{disp}}}{\rho_{\text{disp}} d_{32}} \tag{17}$$

where ϕ_{disp} and ρ_{disp} are the phase fraction and the molar density, respectively. The Sauter mean diameter can be related to various other properties of the system. For example, in stirred vessels the Sauter mean diameter is related to a dimensionless Weber number, which is a function of the power input (Pacek et al., 1998). Correlations are available for the Sauter mean diameter in stirred vessels (Nagata, 1975; Treybal, 1981, Pacek et al., 1998), and in sieve tray columns (Treybal, 1981).

The dimensionless rate constant is

$$\kappa = \frac{k_F}{k_{F,\text{ ref}}} = 10^{(pH_{\text{ref}} - pH)} \tag{18}$$

where $pH_{\text{ref}} = 7.0$. For the physical extraction of Penicillin G, we have

$$y_{n,\text{ penG}} = K_{phy} x_{n,\text{ penG}} \tag{19}$$

where K_{phy} is the distribution coefficient given by (Reschke and Schügerl, 1984a)

$$K_{\text{phy}} = \frac{\rho_{aq}}{\rho_{\text{org}}} \frac{P}{1 + 10^{(pH - pK_A^{\text{penG}})}} \tag{20}$$

and P is the partition coefficient, which is the ratio of the concentration of the undissociated form of Penicillin G in the extract phase to that in the raffinate phase, and ρ_{org}, ρ_{aq} are the molar densities of the extract and raffinate phases.

Equation 5 for the phase equilibrium problem is written in terms of dimensionless flow rates as

$$\left(\frac{S}{F}\right) e_{n+1}\left\{\left(1 - y_{n+1,\,LA2} - y_{n+1,\,\text{penG}-LA2} - y_{n+1,\,\text{penG}}\right)\tilde{\mathbf{y}}_{n+1}\right\} + r_{n-1}\left\{\left(1 - x_{n-1,\,\text{penG}}\right)\tilde{\mathbf{x}}_{n-1}\right\} = \left(\frac{S}{F}\right) e_n \left\{\left(1 - y_{n,\,LA2} - y_{n,\,\text{penG}-LA2} - y_{n,\,\text{penG}}\right)\tilde{\mathbf{y}}_n\right\} r_n\left\{\left(1 - x_{n,\,\text{penG}}\right)\tilde{\mathbf{x}}_n\right\} \tag{21}$$

for $n = 1, 2, \ldots, N$ and $i = 1, 2, \ldots, c$. The terms in the braces are mol fractions of the components in the carrier-water system, considering all of the components present in the extract and raffinate phases.

The extract and the raffinate flow rates are related to the phase fractions obtained by solving the phase equilibrium problem as

$$\frac{e_n}{r_n} = \frac{\phi_n\left(1 - x_{n,\,\text{penG}}\right)}{\left(\frac{S}{F}\right)(1 - \phi_n)\left(1 - y_{n,\,LA2} - y_{n,\,\text{penG}-LA2} - y_{n,\,\text{penG}}\right)} \tag{22}$$

where ϕ_n is the organic phase fraction; $\phi_n = E_n/(E_n + R_n)$.

Note that the overall material balance is equivalent to the sum of the N stagewise material balances, Eqs. 14, 15, 16, and 21, with $e_{N+1} = 1$, $r_0 = 1$, $y_{N+1,\,LA2}$, $x_{0,\,\text{penG}}$, $\tilde{\mathbf{y}}_{N+1} = (1,0)^T$ and $\tilde{\mathbf{x}}_0 = (0,1)^T$. Hence, it is not independent of the set of the N stage balances and we need not consider it in addition to the above material balances.

The fractional recovery of Penicillin G is

$$f_{\text{penG}} = \frac{x_{0,\,\text{penG}} - r_N x_{N,\,\text{penG}}}{x_{0,\,\text{penG}}} \tag{23}$$

where $x_{0,\,\text{penG}}$ is the mol fraction of Penicillin G in the feed.

For the phase equilibrium problem in each of the N reactor-extractors, there are c independent material balance equations and c independent equilibrium equations given by Eqs. 21 and 6, respectively. There are also $2(N+1)$ equations given by Eqs. 7 and 8. For the complexation reaction, there are $3N$ material balance equations and N phase equilibrium relationships for the physical extraction given by Eqs. 14, 15, 16, and 19. This gives a total of $2cN + 6N + 2$ equations. The variables in the problem are (S/F), Da, $\tilde{\mathbf{x}}_n$, $\tilde{\mathbf{y}}_n$, $\tilde{\mathbf{y}}_{N+1}$, $\tilde{\mathbf{x}}_0$, N, e_n, r_n, $x_{n,\,\text{penG}}$, $y_{n,\,\text{penG}}$, $y_{n,\,LA2}$, $y_{n,\,\text{penG}-LA2}$, and pH. Thus, there are $2cN + 2c + 6N + 8$ variables giving $2c + 6$ degrees of freedom. The compositions of the input solvent and input feed streams $\tilde{\mathbf{y}}_{N+1}$ and $\tilde{\mathbf{x}}_0$ are considered given and an additional eight variables need to be specified. We choose N, (S/F), Da, $x_{0,\,\text{penG}}$, $y_{N+1,\,\text{penG}}$, $y_{N+1,\,LA2}$, $y_{N+1,\,\text{penG}-LA2}$ and pH.

Solution Algorithm. (1) The phase equilibrium problem for the entire cascade is solved according to the geometric method given by Minotti et al. (1996). The liquid-liquid equilibrium compositions and phase fractions in each of the N reactor-extractors are calculated using the method by Wasylkiewicz et al., (1996). The liquid-phase nonidealities are modeled with the UNIQUAC equation based on the parameters in Table 1. The organic-phase fractions are then used to relate the extract and the raffinate flow rates from all of the N reactor-extractors by Eq. 22.

(2) We superimpose the reactive components on the phase equilibrium problem, accounting for the distribution of the components between the two liquid phases using partition coefficients. (More sophisticated phase equilibrium models like the UNIQUAC model are typically not available for these components). This is done by solving Eqs. 14, 15, 16, 18, 19, and 20 simultaneously for the entire cascade using a nonlinear equation solver to obtain the mol fractions of the reactive components. Here, the solution was obtained using a modified Powell algorithm and a finite-difference approximation

Table 1. UNIQUAC Equation Model Parameters

Components	r	q
Water	0.92	1.40
Butyl Acetate	4.8274	4.196
p-Xylene	4.6587	3.536
*Binary Interaction Parameters (K) for Water (1) and Butyl Acetate (2)**		
$A_{1,1} = 0.0$	$A_{1,2} = 402.400$	
$A_{2,1} = 234.755$	$A_{1,2} = 0.0$	
*Binary Interaction Parameters (K) for Water (1) and p-Xylene (2)***		
$A_{1,1} = 0.0$	$A_{1,2} = 965.70$	
$A_{2,1}$325.61	$A_{1,2} = 0.0$	

*From Minotti et al. (1998a).
**From Sorensen and Arlt (1979).

to the Jacobian in the IMSL routine NEQNF-DNEQNF (IMSL MATH/LIBRARY, 1987).

(3) The fractional recovery of Penicillin G is calculated from Eq. 23.

Results and discussion for Penicillin G

Figure 2 compares the fractional recovery of Penicillin G by physical extraction to that by reactive extraction at high *Da* in a countercurrent cascade. The recovery decreases as the *pH* increases due to the decrease in the H^+ concentration. However, the drop in reactive extraction occurs at a much higher *pH* than for physical extraction. The introduction of a complexation reaction can give a high fractional recovery of Penicillin G close to the *pH* range of 6 to 8, where Penicillin G is stable.

The effect of the amine feed composition on the fractional recovery of Penicillin G is shown in Figure 3 for high *Da*. As

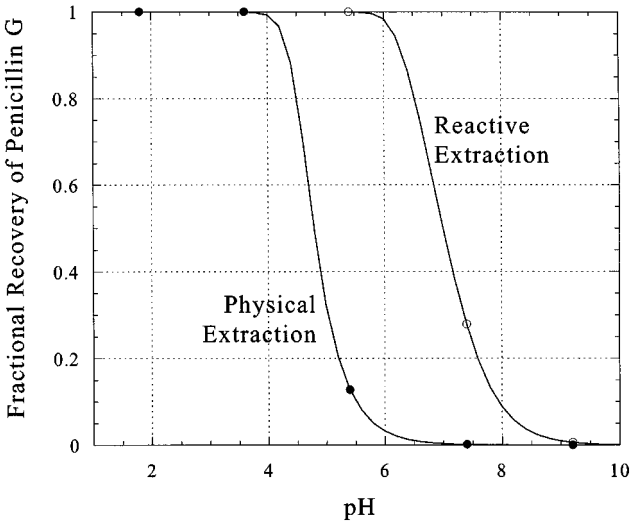

Figure 2. Fractional recovery of Penicillin G as a function of *pH*, vs. physical and reactive extraction.

$N = 4$, $(S/F) = 0.15$, $x_{0,\ penG} = 0.002$, $y_{N+1,\ LA2} = 0.017$, $Da = 100$, equal holdup on each stage.

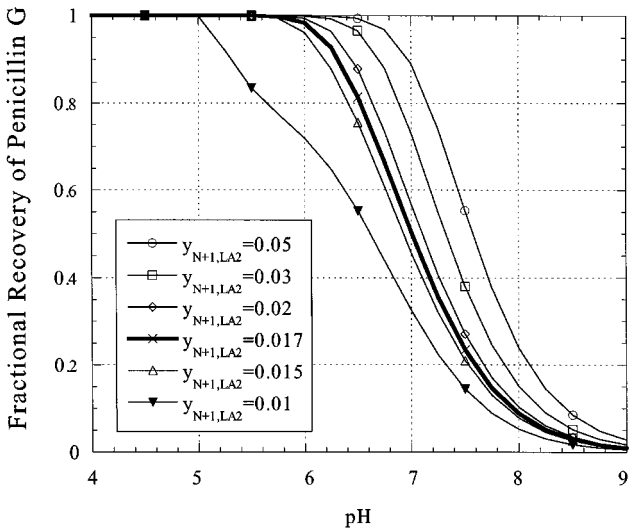

Figure 3. Fractional recovery of Penicillin G as a function of *pH* for varying amine composition in the solvent feed.

$N = 4$, $(S/F) = 0.15$, $x_{0,\ penG} = 0.002$, $Da = 100$, equal holdup on each stage. The bold line is the base-case design.

discussed above, it is desirable to carry out both the reactive extraction, as well as the back extraction of Penicillin G in the *pH* range of 6 to 8, where the Penicillin G is stable. For example, Reschke and Schügerl (1984c) recommended that the reactive extraction be carried out at a *pH* of 5.0 and the back extraction at a *pH* of 7.0. We choose a *pH* of 6.0 for reactive extraction and a *pH* of 8.0 for back extraction. The choice of amine composition in the organic solvent is a trade-off. It should give high recovery of Penicillin G ($\geq 98\%$) at the lower extraction *pH* of 6.0 and low recovery of Penicillin G ($\leq 10\%$) at the higher *pH* of 8.0 for ease of back extraction. A mol fraction of 0.017 of the Amberlite LA-2 in the entering organic solvent stream strikes a balance and is chosen here for a base-case design. The value can be further optimized using the model when cost parameters are available.

Figure 4 shows the effect of the number of reactor-extractor stages on the fractional recovery. For a given number of stages, the recovery increases with increasing *Da*, that is, as the residence time or the interfacial area increase. A limiting value is approached for values of *Da* larger than 50 or so. This limiting value is determined by simultaneous physical and chemical reaction equilibrium. For the same *Da*, the fractional recovery increases as the number of reactor-extractors increases. A high fractional recovery of Penicillin G can be obtained by either a larger number of stages and a relatively low *Da*, or a lower number of stages and a relatively high *Da*. Thus, there is a trade-off between the parameters reflected in the Damköhler number and the number of stages. Using this design model, an optimal value can be determined for each variable if an objective function and parameters are chosen.

The effect of amine composition on the fractional recovery of Penicillin G in a cascade of four reactor-extractors is shown in Figure 5 at $(S/F) = 0.15$. As the amine composition in-

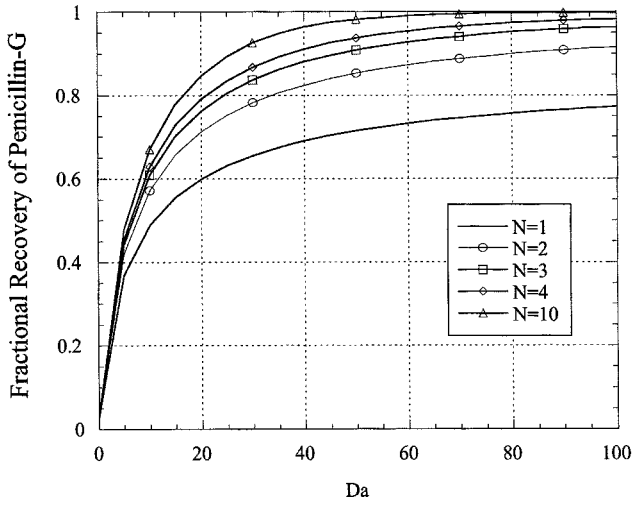

Figure 4. Effect of number of reactor-extractors on fractional recovery of Penicillian G as a function of *Da*.

$(S/F) = 0.15$, $x_{0,\text{ penG}} = 0.002$, $y_{0,LA2} = 0.017$ or $y_{N+1,LA2} = 0.017$), $pH = 6.0$, equal holdup on each stage.

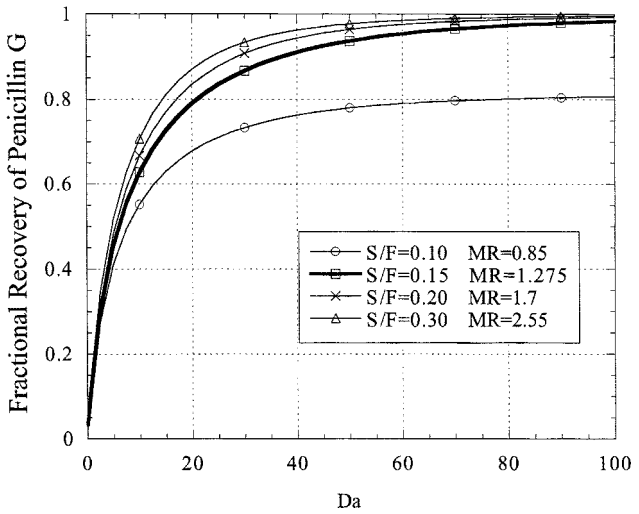

Figure 6. Effect of the molar solvent-to-feed ratio on fractional recovery of Penicillin G.

$x_{0,\text{penG}} = 0.002$, $N = 4$, $y_{N+1,\ LA2} = 0.017$, $pH = 6.0$, equal holdup on each stage. The bold line is the base-case design.

creases, the fractional recovery increases dramatically, especially at lower *Da*, because of the increasing molar ratio of the amine extractant to the Penicillin G. However, as explained earlier, amine compositions $\gg 0.017$ should not be used since that makes the back extraction of the Penicillin G more difficult. Thus, there is also an optimal value for the amine mol fraction.

Figure 6 shows the effect of solvent-to-feed ratio on the fractional recovery four reactor-extractors at a *pH* of 6.0 and an inlet amine mole fraction of 0.017. The recovery increases with *S/F*, but at a diminished rate after $(S/F) \approx 0.2$ for the given amine composition. The decrease in the fractional recovery at low (S/F) is due to an amine loading (mols of the amine per mol of Penicillin G) less than one; at least a stoichiometric amount of the amine extractant must be present to have the potential for high recovery. The relatively small effect of the solvent-to-feed ratio on the fractional recovery is due to the high *pH*, where the physical extraction is negligible.

Based on these results, feasible (but not optimal) designs of the countercurrent reactive extraction cascade giving high fractional recovery of Penicillin G are: $(S/F) = 0.15$, $y_{N+1,\ LA2} = 0.017$, $N \backsim 10$ to 4, $Da \backsim 60$ to 100 and $pH = 6.0$ for an input feed stream with $x_{0,\text{ penG}} = 0.002$. Note that the tradeoffs between N and Da should be optimized.

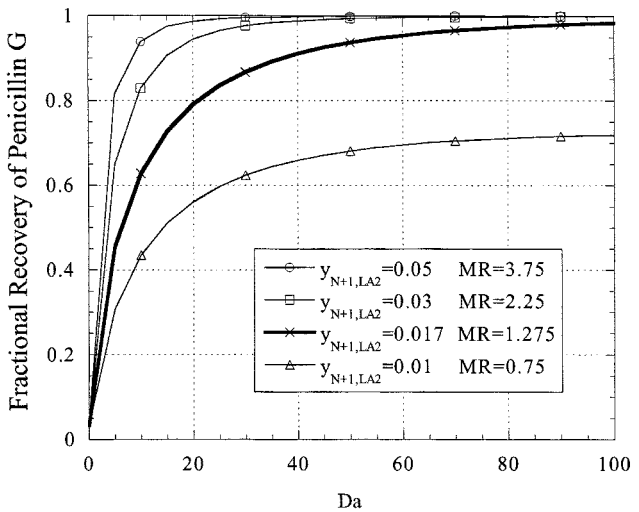

Figure 5. Effect of Amberlite LA-2 composition in the solvent on the fractional recovery of Penicillin G.

$(S/F) = 0.15$, $x_{0,\text{ penG}} = 0.002$, $N = 4$, $pH = 6.0$, equal holdup on each stage. The bold line is the base-case design.

Recovery of Lactic Acid

Lactic acid (2-hydoxypropanoic acid, $CH_3CHOHCOOH$) is a naturally occurring hydroxycarboxylic acid with $pK_A^{HA} = 3.86$. It is present in many foods, such as, as a primary acid component in sour milk and as a constituent in animal blood and muscle tissue. It is extremely soluble in water, but insoluble in most organic solvents. Lactic acid has a wide range of applications in the food and chemical industries. It is used as a raw material for biodegradable polymers, as well as an environmentally friendly solvent.

Commercially, lactic acid is produced by fermentation or synthesis. In fermentation, lactic acid is produced by using homolactic bacteria such as *Lactobacillus delbrueckii, L. bulgarcius* and *L. leichmanii*, at a *pH* of 5.0 to 5.5. Traditional recovery of lactic acid involves the use of calcium carbonate to precipitate lactic acid as calcium lactate. The precipitate is treated with sulfuric acid to regenerate the lactic acid and precipitate the calcium as calcium sulfate. Thus, for every mol of lactic acid produced, one mol of calcium sulfate waste byproduct is generated.

For environmental reasons, there is a large incentive to find an alternative method for the recovery of lactic acid from the fermentation broth. Good recovery of the lactic acid by sol-

vent extraction using organic solvents like ketones, ethers, or alcohols is difficult due to the low solubility of lactic acid in these solvents (Yang et al., 1991). Reversible chemical complexation can be used to increase the effective distribution coefficient of the lactic acid. Baniel (1982) pointed out that carboxylic acids like lactic acid and citric acid can be recovered using mixtures of a water-immiscible tertiary amine and a water-immiscible organic acid. Following that work, there have been a number of studies of the recovery of carboxylic acids from aqueous streams using phosphorus-bonded oxygen-bearing extractants and high molecular weight aliphatic amines as well as quaternary amine salts. Both types of extractant give high effective distribution coefficients of lactic acid. However, the aliphatic amines are slightly more effective and are typically less expensive (Yang et al., 1991). In addition, the use of a base as an extractant gives a selective extraction of the lactic acid over the other nonacidic components in the broth, like glucose, and so on.

Lactic acid fermentations are highly product inhibited (Tamada et al., 1990; Yabannavar and Wang, 1991), so the use of *in-situ* extraction of lactic acid to overcome the product inhibition and bring about high productivity has the potential to be very economically attractive. The extraction can be done either inside the fermenter or in an external extraction unit. However, amine extractants and organic carriers are known to be toxic to the lactic acid-producing cells. Also, since the liquid amine extractants have high viscosities, the carrier helps in reducing the viscosity of the organic phase and helps in stabilizing the acid-amine complex by solvation. Hence, a proper choice of the amine extractants and the carrier has to be made.

Of the various amines, tertiary amines and quaternary amine salts are widely studied on account of their low reactivity with solvents. Tertiary amines are capable of extracting only the undissociated acid and give low fractional recovery under basic conditions. Quaternary amine salts, however, extract both the dissociated, as well as the undissociated, acid and, hence, give high fractional recovery in both acidic as well as basic conditions. This makes a back extraction of the lactic acid by using a *pH* swing more difficult. Yang et al., (1991) studied the effect of *pH* on the extraction of carboxylic acids. They suggested the use of a tertiary amine, Alamine 336, for the reactive extraction of lactic acid followed by back extraction with a *pH* swing. Yabannavar and Wang (1991) and Ye et al. (1996) carried out the extractive fermentation of lactic acid using Alamine 336 in oleyl alcohol at a *pH* of 4.2, which is intermediate to the optimum *pH* for reactive extraction of 3.0 and that for fermentation of 5.0 to 5.5. We consider an example with tri-*n*-octyl amine (TOA) as the amine extractant and xylene as the carrier.

Unlike the case for Penicillin G, in addition to the (1,1) acid-amine complex, HA-TOA, other complexes of the type (2,1) (that is, $HA_2 - TOA$), (3,1), (1,2), and (2,2) complexes appear to be needed to describe the simultaneous reaction and phase equilibrium distribution data (Schügerl et al., 1988; Tamada et al., 1990; Juang and Huang, 1997b). The types of complexes formed depend on the nature of the amine and the carrier, as well as on the concentration of the carboxylic acid. Juang and Huang (1997b) reported on simultaneous reaction and phase equilibrium studies on the reactive extraction of lactic acid using tri-*n*-octyl amine (TOA) in xylene. They found that the formation of the (1,1), (1,2) and (3,1) complexes fit the simultaneous reaction and phase equilibrium distribution data. Similar results are obtained for another tertiary amine, Alamine 336 in chloroform and MIBK (Tamada et al., 1990). We take into account the presence of all three complexes below.

Kinetics of lactic acid reactive extraction

Juang and Huang (1997a) studied interfacial kinetics for reactive extraction of lactic acid using a microporous membrane stirred cell. The rate expressions proposed (Juang and Huang, 1997a) poorly fit the forward reaction rate (obtained from initial rate data) in cases where the lactic acid is in large excess over the amine extractant. Hence, we explain the reaction rate data for the forward reaction using the following alternative mechanism which is similar to the one proposed by Juang and Huang (1997a).

$$HA \rightleftharpoons \overline{HA};\ K'_{\text{eq},1}(\text{fast}) \tag{24}$$

$$2\overline{HA} \rightleftharpoons \overline{(HA)_2};\ k'_2/k'_{-2}(\text{slow}) \tag{25}$$

$$\overline{HA} + \overline{TOA} \rightleftharpoons \overline{HA - TOA}:\ k'_3/k'_{-3}(\text{slow}) \tag{26}$$

$$\overline{HA - TOA} + \overline{TOA} \rightleftharpoons \overline{HA - TOA_2};\ K'_{\text{eq},4}(\text{fast}) \tag{27}$$

$$\overline{HA - TOA} + 2\overline{HA} \rightleftharpoons \overline{HA_3 - TOA};\ K'_{\text{eq},5}(\text{fast}) \tag{28}$$

Taking steps given by Eqs. 25 and 26 as rate-controlling and the other steps to be relatively fast, the rate of the forward reaction is

$$R_F = k'_2 K'^2_{\text{eq},1}[HA]^2 + k'_3 K'_{\text{eq},1}[HA]\left[\overline{TOA}\right] \tag{29}$$

Rearranging Eq. 29, allows a linear plot of the rate data to obtain the reaction rate constants, as shown in Figure 7. The

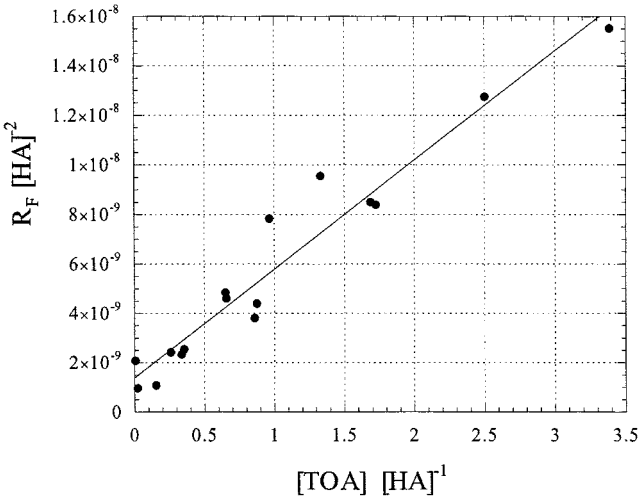

Figure 7. Reactive extraction of lactic acid; determination of reaction rate constants for the forward reaction at 303 K.

The solid line is given by $y = 4.4 \times 10^{-9}x + 1.39 \times 10^{-9}$.

Table 2. Rate and Equilibrium Constants for Reactive Extraction of Lactic Acid*

k'_2	2.233×10^{-6} m^4/(mol·s)
k'_3	7.056×10^{-7} m^4/(mol·s)
$K'_{\text{eq, 1}}$	1.97×10^{-3}
$K'_{\text{eq, 2}}$	0.255 m^3/mol
$K'_{\text{eq, 3}}$	0.665 m^3/mol
$K'_{\text{eq, 4}}$	6.168×10^{-5} m^3/mol
$K'_{\text{eq, 5}}$	0.187 m^6/mol^2

* Regressed from the data of Juan and Huang (1997a,b) for the model in Eqs. 24–28 with Eq. 25 and 26 rate-controlling.

two rate constants for steps given by Eqs. 26 and 27 are obtained from the slope and intercept of the line. The reaction equilibrium constants for reactions given by Eqs. 24–28 are obtained from the simultaneous reaction and phase equilibrium studies conducted by Juang and Huang (1997b). The overall reaction rate is rewritten in terms of the mol fractions, and taking into account that only the undissociated form of the lactic acid takes part in the reaction

$$R_F = k_2\left(\frac{x_{n,\,HA}^2}{\left(1+10^{(pH-pK_A^{HA})}\right)^2}-\frac{y_{n,\,(2,0)}}{K_{\text{eq, 2}}}\right)+ k_3\left(\frac{x_{n,\,HA}}{\left(1+10^{(pH-pK_A^{HA})}\right)}y_{n,\,TOA}-\frac{y_{n,\,(1,1)}}{K_{\text{eq, 3}}}\right) \quad (30)$$

Here k_2 and k_3 are the mol fraction-based forward rate constants and $K_{\text{eq, 2}}$ and $K_{\text{eq, 3}}$ are the corresponding mol fraction-based reaction equilibrium constants. Table 2 gives numerical values for the reaction rate and equilibrium constants.

Mathematical model

We use a steady-state model and assumptions 1–3 and 5–6 as in the previous example. With respect to the additional species, we also make similar assumptions as follows.

(4) Regarding the partitioning of the reactive components and the product complexes:

(a) The amine extractant tri-*n*-octylamine (*TOA*) is essentially insoluble in the aqueous phase (solubility ca. 1.2×10^{-6} vol/vol) (Juang and Huang, 1997a).

(b) The lactic acid dimer $(HA)_2$ and the complexes $HA-TOA$, $HA-TOA_2$ and HA_3-TOA are also essentially insoluble in the aqueous phase.

(c) Lactic acid is extracted physically as well as by reaction into the extract phase. For reactive extraction with tertiary amines, only the undissociated acid is extracted (Juang and Huang, 1997b; Yang et al., 1991).

The mathematical model for the cascade must be modified to account for the additional species (Pai, 2001).

Arguments similar to those used in the first example show that there are $2c+9$ degrees of freedom in this model. This increase of 3 over the Penicillin example is due to the three additional species. Considering the compositions of the input carrier and input feedstreams $\tilde{y}_{N+1}$ and $\tilde{x}_0$ as given, 11 variables need to be specified. We choose N, (S/F), Da, $x_{0,\,HA}$, $y_{N+1,\,HA}$, $y_{N+1,\,TOA}$, $y_{N+1,\,(1,1)}$, $y_{N+1,\,(2,0)}$, $y_{N+1,\,(1,2)}$, $y_{N+1,\,(3,1)}$ and pH.

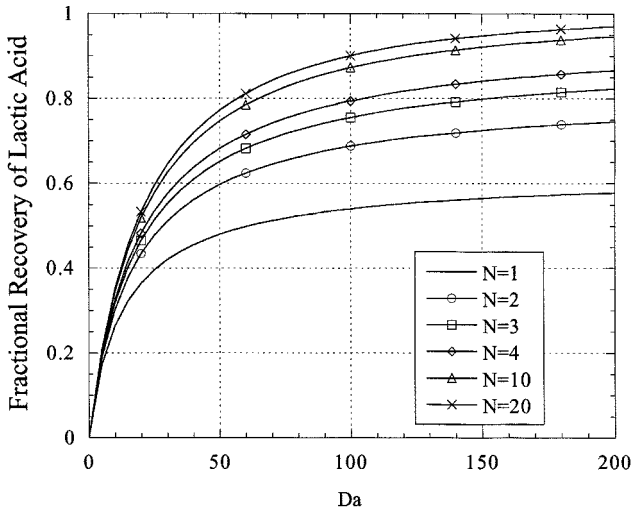

Figure 8. Effect of number of reactor-extractors on the fractional recovery of lactic acid as a function of *Da*.

$(S/F)=0.1$, $x_{0,\,HA}=0.01$, $y_{N+1,\,TOA}=0.3$, $pH=3.0$, equal holdup on each stage.

Results and discussion for lactic acid

Figure 8 shows the effect of the number of reactor-extractors on the fractional recovery of lactic acid at $pH=3$. For a given number of stages, the fractional recovery increases with *Da*, approaching a limiting value determined by simultaneous physical and chemical reaction equilibrium. This limit is not closely approached until much larger values of *Da* than in the previous example. For a constant *Da*, the fractional recovery increases as the number of stages increases. Figure 8 shows that a large number of stages (≈10) is essential for high fractional recovery. High recovery ($\geq90\%$) cannot be obtained by a high Damköhler number and lower number of stages, in contrast to the previous example. That is, no tradeoff is apparent between the Damköhler number and the number of stages. Hence, a relatively large number of stages in the countercurrent cascade is necessary, and a cascade of 10 stages is employed for studying the effect of other process parameters below. In a similar manner, the fractional recovery of lactic acid in a countercurrent cascade as a function of *Da* at the *pH* of the extractive fermentation ($pH=4.2$, Yabannavar and Wang, 1991) can be calculated. The fractional recovery of the lactic acid decreases significantly as the *pH* increases.

The effect of the inlet tri-*n*-octylamine composition (at a solvent flow $S/F=0.1$) on the fractional recovery of lactic acid is shown in Figure 9. As the amine composition increases, the fractional recovery increases significantly. However, high amine compositions should not be used since the back extraction of lactic acid by a *pH* swing may be hindered, and there is a tradeoff regarding the amine composition. Also, a high amine composition in the organic phase

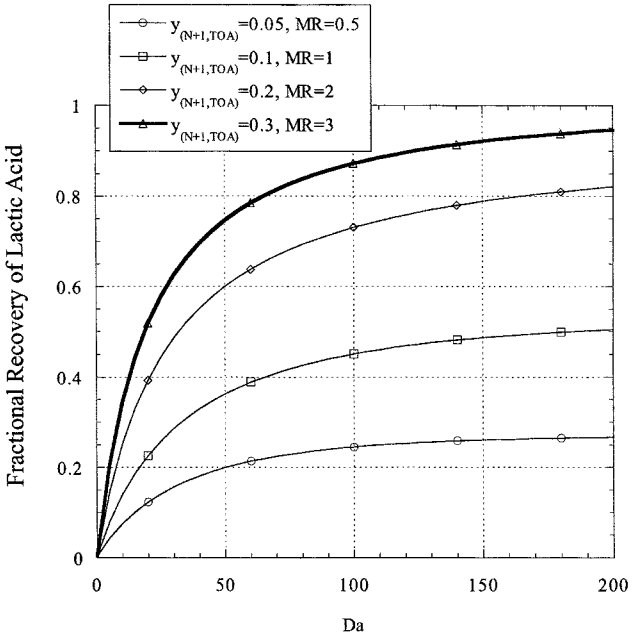

Figure 9. Effect of tri-*n*-octylamine composition in solvent on fractional recovery of lactic acid.

$(S/F) = 0.1$, $x_{0,\,HA} = 0.01$, $N = 10$, $pH = 3.0$, equal holdup on each stage. The bold line is the base-case design.

increases the viscosity which may lead to difficulties in obtaining good mixing and mass transfer.

Figure 10 shows the effect of molar solvent-to-feed ratio on the fractional recovery of lactic acid at a *pH* of 3 and a TOA feed mole fraction of 0.3. The recovery increases significantly as (S/F) increases.

Based on these results, feasible (but not optimal) designs of the countercurrent reactive extraction cascade giving high

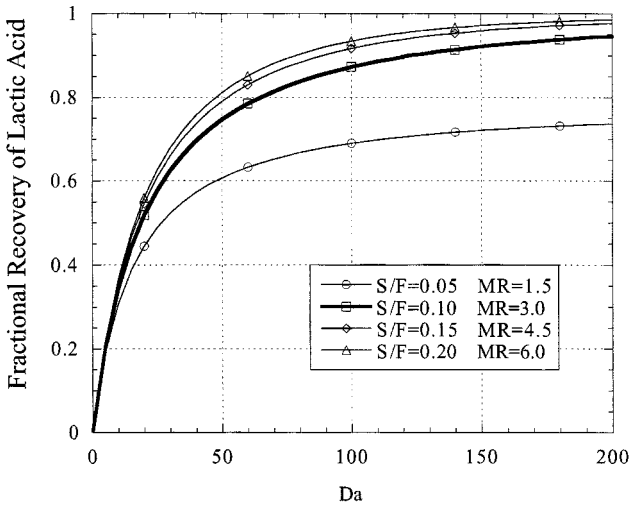

Figure 10. Effect of solvent-to-feed ratio on fractional recovery of lactic acid.

$x_{0,\,HA} = 0.01$, $N = 10$, $y_{N+1,\,TOA} = 0.3$, $pH = 3.0$, equal holdups on each stage. The bold line is the base-case design.

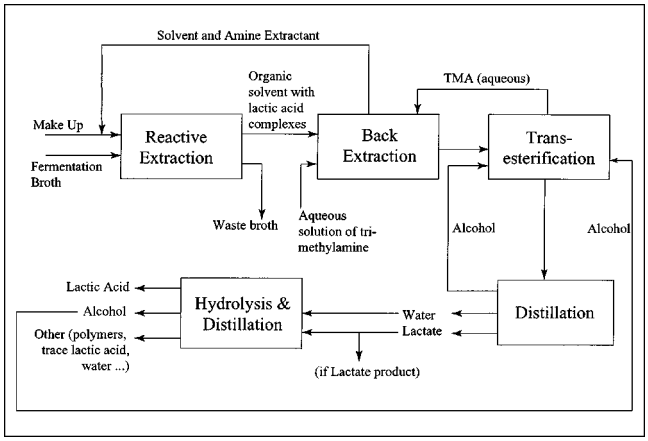

Figure 11. Complete flowsheet for recovery and purification of lactic acid.

The lactate can also be made as a co-product; additional alcohol feed is required in that case.

fractional recovery of lactic acid are: $(S/F) = 0.1$, $y_{N+1,\,TOA} = 0.3$, $N \approx 10$, $Da \approx 200$ and $pH = 3.0$ for an input feedstream with $x_{0,\,HA} = 0.01$.

Back extraction and purification of lactic acid

A flowsheet for the recovery of lactic acid from a fermentation broth is shown in Figure 11. Following the reactive extraction, further recovery of the lactic acid involves a *pH* swing as suggested by Yang et al., (1991). In another study, Tung and King (1994a,b) examined extraction, as well as regeneration aspects for a variety of carboxylic acids, including lactic acid. Back extraction of lactic acid can be done by contact with an aqueous solution containing a base which causes the *pH* swing resulting in the back extraction of acid. Poole and King (1991, 1995) studied the back extraction using aqueous solution of a volatile base, tri-methylamine [$N(CH_3)_3$, TMA] which takes place via

$$RCOO^- + H^+ + N(CH_3)_3 \rightarrow RCOO^{-+}HN(CH_3)_3 \quad (31)$$

The tri-methylamine is then recovered in the next step, where the tri-methyl ammonium carboxylate is decomposed thermally by the following reaction

$$RCOO^{-+}HN(CH_3)_3 \rightleftharpoons RCOOH + N(CH_3)_3 \uparrow \quad (32)$$

The thermal decomposition step is effective for carboxylic acids, like succinic and fumaric acids. However, in the case of lactic acid, thermal decomposition of the lactate is much more difficult due to the high solubility of lactic acid in water and tendency of the lactic acid to polymerize. Poole and King (1991) found that prolonged heating of the tri-methyl ammonium lactate results in evolution of only 62% of the TMA, leaving behind a viscous solution of water, TMA, lactic acid, and lactic acid polymers. As an alternative, Tung and King (1994b) considered transesterification with an alcohol for the recovery of the lactic acid from trimethylammonium lactate

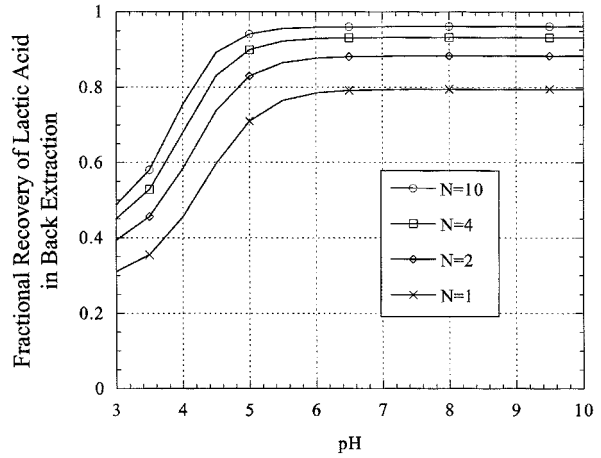

Figure 12. Fractional recovery of lactic acid during back extraction as a function of the *pH*.

($S/F = 0.1$, $Da = 200$, equal holdup on each stage). Entering solvent composition is the same as the composition of the organic phase leaving a countercurrent cascade ($S/F = 0.1$, $N = 10$, $Da = 200$, $x_{0,HA} = 0.01$, y_{N+1}, $TOA = 0.3$, $pH = 3.0$, equal holdup on each stage).

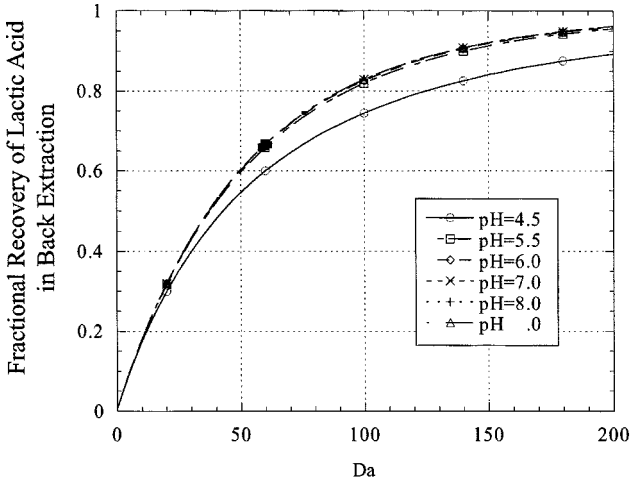

Figure 13. Fractional recovery of lactic acid during back extraction as a function of the Damköhler number ($S/F = 0.1$, $N = 10$, equal holdup on each stage).

Entering solvent composition is the same as the composition of the organic phase leaving a countercurrent cascade ($S/F = 0.1$, $N = 10$, $Da = 200$, $x_{0,\ HA = 0.01,\ yN+1}$, $TOA = 0.3$, $pH = 3.0$, equal holdup on each stage).

by the reaction

$$RCOO^{-+}HN(CH_3)_3 + R'OH \rightleftharpoons RCOOR' + N(CH_3)_3\uparrow + H_2O \quad (33)$$

which is driven to the right by the removal of TMA and some of the water in the vapor. The liquid mixture is then distilled to recover the excess alcohol, which is recycled and the lactate product is obtained.

As an alternative, we examine the performance of reactive extraction cascades for the back extraction of lactic acid. For the reactive extraction of lactic acid, the *pH* in each reactor-extractor was a design variable. The *pH* can be adjusted using buffer solutions or mineral acids or bases. However, for the back extraction of lactic acid, the *pH* should not be adjusted using mineral acids or bases to avoid contamination of the lactic acid product. Thus, the *pH* is determined physically from the amount of tri-methylamine and lactic acid present in the aqueous phase. However, the use of tri-methyl amine concentration as a design variable gives rise to convergence problems in the model because of the sensitivity of *pH* to composition. Hence, we use *pH* as the design variable and subsequently calculate the corresponding concentrations as necessary.

Figure 12 shows the effect of *pH* on the fractional recovery by back extraction of lactic acid in countercurrent cascades for $Da = 200$. For a given number of stages, the fractional recovery increases as the the *pH* increases. However, beyond a *pH* of 5.5, the fractional recovery in back extraction is essentially constant. Figure 13 shows the effect of *Da* on the fractional recovery in a countercurrent cascade of 10 reactor-extractors at various *pH* values. The fractional recovery is insensitive to *pH* above values of 5.5 over the entire range of *Da*. Hence, instead of performing cascade calculations at a decreasing *pH* along the cascade (which corresponds to a given mol ratio of tri-methylamine to the lactic acid entering into the cascade), calculations at a constant *pH* throughout the cascade give a very good approximation of the cascade performance, provided $pH \geq 5.5$. The use of the *pH* as a design variable for the back extraction case is convenient, and its value in the cascade calculation can then give a good approximation of the required tri-methylamine composition.

Feasible (but not optimal) designs of the countercurrent back extraction cascade are: $(S/F) = 0.1$, $N \approx 4$, $Da \approx 200$, and molar ratio of TMA: lactic acid = 1.0 (corresponding to $pH = 7.0$) for an entering solvent composition, which is the same as the composition of the organic phase leaving a countercurrent cascade performing the reactive extraction ($(S/F) = 0.1$, $N = 10$, $Da = 200$, $x_{0,\ HA} = 0.01$, $y_{N+1,\ TOA} = 0.3$, $pH = 3.0$, equal holdup on each stage).

Conclusions

We have developed a design method for reactive extraction systems, suitable for use to describe bioproduct recovery from aqueous solutions. The procedure quantifies the viability of the reactive extraction process and estimates ranges for the design variables, including the influence of the cascade configuration, number of reactor-extractor stages, solvent-to-feed ratio, the solvent composition, the *pH* of the extraction, and the Damköhler number. For the two examples studied, a countercurrent cascade is preferred over the cocurrent arrangement. A similar approach was also used to examine the back extraction of lactic acid, which is the second step in the recovery and purification of lactic acid.

Acknowledgment

We are grateful to the sponsors of the Process Design Center, University of Massachusetts, Amherst. Financial support from the National Science Foundation (grant No. CTS-9613489) is gratefully acknowledged.

Notation

$\underline{a}$ = interfacial area per mol of holdup in the reacter-extractor
$[A]$ = concentration of component A mol/m^3
c = number of components in the carrier-water system
Da = Damköhler number, dimensionless
d_{32} = Sauter mean diameter of the droplets of the dispersed phase, m
e_n = dimensionless extract flow rate leaving the nth reactor-extractor
$\hat{E}_n$ = total molar flow rate in the extract phase leaving the nth reactor-extractor, mol/s
$E_{n,\ A}$ = molar flow rate of component A in the extract phase leaving the nth reactor-extractor, mol/s
f_A = fractional recovery of component A, *dimensionless*
F_A = molar flow rate of component A in the feed, mol/s
H_n = liquid holdup in the nth reactor-extractor, mol
H_T = total liquid holdup in the cascade, mol
HA = lactic acid
K'_{eq} = concentration-based reaction equilibrium constant for Penicillin G, m^6/mol^2
K_{eq} = mol fraction-based reaction equilibrium constant for Penicillin G, dimensionless
$K'_{\text{eq},\ j}$ = concentration-based reaction equilibrium constant of reaction j for lactic acid units in Table 2
$K_{\text{eq},\ j}$ = mol fraction-based reaction equilibrium constant of reaction j for lactic acid, dimensionless
k'_F = concentration-based forward rate constant for Penicillin G, m^7/mol$^2\cdot$s
k_F = mol fraction-based forward rate constant for Penicillin G, mol/m$^2\cdot$s
k'_j = concentration-based forward rate constant of reaction j ($=2, 3$) for lactic acid, m^4/mol$\cdot$s
k_j = mol fraction-based forward rate constant of reaction j ($=2, 3$) for lactic acid, mol/m$^2\cdot$s
$LA2$ = Amberlite LA-2
MR = molar ratio of the amine extractant to the product, dimensionless
N = number of reactor-extractors in the cascade
P = partition coefficient of Penicillin G
pen$G$ = Penicillin G
penG^- = Penicillin G anion
pen$G - LA2$ = Penicillin G-Amberlite LA-2 complex
pK_A = dissociation constant
$R_{n,A}$ = molar flow rate of component A in the raffinate phase leaving the nth reactor-extractor, mol/s
$\hat{R}_n$ = total molar flow rate in the raffinate phase leaving the nth reactor-extractor, mol/s
r_n = dimensionless extract flow rate leaving the nth reactor-extractor
S_A = molar flow rate of component A in the solvent, mol/s
(S/F) = molar ratio of solvent to feed, dimensionless
TOA = tri-n-octylamine
w_n = holdup fraction in the nth reactor-extractor, dimensionless
$x_{n,A}$ = mol fraction of component A in the raffinate phase leaving the nth reactor-extractor
$\tilde{x}_n$ = vector of c mol fractions in the raffinate phase leaving the nth reactor-extractor
$y_{n,A}$ = mol fraction of component A in the extract phase leaving the nth reactor-extractor
$\tilde{y}_n$ = vector of c mol fractions in the extract phase leaving the nth reactor-extractor

Greek Letters

κ = dimensionless ratio of rate constant to reference rate constant
ρ_{aq}, ρ_{org} = molar densities in the aqueous and organic phases, mol/m^3
ϕ_n = organic phase fraction in the nth reactor-extractor

Superscripts and subscripts

(1,1) = lactic acid tri-n-octylamine (1,1) complex
(1,2) = lactic acid tri-n-octylamine (1,2) complex
(2,0) = lactic acid dimer
(3,1) = lactic acid tri-n-octylamine (3,1) complex
C = carrier
disp = dispersed phase
HA = lactic acid
$LA2$ = Amberlite LA-2
n = stage number of the reactor-extractor in cascade
—— = species in the organic phase
pen$G$ = Penicillin G
penG^- = Penicillin G anion
pen$G - LA2$ = Penicillin G-Amberlite LA-2 complex
TOA = tri-n-octylamine
W = water

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Manuscript received Feb. 12, 2001, and revision received Sept. 21, 2001.