

# Computerized Design of Solvents for Extractive Processes

by

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# Declaration

I, the undersigned, hereby declare that the work contained in this dissertation is my own original work and that I have not previously in its entirety or in part submitted it at any university for a degree.

Date: 07/09/2001

## Synopsis

Separation processes are an integral part of chemical engineering. The purity of a chemical product is among the principal factors influencing its value. Therefore, any method that can increase the purity of a product or decrease the cost of purification will have a direct effect on the profitability of the entire plant.

An important class of separation processes is the solvent-based separations. This includes processes like extractive distillation, liquid-liquid extraction and chromatographic separation. Heterogeneous azeotropic distillation is closely related to these processes. The most important variable in the design of a solvent-based separation process is the choice of solvent.

A genetic algorithm for the computer-aided molecular design of solvents for extractive distillation had been previously developed by the author. This algorithm was improved and expanded to include liquid-liquid extraction, heterogeneous azeotropic distillation, gas-liquid chromatography and liquid-liquid (partition) chromatography. At the same time the efficiency of the algorithm was improved, resulting in a speed increase of up to 500% in certain cases. An automatic parameter tuning algorithm was also implemented to ensure maximum efficiency of the underlying genetic algorithm.

In order to find suitable entrainers for heterogeneous azeotropic distillation a method is required to locate any ternary heterogeneous azeotropes present in a system. A number of methods proposed in the literature were evaluated and found to be computationally inefficient. Two new methods were therefore developed for ternary systems. A methodology for applying these methods to quaternary and higher systems was also proposed.

Two algorithms to design blended solvents were also developed. Blended solvents allow the use of simpler and thus cheaper solvents by spreading the active functional groups over several molecular backbones. It was observed in a number of cases that the blended solvents performed better than their individual components. This was attributed to synergistic interactions between these components. Experimental evidence for this effect was also found.

The algorithm was applied to a number of industrially important separation problems, including the extremely difficult final purification process of alpha olefins. In each case solvents were found that are predicted to perform substantially better than those that are currently used in industry. A number of these predictions were tested by experiment and found to hold true.

## Opsomming

Skeidingsprosesse is 'n integrale deel van chemiese ingenieurswese. Die suiwerheid van 'n chemiese produk is een van die hoof faktore wat die waarde daarvan bepaal. Derhalwe sal enige metode wat die suiwerheid van 'n produk kan verbeter, of die koste van die suiwing daarvan kan verlaag, 'n direkte effek op die winsgewendheid van die hele aanleg hê.

'n Belangrike groep skeidingsprosesse is die oplosmiddel-gebaseerde skeidings. Dit sluit prosesse soos ekstraktiewe distillasie, vloeistof-vloeistof ekstraksie en chromatografiese skeidings in. Heterogene azeotrope distillasie is nou verwant aan hierdie prosesse. Die belangrikste veranderlike in die ontwerp van so 'n oplosmiddel-gebaseerde proses is die keuse van oplosmiddel.

'n Genetiese algoritme vir die rekenaargesteunde molekulêre ontwerp van oplosmiddels vir ekstraktiewe distillasie is voorheen ontwikkel deur die skrywer. Hierdie algoritme is verbeter en uitgebrei om vloeistof-vloeistofekstraksie, heterogene azeotrope distillasie, gas-vloeistof chromatografie en vloeistof-vloeistof (verdelings) chromatografie in te sluit. Ter selfde tyd is die doeltreffendheid van die algoritme verbeter, wat 'n verbetering in spoed van tot 500% in sekere gevalle tot gevolg gehad het. 'n Algoritme om die parameters van die onderliggende genetiese algoritme outomaties te verfyn is ook geïmplementeer om die optimale werksverrigting van die algoritme te verseker.

Om gepaste saamsleepmiddels vir heterogene azeotrope distillasie te vind, word 'n metode benodig om enige ternêre heterogene azeotrope aanwesig in 'n stelsel op te spoor. 'n Aantal sulke metodes wat in die literatuur voorgestel is, is geëvalueer en daar is gevind dat hierdie metodes ondoeltreffend is. Twee nuwe metodes is derhalwe ontwikkel vir ternêre

stelsels. 'n Metodiek om hierdie metodes op kwaternêre en hoër stelsels toe te pas, is ook voorgestel.

Twee algoritmes vir die ontwerp van gemengde oplosmiddels is ook ontwikkel. Gemengde oplosmiddels laat die gebruik van eenvoudiger en dus goedkoper oplosmiddels toe, deur die aktiewe funksionele groepe oor 'n aantal molekulêre strukture te versprei. Daar is 'n aantal gevalle waargeneem waar die mengsel beter skeiding bewerkstellig het as die individuele oplosmiddels waaruit dit bestaan. Dit is toegeskryf aan 'n sinergistiese wisselwerking tussen die komponente van die mengsel. Eksperimentele getuienis vir hierdie effek is ook ingewin.

Die algoritme is toegepas op 'n aantal belangrike skeidingsprobleme vanuit die bedryf, insluitende die uiters moeilike finale suiwering van alfa olefiene. In elke geval is oplosmiddels gevind wat volgens voorspelling aansienlike beter skeidings sal bewerkstellig as dié wat tans in die bedryf gebruik word. 'n Aantal van hierdie voorspellings is eksperimenteel getoets en korrek bewys.

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# 1 Solvent Selection Methods

## 1.1 Introduction

Separation processes have always been an integral part of chemical engineering. One of the earliest examples is the design of the Glover tower for the recovery of nitrates during the production of sulphuric acid, by John Glover in 1859. In the same year Edwin Drake found oil in Pennsylvania. By 1860 there were fifteen refineries in operation using “tea kettle” stills. This was almost thirty years before chemical engineering became an official discipline with the introduction of ‘Course X’ (ten), the first four-year degree course in chemical engineering at the Massachusetts Institute of Technology, by Professor Lewis Norton in 1888 (Pafko, 2000).

The purity of product streams is among the principal factors influencing the final price of a chemical product. Any method that can increase the purity of a product or decrease the cost of purification will therefore have a direct effect on the profitability of the entire plant. This has served as a driving force for vast amounts of research in separation technology, which has led to numerous new and improved techniques of separating mixtures.

An important class of separation methods is the solvent-based techniques. These methods include liquid-liquid extraction, extractive distillation and chromatographic separations. Azeotropic distillation is also closely related to these methods.

All of these methods rely on the interaction of an added chemical species (the solvent or entrainer) with the components of the mixture. If this solvent interacts differently with the key components, a separation may be accomplished. The selection of the solvent is arguably the most important step in the design of a solvent-based separation process. This begs the question as to how the optimal solvent (or solvents) for a given separation may be found.

## ***1.2 Solvent Selection Methods***

Many solvent selection methods have been proposed in the literature, some of which are summarised in (Seader et al, 1997) and (Van Dyk, 1998). These methods may be classified into two types: heuristics and database searches.

Database searches have the benefit that they are based on experimental phase equilibrium data, rather than models and predictions. They are however limited to the contents of the database. Many databases are limited to a few hundred combinations, with the Dortmund Databank, probably the largest of its kind, containing 21 800 sets of VLE data. Unfortunately, most of the data contained on these databases are for binary mixtures, whereas even the simplest solvent-based separation would require at least ternary data.

This lack of multi-component data is not the only failing of database searches. The contents of the database must by necessity be limited to



those mixture-solvent combinations that have already been investigated. This excludes the possibility of finding newer and better solvents.

The heuristic methods, although numerous and varied, are almost always based on a single property and are mostly qualitative. Such a method may also recommend multiple possible solvents, without an indication as to the relative suitability of the candidates. An example of this is the use of the Robbins chart (Robbins, 1980) to find a solvent to separate acetone and methanol with extractive distillation. According to the Robbins chart, all of the following may be considered:

- Alcohols / water
- Multi-haloparaffins with active hydrogen atoms
- Ketones / amides with no hydrogen atoms bonded to the nitrogen / sulfone / phosphine oxide
- Tertiary amines
- Esters / aldehydes / carbonates / phosphates / nitrates / nitrites / nitriles / intramolecular bonding compounds e.g. o-nitrophenol

No indication is given as to the extent to which any of these compounds will influence the relative volatility.

It is also not uncommon for these methods to produce contradictory results, especially when the species under consideration have multiple functional groups.

These problems leave a lot of room for better methods of solvent selection. Computer-aided molecular design (CAMD) is one such method.

### **1.3 CAMD in Chemical Engineering**

The application of computer-aided molecular design to chemical engineering problems started in the early 1980's when Gani and co-workers used a CAMD algorithm to design solvents for liquid-liquid extraction (Gani and Brignole, 1983). Their method builds molecular structures from sub-molecular groups according to a set of rules for physical viability. The macroscopic properties of these molecules are then estimated with various group contribution methods. In this manner an optimal molecular structure is found within the search space of the method.

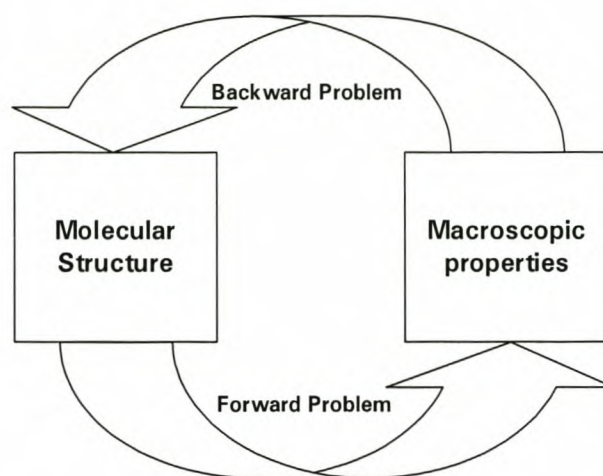
The application of CAMD in chemical engineering is not limited to designing solvents for liquid-liquid extraction. Different CAMD methods have been applied to the problems of designing solvents for extractive distillation problems (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000), coolants for refrigeration cycles (Joback and Stephanopoulos, 1989) as well as polymers and polymer blends (Venkatasubramanian et al, 1994).

A number of different CAMD algorithms have been proposed (Brignole et al, 1986; Joback and Stephanopoulos, 1989; Macchietto et al, 1990; Nielsen et al, 1990; Gani et al, 1991; Naser and Fournier, 1991; Pretel et al, 1994; Venkatasubramanian et al, 1994; Churi and Achenie, 1996; Maranas, 1996; Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000). These algorithms may be broadly classified into five groups:

- Interactive Methods
- Combinatorial Methods
- Construct-and-Test Methods
- Mathematical Programming Methods
- Evolutionary Methods

These methods will be discussed in detail in the following chapter.

The various methods may differ in the details of their implementation, but share a common objective – to solve the backward problem, as depicted in Figure 1.1.



**Figure 1.1 The Forward and Backward Problems in Molecular Design**

Like in Gani's method, the backwards problem is typically solved through the construction of candidate molecules using sub-molecular groups and then estimating the macroscopic properties of these structures. This estimation process entails solving the forward problem, and is mostly done with group-contribution methods. This process continues until the structure is found that best satisfies all of the specified requirements. It is only in the construction of the molecular structures that the methods differ. However, as with all numerical methods, these differences can have a very significant effect on the speed of the method as well as the results produced by it.

## ***1.4 Opportunities for Improvement***

The individual merits and shortcomings of the various CAMD algorithms will be discussed in detail in the following chapter. At this point a number of general issues may be considered.

### **1.4.1 Blended Solvents**

As will be seen in the detailed discussion of the various CAMD algorithms, most of the work up to this point has been on the design of pure solvents. This is simply because it is easier to construct a single molecular structure than a mixture of different molecules.

Blended solvents have the attraction that it may be possible to use simpler, and thus cheaper, solvents to effect a given separation. These blends would make use of synergistic effects to increase the selectivity of the blend beyond that of its individual components. This may have a dramatic influence in especially extractive distillation and liquid-liquid extraction.

Some of the methods mentioned above present the possibility of designing blended solvents. This is more often a side effect of not being able to construct a single viable molecule from the functional groups that the search algorithm returned. The molecules that are constructed in this manner are often rejected, as they do not individually conform to all of the design requirements.

The design of blended solvents should receive more attention as the research in CAMD advances and the single solvent algorithms are improved upon.

### **1.4.2 Chromatographic Separations**

Although CAMD has been applied to many different problems in chemical engineering, the focus in solvent design has been only on liquid-liquid extraction and later on extractive distillation. Other solvent-based processes like chromatographic separations have been almost completely ignored up to this point.

Chromatographic separations, although not widely used for bulk separations, are of utmost importance in chemical analysis. For the separation and purification of pharmaceuticals and naturaceuticals (pharmaceutically active compounds of natural origin), there is a strong trend towards using preparative chromatographic techniques (Cramer and Jayaraman, 1993).

Gas-liquid chromatography has long been used to find UNIFAC interaction parameters (Zarkarian et al, 1979). It is thus rather surprising that the process has not been reversed to find improved mobile and/or stationary phases for chromatographic separations.

### **1.4.3 Azeotropic Distillation**

As with the chromatographic separations, the computer-aided molecular design of entrainers for azeotropic distillation has also received virtually no attention. Azeotropic distillation remains a very important method of separating close-boiling or azeotropic mixtures (Seader and Henley, 1998). Finding better entrainers to effect these separations more economically or in a more environmentally friendly manner should be a priority in separations research.

## ***1.5 The Road Ahead***

The use of CAMD to find solvents for separation processes has a number of advantages over older methods. The search space of CAMD methods is vast, including billions of possible candidates. In contrast to this database searches are usually limited to a few hundred or thousand molecules. As the selectivity of candidate solvents are determined through estimation methods like UNIFAC, the problem of unavailability of multi-component VLE or LLE data is circumvented. In contrast to heuristic methods, the results produced by CAMD methods are quantitative - the extent to which

candidates match the requirements are given numerically. When more than one solvent is suitable, they may be ordered according to suitability.

A number of opportunities for improving on current methods of solvent design have been identified. Before possible solutions to these shortcomings may be discussed, the different algorithms should first be considered in more detail.

A review of these methods will allow the strengths and weaknesses of each to be identified. We will then attempt to improve on one of these methods, the SolvGen algorithm (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000), not only by seeking to eliminate some of its more obvious shortcomings, but also by extending the basic algorithm to include all of the separation processes discussed in this section.

The success of these modifications will then be tested by applying the improved algorithm to a number of case studies, including problems in extractive distillation, liquid-liquid extraction, heterogeneous azeotropic distillation and chromatographic separation.

# 2

## 2 Algorithms for Solvent Design

### ***2.1 Introduction***

The various algorithms for the computer-aided molecular design of solvents were very briefly described in the previous chapter. In order to better understand the benefits and problems associated with the different types of algorithms, an example of each type will be discussed in detail.

### ***2.2 Interactive Methods***

Interactive methods depend on the user's knowledge and experience to find a set of functional groups that may be combined into molecules with the required properties. Once this set of functional groups has been found, another method (e.g. an exhaustive search) must be used to construct a molecule, or molecules, using the entire set.

The interactive methods make use of linear group contribution methods. In linear methods, the individual contributions of all the functional groups are added to find the molecular property. This allows the molecule to be assembled group-by-group, independent of the order in which the groups are added. Given a requirement such as a boiling point higher than 500K,

groups are simply added and the resulting molecular property evaluated until the constraint is met.

The decision as to which groups are added or excluded is solely up to the user. The task of the computer is generally only to compute the properties for the molecule at each step in the design process.

The complexity of the process increases rapidly as more properties are specified. For such cases Joback proposed a graphical method (Joback and Stephanopoulos, 1989). In this method the contribution of each functional group to the specified properties is written as a vector. As functional groups are added, the vectors are plotted on the design space to give a graphical representation of each group's contribution towards reaching the design objective. Because of its graphical nature, it is obvious that this method is best suited to problems where two, or at best three, physical properties are involved (Joback and Stephanopoulos, 1989).

Fortunately, many physical properties are highly intercorrelated (Cramer, 1980; Cramer, 1980; Joback and Stephanopoulos, 1989). This allows one physical property to be replaced with a function of the other specified properties. This may be done using statistical techniques like principal factor analysis or principal curves, or through thermodynamic relations. In this manner it may be possible to reduce the number of design parameters to such an extent that the graphical technique is again feasible. Joback reports that it was possible to replace up to nine physical properties with three factors extracted in this manner (Joback and Stephanopoulos, 1989).

Unfortunately the group contribution methods used to calculate activity coefficients (UNIFAC and ASOG) are not linear. This complicates the application of the graphical design technique to the design of solvents for



separation processes. It will not be possible to calculate contribution vectors for each functional group a priori, as the contribution of the groups will strongly depend on the groups that are already present as well as other factors, e.g. temperature.

Although the interactive design methods are simple to implement, they are limited by the knowledge of the user. The ability of the computer to do the repetitive calculations needed for optimisation and search algorithms is not utilised at all. To make effective use of the computer, the process of selecting functional groups must be automated.

### 2.3 Combinatorial Methods

In its crudest form, the combinatorial method is a brute force search method. All possible combinations of functional groups are tested until a set of groups is found that could be used to construct molecules with the required properties. With even the simplest group contribution methods, with small sets of functional groups, this method will be so resource intensive as to be utterly impractical.

The first step is to select all the groups from which the molecule may be constructed. Joback (Joback and Stephanopoulos, 1989) gives the groups in Table 2.1 as an example of an initial set for designing a refrigerant.

**Table 2.1 Initial Groups for Refrigerant Design (Joback and Stephanopoulos, 1989)**

-CH <sub>3</sub>	>CH <sub>2</sub>	>CH-	>C<	=CH <sub>2</sub>	=CH-	=C<
=C=	≡CH	≡C-	-F	-Cl	-Br	-I
-OH	-O-	>CO	-CHO	-COOH	-COO-	=O
-NH <sub>2</sub>	>NH	>N-	-CN	-NO <sub>2</sub>	-SH	-S-

At least two groups will be needed to construct a molecule. A maximum number of groups must also be specified to limit the search to molecules of a practical size.

The simple combinatorial process would start by constructing subsets of these functional groups. First all possible combinations of two groups are constructed, then all possible combinations of three groups and so forth up to the maximum number of groups allowed. Without such a limit, the construction of molecules would continue until all the available sub-molecular groups have been combined into a single molecule.

The number of possible combinations may be calculated with using Equation 2.1.

#### Equation 2.1

$$\Omega = \sum_{n=2}^{\max} N^n$$

With

- $\Omega$ : Total number of combinations
- $N$ : Total number of groups to select from
- $n$ : Number of groups selected

Setting an upper limit of six groups and using the groups in Table 2.1, this will give 499,738,064 possible combinations.

The number of unique combinations may be calculated using Equation 2.2

#### Equation 2.2

$$\Omega^{\circ} = \sum_{n=2}^{\max} \sum_{r=1}^n \left[ \binom{N}{r} \binom{n-1}{r-1} \right]$$

With

- $\Omega^{\circ}$ : Number of unique combinations
- N: Total number of groups to select from
- n: Number of groups selected

This shows that only 1,344,875, or 0.27% of these combinations are unique! Most of these would not represent physically viable molecules. This should give some idea of how wasteful of resources the brute force method is.

Each of the sets may be stored as a vector. Ethane, for example, would be written as:

$$[2 \ 0 \ 0 \ 0 \ 0 \ \dots \ 0 \ 0]$$

Using the brute-force approach, all the specified properties must now be calculated for each of these vectors. Each vector must also be tested for physical viability, using rules such as those in Table 2.2.

Clearly this process would require an enormous amount of computer resources and time. Merely storing all of the possible vectors would require more than 13 gigabytes of RAM!

Joback and Stephanopoulos (Joback and Stephanopoulos, 1989) proposed a method designed to reduce the search space in which a combinatorial search must take place.

**Table 2.2 Structural Constraints Based On Octet Rule**  
**(Joback and Stephanopoulos, 1989)**

1. A collection of groups must contain at least two groups
2. If a collection contains both cyclic and acyclic groups, then it must also contain mixed groups.
3. The number of groups in a collection having an odd number of free bonds must be even.
4. If a collection contains $n$ groups with $b$ free bonds, then $\frac{b}{2} \leq \frac{1}{2}n(n-1)$
5. If a collection contains $n$ groups that are all acyclic, and $n_i$ denotes the number of groups with a global valence of $i$ then $n_1 = 2 + n_3 + 2n_4 + \dots + (i-2)n_i + \dots$

To reduce the size of the problem, Joback proposed the use of *meta-groups* and *meta-molecules*. Meta-groups are formed by abstracting the functional groups of Table 2.1 into clusters of groups. Instead of combining groups from Table 2.1 into molecules, these meta-groups are combined into meta-molecules.

A meta-molecule that contains two members of the first meta-group will be written as:

$$[2 \ 0 \ 0 \ 0 \ 0 \ \dots \ 0 \ 0]$$

The representation is the same as previously, but now each component of the vector represents not an individual functional group, but a set of functional groups.

Each meta-molecule represents a set of molecules that may be expanded by taking all possible combinations of the individual groups from the meta-groups in each meta-molecule.

The meta-groups in Table 2.3 were formed by grouping the functional groups in the initial set by the number of free bonds in each group. Double and triple bonds are counted as single bonds.

**Table 2.3 Example Meta-groups (Joback and Stephanopoulos, 1989)**

<b>Meta-group 1</b>	-CH <sub>3</sub>	=CH <sub>2</sub>	≡CH	-F	-Cl	-Br
	-I	-OH	-CHO	-COOH	=O	-NH <sub>2</sub>
	-NO <sub>2</sub>	-CN	-SH			
<b>Meta-group 2</b>	>CH <sub>2</sub>	=CH-	=C=	≡C-	>CO	-COO-
	-O-	>NH	-S-			
<b>Meta-group 3</b>	=C<	>CH-	>N-			
<b>Meta-group 4</b>	>C<					

As an example, these meta-groups will be used to find a molecule containing two to four functional groups and possessing a boiling point of more than 500K.

The first step is to generate all the possible meta-molecules that contain two to four meta-groups. According to Equation 2.1 this gives a total of 336 meta-molecules of which 65 are unique (Equation 2.2).

These meta-molecules are then tested against the physical constraints listed in Table 2.2. After this test, only four meta-molecules remain. These are listed in Table 2.4.

For each of these meta-molecules, a boiling point is computed using an additive group contribution method like that of Joback (Joback and Reid, 1987) or one of the linear methods proposed by Marrero-Morejón and Pardillo-Fontdevila (Marrero-Morejón and Pardillo-Fontdevila, 1999). As the meta-molecules are actually sets of molecules, their boiling points will also be sets. As a practical measure these sets are written as closed intervals.

This means that only the highest and lowest boiling points possible in each set need be calculated and stored.

Once the physical properties for the meta-molecules have been calculated, these are tested against the requirements in the design specification. In this example, only those meta-molecules with an upper bound higher than 500K are retained, which includes all four of the meta-molecules that passed the physical constraint tests.

**Table 2.4 Property Values for the Meta-molecules (Joback and Stephanopoulos, 1989)**

Meta-molecule	$T_b$
(2 0 0 0)	[177.18, 536.36]
(2 1 0 0)	[199.60, 617.46]
(3 0 1 0)	[178.42, 729.59]
(2 2 0 0)	[222.02, 698.56]

At this stage, the search space has been reduced from an initial 637392 possible combinations (Equation 2.1), to 30,600 possible combinations, a reduction of 95.2%!

To further reduce the number of candidates, the remaining meta-molecules are expanded in a step-wise manner by dividing the meta-groups into smaller groups. This division is based on the chemical and/or physical properties of the groups.

The first meta-group may be divided into two smaller meta-groups as seen in Table 2.5. This division was done on the basis of boiling point contributions.

**Table 2.5 Divided Meta-groups**

	Functional groups						$\Delta T_b$
Meta-group 1,1	-CH <sub>3</sub>	=CH <sub>2</sub>	≡CH	-F	-Cl	-Br	[-10.50, 90.84]
	-I	-OH	-CHO	=O	-NH <sub>2</sub>	-SH	
Meta-group 1,2	-COOH	-NO <sub>2</sub>	-CN				[125.66, 169.09]

All the meta-molecules containing meta-group 1 must be expanded as well. Again all possible combinations of meta-groups 1,1 and 1,2 are taken for each meta-molecule. For example, meta-molecule (2 0 0 0) may be expanded into three new meta-molecules: (2 0 0 0 0), (0 2 0 0 0) and (1 1 0 0 0). In the process the dimensionality of the vectors was increased from four to five.

The property intervals for each of these new meta-molecules are now calculated and tested against the required values. Those not satisfying the design specifications are eliminated. The process is repeated for another meta-group until all the meta-groups have been fully expanded. At this point every meta-molecule represents only one actual molecule.

The functional groups in each of these sets must then be combined into actual molecules, using a brute-force or other combinatorial method.

Joback's method greatly reduces the search space for combinatorial methods, but is sensitive to the way in which meta-groups are divided. The best division of meta-groups is also not obvious when multiple physical properties are specified.

Further complications arise when this method is applied to the design of solvents. The UNIFAC method that is used to calculate activity coefficients is not a purely additive method. This makes it difficult to calculate the intervals of contributions for the different meta-groups.

The method may be used to design either aliphatics or aromatics, but not simultaneously, unless the physical constraints are expanded.

## **2.4 Construct-and-Test Methods**

The method developed by Gani and co-workers (Gani and Brignole, 1983; Brignole et al, 1986; Nielsen et al, 1990; Gani et al, 1991), uses knowledge of the physical and chemical properties of the functional groups to limit the search space to physically viable molecules.

The method uses a classification of the UNIFAC groups according to the number of free attachments and chemical and physical considerations (see Table 2.6). Structures are built by combining these groups in compliance with a set of conditions. These conditions are applied at every step, so that only feasible structures are assembled.

The primary conditions set for these molecular structures are:

1. The final structure must have no free bonds.
2. Certain restriction are placed on the manner in which groups of categories 2 to 5 (Table 2.6) may be combined with other groups.

Table 2.7 gives a summary of the combinations that will satisfy these conditions. There are also a number of secondary conditions:

1. Only groups with known parameters for the group contribution methods may be used.
2. Highly branched structures are to be avoided.
3. Structures that may exhibit proximity effects, e.g. two or more large structures bonded to adjacent carbon atoms, are to be rejected.



The method of combining functional groups requires that different types of molecular structures, e.g. straight chain aliphatics, branched aliphatics, naphthenes or aromatics, be considered separately.

Table 2.6 Classification of UNIFAC groups (Gani et al, 1991)

Category					
Class	1	2	3	4	5
1	CH <sub>3</sub>	CH <sub>2</sub> CN	CH <sub>3</sub> CO	OH	CCl <sub>2</sub> F
		CH <sub>2</sub> NO <sub>2</sub>	CONH <sub>2</sub>	CHO	CH <sub>2</sub> SH
		CH <sub>2</sub> NH <sub>2</sub>	CONHCH <sub>3</sub>	COOH	CH <sub>3</sub> NH
			CON(CH <sub>3</sub> ) <sub>2</sub>	CH <sub>2</sub> Cl	CHCl <sub>2</sub>
				I	C <sub>4</sub> H <sub>3</sub> S
				Br	SH
				F	C≡CH
				Cl	COO
				CH <sub>3</sub> COO	CCl <sub>3</sub>
				CH <sub>3</sub> O	CH <sub>2</sub> NH <sub>2</sub>
				C <sub>2</sub> H <sub>5</sub> O <sub>2</sub>	CCl <sub>2</sub> F
				CH <sub>3</sub> S	CHClF
	2	CH <sub>2</sub>	CHNO <sub>2</sub>	CH <sub>2</sub> CO	CHNH <sub>2</sub>
			CH <sub>2</sub> COO	CH <sub>2</sub> NH	CH <sub>2</sub> =C
			CH <sub>2</sub> O	CHCl	C <sub>4</sub> H <sub>2</sub> S
			CONCH <sub>3</sub> CH <sub>2</sub>	CONHCH <sub>2</sub>	CH <sub>3</sub> N
				C <sub>2</sub> H <sub>4</sub> O <sub>2</sub>	C≡C
				CH <sub>2</sub> S	
3	CH		CON(CH <sub>2</sub> ) <sub>2</sub>	CHNH	CH=C
				CH <sub>2</sub> N	CCL <sub>2</sub>
				CCl	
				CH-O	
			CHS		
4	C				C=C
5	ACH		ACCH <sub>2</sub>	ACCH <sub>3</sub>	ACOH
			ACCH		ACNH <sub>2</sub>
			AC		ACCl
					ACNO <sub>2</sub>

**Table 2.7 Rules Related to the Primary Conditions (Gani et al, 1991)**

Total No. of Groups	Largest Class of Group	Groups from Largest Class	Max. Number. of Groups Allowed from Categories				
			3	4	5	3+4+5	4+5
<b>Non-aromatic Compounds</b>							
2	1	2	2	1	1	2	1
3	2	1	2	1	1	2	1
4	3	1	2	1	1	2	1
4	2	2	2	2	1	2	2
5	4	1	2	1	1	2	1
5	3	1	2	2	1	2	2
5	2	3	3	2	1	3	2
6	4	1	3	2	1	3	2
6	3	2	3	2	1	3	2
6	3	1	3	2	1	3	2
6	2	4	3	3	1	3	3
7	4	1	3	2	1	3	2
7	3	2	3	3	1	3	3
7	3	1	3	3	1	3	3
7	2	5	4	3	1	4	3
8	4	2	3	2	1	3	2
8	4	1	3	3	1	3	3
8	3	3	3	2	1	3	2
8	3	2	3	3	1	3	3
8	3	1	3	3	1	3	3
8	2	6	4	3	1	4	3
<b>Aromatic Compounds</b>							
6	5	6	0	3	1	3	3
7	5	5	1 (1)*	2	1	3	2
8	5	5	2 (1)	2	1	3	2
8	5	5	1 (2)	2	1	3	2
9	5	5	3 (1)	0	0	3	0
9	5	5	1 (3)	2	1	3	2
9	5	5	1(1) + 1(2)	1	1	3	1

\* Values in parentheses indicate the number of free attachments after ring completion.

The first step in applying this method is to select the type of molecular structure, e.g. aliphatic or aromatic, and select the functional groups that will be considered. The algorithm is summarised in Table 2.8.

**Table 2.8 The Construct-and-Test Algorithm**

<b>Variables</b>	
$M_A$ :	minimum number of groups in a molecule
$M_B$ :	maximum number of groups in a molecule
$M_C$ :	category in table 2.6 to be used
$M_2$	} utility variables
$M_3$	
$M_4$	
$M_5$	
<b>Algorithm</b>	
Step 1:	
1.1	Input $M_A$ and $M_B$
1.2	$M_C \rightarrow 1$
Step 2:	
2.1	$M_2 \rightarrow M_B - 1$
2.2	For non-aromatic compounds:
	Choose a group from category $M_C$ and class $M_2$
	If $M_2 > 4$ then
	Choose from category $M_C$ or category 5 and class 4
	$M_2 \rightarrow 4$
	End if
2.3	For aromatic compounds:
	Choose a group from category $M_C$ or category 5 and class 5
2.4	For either case:
	If more than one group exists in the specified class and category then create a molecular structure for each case.

## Step 3:

3.1  $M_3 \rightarrow M_B - M_2$

3.2 If  $M_3 = 1$  then

Terminate structures by choosing  $M_2$  groups from class 1 and any category that satisfies the primary and secondary conditions (see above and Table 2.7).

Repeat until all the structures formed in step 2 have been considered.

End if

3.3 If  $M_3 > 1$  then

Continue with step 4

Else

Go to step 6

End if

## Step 4:

4.1  $M_4 \rightarrow M_B - M_2$

4.2 If  $M_4 > 4$  then

$$M_4 \rightarrow 4$$

End if

4.3 Choose a group from class  $M_4$  and category that satisfies the primary and secondary conditions (see above and Table 2.7).

4.4 Repeat 4.3 for all allowable categories in class  $M_4$

4.5 Repeat 4.3 – 4.3 until all the structures created in step 3 have been considered.

## Step 5:

5.1  $M_5 \rightarrow M_B - M_2 + 1$

5.2 If  $M_5 = 1$  then

Go to step 3

Else

Choose a group from class  $M_5$  and any category that satisfies the primary and secondary conditions (see above and Table 2.7).

Repeat 4.3 – 4.3 until all the structures created in step 3 have been considered.

End if

5.3  $M_2 \rightarrow M_2 + 1$

5.4 Go to step 4

Step 6:

6.1  $M_C \rightarrow M_C + 1$

6.2 If  $M_C \geq 5$  then

    Go to step 7

    Else

        Go to step 2

    End if

Step 7:

7.1  $M_B \rightarrow M_B - 1$

7.2 Repeat from step 2 until  $M_B = M_A$

7.3 If  $M_B < M_A$  then

    Select new type of structure and repeat from step 1.

    End if

End.

This algorithm will construct all possible molecular structures that are feasible under the conditions given above. These structures are then tested against the property specifications.

Properties are classified into four groups according to the methods that are available to estimate their values (Gani et al, 1991):

- Primary pure component properties
- Secondary pure component properties
- Primary mixture properties
- Secondary mixture properties

The primary properties are those, which may be estimated directly from the molecular structure. The methods for secondary properties require that other property values be available.

The properties are calculated in the order as given above. This allows properties that are easier to calculate to be tested first. Each property is tested against the requirements before further properties are calculated.

Like Joback's combinatorial method discussed above, the construct-and-test method is an attempt to limit the search space of an essentially brute-force method. While Joback attempts to eliminate candidates based on their physical properties, Gani et al (Gani et al, 1991) eliminate candidates based on physical viability.

Due to the complexity of the natural laws that govern the stability of chemical compounds, the set of rules used by Gani et al will by necessity have some exceptions. This may cause feasible candidates not to be considered and possibly include some non-feasible candidates. It is up to the user to check for these eventualities. Continued research on this topic should increase the accuracy and generality of these rules.

## ***2.5 Mathematical Programming Methods***

A number of mathematical programming methods for CAMD have been proposed (Macchietto et al, 1990; Naser and Fournier, 1991; Churi and Achenie, 1996; Maranas, 1996; Vaidyanathan and El-Halwagi, 1996). Most of these methods are based on variations of mixed integer non-linear programming (MINLP), though Macchietto and Naser both relaxed the integer specification and employed continuous optimisation algorithms in their methods.

In all of these methods, the variable that is optimised is the number of each sub molecular group that is present in the structure. The goal function includes all the required properties and is either minimised or maximised depending on the formulation of the goal function. After sets

of functional groups have been assembled, molecules must be built from these sets. These molecules are usually assembled with combinatorial or exhaustive search algorithms.

Constraints are often set to ensure that the assembled groups form viable molecules. As most of these methods were developed to design polymers and polymer blends, only certain physical viability aspects are checked. Certain groups like C=C and C≡C are usually excluded beforehand.

The method of Macchietto et al (Macchietto et al, 1990) will be considered in more detail. As mentioned above, the primary variables in the optimisation problem is the number of each structural group present in the molecule. The number groups of type  $i$  present, is defined as  $n_i$ , where  $i$  is a member of  $I$ , the set of structural groups. The objective function ( $n$ ) must be maximised. The solvent design problem can be written as follows:

### Equation 2.3

$\max_{n_i, i \in I} \text{of } (n)$	(e.g. maximise selectivity)
subject to: process constraints	(e.g. mass balance, equilibrium equations)
design constraints	(e.g. solute recovery $\geq 80\%$ )
constraints on physical properties	(e.g. $200^\circ\text{C} \leq \text{boiling point} \leq 270^\circ\text{C}$ )
structural constraints on solvent molecule	

The structural constraints are included to ensure the physical viability of the molecule. Macchietto et al divide the structural groups into four categories: terminators (e.g.  $-\text{CH}_3$ ), extenders (e.g.  $-\text{CH}_2\text{-O-}$ ), branchers (e.g.  $-\text{CH}<$ ) and molecules (e.g.  $\text{H}_2\text{O}$ ). The last group is included to handle the molecular groups defined in the UNIFAC method (Fredenslund et al, 1975). To satisfy the octet rule, the structure must satisfy the following equality:



**Equation 2.4**

$$\sum(\text{terminators}) - \sum(\text{branches}) = 2q$$

With

$q = 1$  for acyclic molecules

$q = 0$  for non-aromatic, single ring molecules

$q = -1$  for non-aromatic, double ring molecules

Further requirements for physical viability are similar to those used by Gani et al (Gani et al, 1991). The requirements for acyclic molecules are expressed in Equation 2.5

**Equation 2.5**

$$k = m + \frac{j}{2} + p$$

With

$k$ : The number of severely restricted attachments (e.g. – OH)

$m$ : The number of unrestricted carbon attachments in single and linear dual valency groups (e.g. – CH<sub>3</sub>)

$j$ : The number of unrestricted carbon attachments in radial dual valency groups (e.g. – CH<sub>2</sub>– )

$p$ : The number of unrestricted carbon attachments in radial triple valency bonds (e.g. – CH<).

Similar requirements are formulated for cyclic and aromatic compounds. Restraints may also be placed on the maximum or minimum number of a certain structural group present in the molecule and on the total number of structural groups used.

The optimisation problem has integer variables (the number of each structural group present) and should be treated as a MINLP (mixed integer

non-linear programming) problem. Macchietto et al propose that the integer constraint may be relaxed in order to use continuous non-linear programming techniques. They used a so-called infeasible path gradient-based method to solve the problem formulated in Equation 2.3.

Due to the large number of constraints, integer solutions are often found. This is especially so when only a few structural groups are used (Macchietto et al, 1990). It is also possible to add further constraints to force an integer solution. For example:

#### Equation 2.6

$$\sum_i [(\bar{n}_i - n_i)(1 + \bar{n}_i - n_i)] = 0$$

With

$\bar{n}_i$  : The integer part of  $n_i$

This constraint will ensure that the number of each group is rounded either up or down to an integer value.

As an example, the recovery of acetic acid from water with liquid-liquid extraction is considered. UNIFAC is used to calculate the liquid-liquid equilibria and the method of Lai et al (Lai et al, 1987) is used to estimate pure component boiling points. The structural groups listed in Table 2.9 will be used.

**Table 2.9 Initial Groups for Solvent Design (Macchietto et al, 1990)**

CH <sub>3</sub>	CH <sub>2</sub>	CH	CH <sub>3</sub> CO	COOH
CHO	CH <sub>3</sub> COO	CH <sub>3</sub> O	CH <sub>2</sub> O	CH-O

The objective function is defined as the product of the selectivity and the solvent capacity at ambient temperature. To facilitate recovery of the

solvent, its boiling point is required to be 20K higher or lower than that of the pure solute. As starting point, the structure of an industrial solvent is used. The intermediate results of the step-wise optimisation are shown in Table 2.10.

**Table 2.10 Solvent Design for Recovery of Acetic Acid from Water**  
(Macchietto et al, 1990)

<b>Low Boiling Solvent (<math>T_b \leq 98^\circ\text{C}</math>)</b>		
Iteration	Structure	Objective Function
0	$\text{CH}_3\text{CH}_2\text{CH}_3\text{COO}$ (ethyl ethanoate)	71.71
1	$(\text{CH}_3)_{1.1}(\text{CH}_2)(\text{CH})_{0.1}(\text{CH}_3\text{COO})_{0.8}(\text{CH}_3\text{O})_{0.7}$	100.70
2	$(\text{CH}_3)_3\text{CH}_2\text{CHCH}_3\text{O}$	192.50
3	$(\text{CH}_3)_2(\text{CH}_2)_5$	304.50
4	$(\text{CH}_3)_{4.6}(\text{CH})_{2.6}$	329.23
Integer solution	$(\text{CH}_3)_4\text{CH}_2(\text{CH})_2$ (2,4 dimethyl pentane)	320.43
<b>High Boiling Solvent (<math>T_b \geq 138^\circ\text{C}</math>)</b>		
Iteration	Structure	Objective Function
0	$\text{CH}_3(\text{CH}_2)_3\text{CH}_3\text{CO}$ (methyl isobutyl ketone)	20.22
1	$(\text{CH}_3)_{2.7}(\text{CH}_2)_{4.7}(\text{CH})_{1.7}\text{CH}_3\text{COO}$	173.64
2	$(\text{CH}_3)_{3.4}(\text{CH}_2)_5(\text{CH})_{1.5}(\text{CH}_3\text{COO})_{0.1}$	421.55
3	$(\text{CH}_3)_{2.2}(\text{CH}_2)_5(\text{CH})_{0.2}$	360.04
4	$(\text{CH}_3)_{3.4}(\text{CH}_2)_{5.2}(\text{CH})_{1.4}$	426.22
5	$(\text{CH}_3)_{3.5}(\text{CH}_2)_5(\text{CH})_{1.5}$	429.33
Integer solution	$(\text{CH}_3)_6(\text{CH}_2)_4$ (tetra-methyl hexane) or $(\text{CH}_3)_4(\text{CH}_2)_4(\text{CH})_2$ (2,7 dimethyl octane) or $(\text{CH}_3)_3(\text{CH}_2)_6(\text{CH})$ (methyl nonane)	421.91 421.51 421.42

More than one integer result may be found from the final real value solution. In the case of the high boiling solvent three possible solutions were found.

The mathematical programming methods are computationally inexpensive when compared to other methods. Unfortunately they are not guaranteed to find the global optimum, as the gradient methods, such as that used by Macchietto et al (Macchietto et al, 1990) to solve Equation 2.3, tend to be susceptible to local minima traps. Furthermore, when convenient industrial solvents are not available to use as starting points, these methods may be very susceptible to poor initial estimates.

The methods used to assemble molecules from the returned sets of functional groups (typically either brute force or combinatorial methods), are computationally more expensive, but operate on a much smaller number of groups. As such they contribute little to the total amount of processing time required.

If the structural constraints are relaxed it may be possible for the post-processing step to construct more than one molecule from the returned set. In this case the physical properties must be recalculated. If each of the molecules constructed in this manner do not meet the requirements, the entire set must be discarded. This is often the case, as the answer to the optimisation problem was the entire set.

## ***2.6 Evolutionary Methods***

In 1975 John Holland published a paper describing how the Darwinian principles of evolution may be applied to optimisation problems (Holland, 1975). The Genetic Algorithms (GA) he described were found to be efficient, robust optimisation techniques that work in the most difficult search spaces without problems like susceptibility to local minima traps.

These algorithms have also been applied to CAMD problems, both for the design of polymers (Venkatasubramanian et al, 1994) and for the design of solvents for extractive distillation (Van Dyk, 1998) (Van Dyk and Nieuwoudt, 2000). Further publications describing the use of CAMD for liquid-liquid extraction emanated from this work (Van Dyk and Nieuwoudt, 2001).

These methods are fast and efficient; do not require vast amounts of computing resources (Davis, 1991; Koza, 1992) and function without problem in the difficult search spaces of CAMD problems (Venkatasubramanian et al, 1994).

In order to explain the SolvGen algorithm proposed by Van Dyk and Nieuwoudt, a brief discussion of genetic algorithms is appropriate. A more detailed treatment of the topic may be found in (Davis, 1991), (Holland, 1975), (Koza, 1992) or (Van Dyk, 1998).

### **2.6.1 A Brief Introduction to Genetic Algorithms**

The basic premise of evolution through natural selection is that those individuals that are better suited to their environment will have a better chance of surviving and reproducing. The genetic material that gave them this enhanced fitness will then be passed on to their offspring, who will in turn also have a better chance to reproduce. In time the entire population will have the characteristics that make them more suited to their environment.

This *survival of the fittest* principle may be used to solve optimisation problems. A fitness function suited to the problem is defined and candidate solutions are tested against this function. The fitness function may take any form, but better solutions to the problem must have higher fitness values.

### ***2.6.1.1 The Encoding Scheme***

Candidate solutions are encoded in linear structures that are called chromosomes in reference to their biological counterparts. The elements comprising the chromosomes are similarly called genes.

### ***2.6.1.2 The Evaluation Scheme***

Once the chromosomes have been encoded, a method must be found to decode the chromosome into the parameters that are to be optimised and calculate the fitness of the individual. In CAMD this is done with the group contribution methods that convert the structural information stored in the chromosome into physical properties.

### ***2.6.1.3 The Population Scheme***

Evolution does not influence the extent to which an individual is suited to its environment, but instead will strive to improve the average fitness of the population as a whole. For a GA to mimic this natural phenomenon, a population scheme is required.

Unlike most optimisation techniques, a GA does not sample the solution space at a single point at a time. Instead, a GA is hugely parallel.

A population of chromosomes is maintained, typically containing hundreds to thousands of individuals. The selection of individuals to reproduce is done probabilistically and the selection probability of each chromosome is directly proportional to its fitness.

A method that is often used is the so-called Roulette Wheel method (Davis, 1991; Van Dyk, 1998). In this method, a selection probability is assigned to each chromosome. A random number is then generated and

scaled to fall between zero and the sum of the selection probabilities of all the chromosomes. An accumulator is initialised to zero and the selection probabilities of the chromosomes are added to it, one at a time, until its value exceeds that of the random number. The last chromosome of which the selection probability was added is then selected to become a parent.

The two population schemes most often used, are steady-state reproduction and generational reproduction. In steady-state reproduction, new individuals will immediately replace their parents if they have higher fitness values and so the population size remains constant. In generational reproduction, the new chromosomes that are produced are stored in a second population – the new generation – regardless of whether their fitness is higher than that of their parents. When the construction of the new generation is complete, the entire parent generation is discarded and replaced with the new generation.

Both methods have certain benefits, but some researchers claim that generational reproduction is superior to steady-state reproduction (Davis, 1991).

A useful variation on generational reproduction is to implement an elitist strategy. With an elitist strategy, the best individuals (typically 5% – 10%) of each generation are copied unchanged into the next generation. The rest of the generation is then filled as before by generating offspring from the parent generation.

This usually has the effect of speeding up convergence in the GA, as good solutions are not lost due to random mutations. (Davis, 1991; Koza, 1992)

### **2.6.1.4 The Reproduction Scheme**

The reproduction scheme determines the manner in which chromosomes reproduce to form new individuals. This is done by having certain genetic operators perform manipulations on the chromosomes.

The two most commonly used operators are point mutation and crossover. During a point mutation operation, a single gene on a chromosome is randomly changed. The manner in which it is changed will depend on the details of the encoding scheme.

During a crossover, two chromosomes are both divided into two or more parts that are then joined across to form two new individuals. The one point crossover, where the parent chromosomes are split into two parts, is most commonly used. The crossover point(s) on each chromosome may be determined randomly or the midpoint of each chromosome may be used.

Other operators include the insertion of random genes and the deletion of genes from a chromosome. The point on the chromosome where these operators will act is determined randomly. In these cases the length of the chromosome may vary. This type of GA is called a 'messy' GA. (Koza, 1992).

Which operator is used, is determined probabilistically, using the same Roulette Wheel method as for the selection of parent chromosomes.

## **2.6.2 The Application of GA to Solvent Design - SolvGen**

### **2.6.2.1 The Encoding Scheme**

The first step in applying GA to molecular design is to decide on an encoding scheme. Although binary strings would be perfectly adequate, experience shows that enumerated types are much easier to implement in



CAMD problems. Using enumerated types entails assigning numbers to certain sub-molecular groups and then storing a list of these numbers instead of the binary string. Each of these groups represents a single gene. The structures of these groups are determined by the group contribution methods that are used.

In solvent design the most important group contribution method used would be UNIFAC (Fredenslund et al, 1975; Hansen et al, 1991) or one of its modified versions (Gmehling et al, 1998). This is used to calculate phase equilibria. Group contribution methods for other properties must then be found that use structures that are compatible with the UNIFAC groups. The methods of Marrero-Morejón and Pardillo-Fontdevila (Marrero-Morejón and Pardillo-Fontdevila, 1999) or Joback (Joback and Reid, 1987) may for example be used to estimate boiling and freezing points.

#### *2.6.2.1.1 The Genes*

Once the estimation methods have been chosen, the set of structural groups is fixed. Naturally, all the groups in the set do not have to be used. These groups must now be combined into molecules.

Since the genetic operators require that the genes combine linearly to form the chromosomes, the structural groups cannot be directly used as genes without discarding all those that do not have either one or two free bonds. This would also limit the algorithm to designing linear molecules. An effective solution to this problem is to predefine genes from combinations of these structural groups.

Using these predefined genes has a number of advantages:

1. It allows the construction of more complex molecules than simple linear combinations of UNIFAC groups. Genes of arbitrary complexity

may be constructed. This removes most of the constrictions caused by the requirement of linear combinations.

2. It allows the mixing of aromatic and aliphatic groups. This has been a problem in some of the algorithms published previously and was usually solved by designing aromatic and aliphatic solvents in separate cycles of the algorithm.
3. It prevents most unrealistic and reactive combinations of functional groups. In methods like those of Gani (section 2.4), a lot of effort has gone into deriving rules for the physical viability of candidate molecules. Due to the complexity of the natural laws that govern the feasibility of molecular structures, these rules have many exceptions. These exceptions could cause viable candidates to be mistakenly discarded or infeasible candidates to be accepted. Using predefined genes to build molecules largely circumvents this problem.

Although predefined genes may be seen to limit the solution space, a sufficiently large set of genes will include all feasible combinations of the available structural groups.

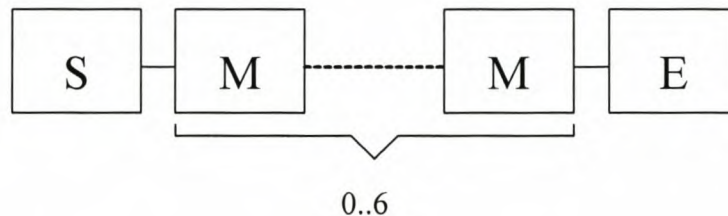
The linear combination of genes into chromosomes requires that two sets of genes be defined. The first set includes those genes that have one free bond and will be used as the first and last genes in each chromosome. The second set includes those genes with two free bonds and will be used to construct the middle part of each chromosome. Should cyclic molecules be desired, it is merely necessary to omit the first and last genes in the chromosome.

#### 2.6.2.1.2 *The Chromosomes*

As discussed above, the chromosomes are constructed by a linear combination of genes from the two sets (end groups and middle groups). As a practical matter, the size of a chromosome is limited to a maximum

of six middle genes. Larger molecules will have higher melting points and are no longer in the liquid phase at the temperatures that are normally of interest. For large molecules the accuracy of the group-contribution methods also becomes questionable.

The specific limit in the number of genes is determined by the gene set that is used. If the genes each consist of a large number of structural groups, the limit should be reduced. Likewise, if the genes consist of only one or two structural groups each, the number of genes allowed in a chromosome could be increased. Figure 2.1 shows the structure of a typical chromosome.



**Figure 2.1 A Typical Chromosome**

To accommodate cyclic molecules in this structure, an empty gene is defined as part of the set of start and end genes. This also allows the molecular UNIFAC groups (e.g. H<sub>2</sub>O) to be handled without a change in the data structures. The molecular UNIFAC groups is simply used as the start group and the empty gene as the end gene. The number of middle genes is of course set to zero.

### **2.6.2.2 The Evaluation Scheme**

The choice of fitness function is determined by the specific CAMD problem that is to be solved. The specification for a solvent for extractive distillation would for example, include the following:

- The selectivity of the solvent for one of the key components must be high.
- No unwanted azeotropes must form between the solvent and any of the feed components.
- The solvent must have a high boiling point so as to remain almost exclusively in the liquid phase.
- The formation of two liquid phases must preferably be avoided.
- The melting point must preferably be below ambient temperature

For liquid-liquid extraction, the specifications would differ in that the formation of two liquid phases is crucial and the boiling point of the solvent of lesser concern. It must also be possible to recover the solvent without leaving contamination in the product.

The selectivity may be determined through the use of an activity coefficient model like UNIFAC. Other properties, like boiling and freezing points, may be estimated through various group contribution methods.

It is an unfortunate fact that group contribution methods are not always very accurate. When the only method available to estimate a property is of dubious accuracy, it may be better not to specify requirements for these properties, or to give it a very low contribution to the fitness function.

The multiple requirements that must be satisfied must be combined into a single fitness value. This is done by calculating a fitness value for each property and then using a weighted mean as the overall fitness of the chromosome. The weights assigned to each property are determined by the specific problem under consideration and the perceived quality of the group-contribution method for this particular property.

Most of the requirements used in solvent design are one-sided, i.e. a property value must be above or below a certain value for the candidate to be acceptable. The boiling point of the solvent is an exception, since too high a boiling point will prevent the solvent from being reclaimed in a pure form. This problem may be solved by using two one-sided specifications: one for a minimum boiling point and one for a maximum boiling point. It would also be convenient to have fitness values within the interval  $[0; 1]$ , as this would make calculation of the weighted mean simpler and thus faster.

There are two types of functions that would be well suited to all of these requirements: a step-function (or Boolean function) and a sigmoidal function.

Although the Boolean function is suitable for requirements like the formation of two liquid phases, it is ill suited for properties that vary continuously (Van Dyk, 1998). This is easily demonstrated through an example.

Suppose a minimum value for the selectivity is required. Two chromosomes are considered: the first has a selectivity much lower than the required value; the other's is just below the requirement.

It is very probable that the second chromosome will contain genetic material (functional groups) that assists the desired separation, whereas the first probably does not.

Should a Boolean fitness function be used, the same low fitness will be assigned to each of these chromosomes. The desired genetic material of the second chromosome will have no better chance of surviving into the next generation than the undesired genetic material of the first

chromosome. This failure to identify desired traits in candidates could prove detrimental to the algorithm.

If a sigmoidal fitness function is used, the second chromosome will have a significantly higher fitness value assigned to it than the first. The probability that the desirable functional groups from this chromosome will be used to construct candidates for the next generation is now much better.

Equation 2.7 is an example of a sigmoidal property fitness function that may be used.

#### Equation 2.7

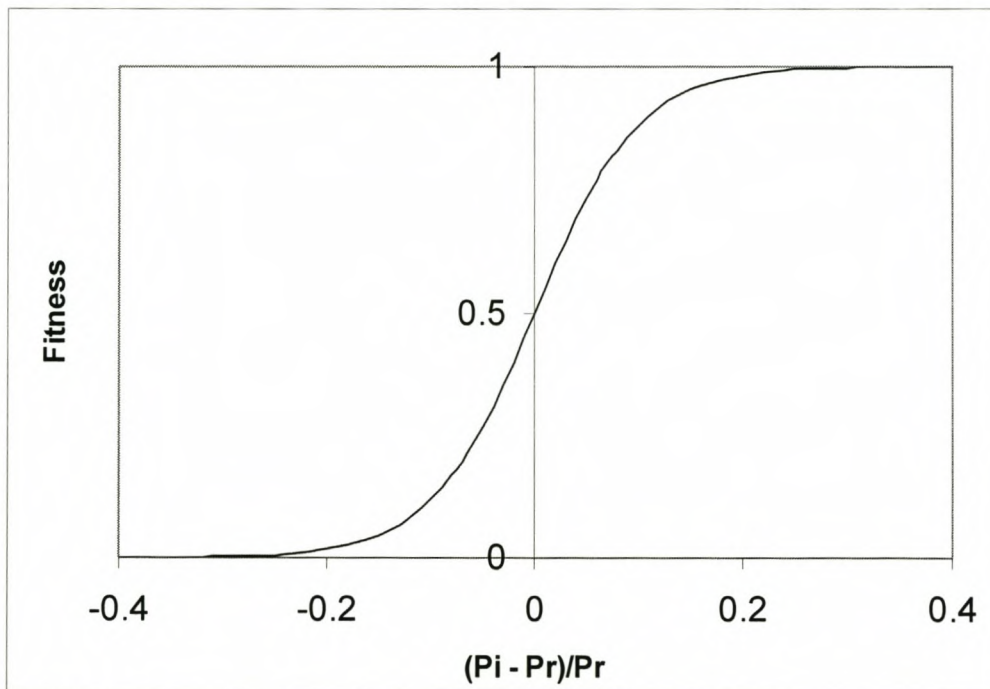
$$F = \frac{1}{1 + \exp\left[-\beta\left(\frac{P_i - P_r}{P_r}\right)\right]}$$

With

- $F$ : The property fitness
- $P_i$ : The property value for the  $i$ -th chromosome
- $P_r$ : The required value for the property
- $\beta$ : A gradient parameter

This function has the following properties (see Figure 2.2):

1. At the required value the fitness is 0.5.
2. For values higher than the requirement, the fitness approaches unity.
3. For values lower than the requirement, the fitness approaches zero.
4. The slope of the function may be controlled with the  $\beta$  parameter.
5. The function is smooth and continuous.
6. The slope of the function can be varied based on the characteristics of the problem at hand and it can thus be made to approach a Boolean function if desired.



**Figure 2.2 The Sigmoidal Fitness Function**

### ***2.6.2.3 The Population Scheme***

A random initial population is used. As stated above, generational reproduction is considered to be superior to steady-state reproduction. An elitist policy is also implemented to help speed conversion by preventing the loss of good candidates to random changes. Retaining the best 10% of candidates has been found to give good results (Van Dyk, 1998).

### ***2.6.2.4 The Reproduction Scheme***

Four genetic operators are used. These are point mutation, one point crossover, insertion and deletion.

The use of the insertion and deletion operators is limited by the restrictions in the structure of a chromosome. Start and end genes may not be inserted or deleted. The maximum number of middle genes is also fixed at six.

When applying the crossover operator two new chromosomes are created. This is only allowed if there is enough space for both in the generation that is being constructed. The crossover point is determined randomly within a small interval around the centre of each chromosome.

### ***2.6.2.5 The Basic Algorithm***

The basic genetic algorithm is summarised in Table 2.11.



**Table 2.11 The Basic Algorithm**

1. Initialise a population of chromosomes.
2. Evaluate each chromosome in the population. 2.1. Estimate the properties. 2.2. Calculate the property fitness values. 2.3. Calculate the global fitness.
3. Choose best 10% and copy them to the new generation.
4. Create new chromosomes. 4.1. Choose an operator. 4.2. Choose parent chromosome(s). 4.3. Apply the operator to the parent chromosome(s).
5. Copy the new chromosomes to the new generation until this generation has been filled.
6. Replace the current generation with the new generation.
7. If time is up, go to step 8, else repeat from step 2.
8. Evaluate each chromosome in the population.
9. Return the best solution

Van Dyk and Nieuwoudt also included a number of enhancements to this basic algorithm (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000). These include penalty functions for handling missing interaction parameters, a scheme for biasing gene selection based on the Robbins chart (Robbins, 1980), seeding of the initial population, evolving fitness functions and further checks for physical viability.

## **2.7 Conclusions**

Although CAMD methods have been applied with great success in many areas of chemical engineering, it has yet to become part of the standard toolbox for process design engineers. This is to some extent the direct effect of the amount of processing power required by some of the earlier algorithms. Much effort has gone into developing faster and more efficient algorithms. The SolvGen algorithm is both fast and efficient, but could still be improved on in both of these areas, especially by making use of the current trend towards multi-processor desktop computers.

In order to further the use of CAMD it is also important that it be applied in more areas of importance. As discussed in the previous chapter, little or no work has been done in the design of blended solvents for extractive distillation and liquid-liquid extraction. Likewise, the design of entrainers for azeotropic distillation and solvents for chromatographic separations has been neglected.

In the following chapters we will attempt to address these problems. First some of the shortcomings in the SolvGen algorithm mentioned here will be rectified. The improved algorithm will then be extended further to include blended solvents as well as other separation processes like azeotropic distillation and chromatography.

# 3

## **3 Improvements to the SolvGen Algorithm**

### ***3.1 Introduction***

The SolvGen algorithm described in chapter 1 has been found to perform very well in designing solvents for extractive distillation (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000). The basic genetic algorithm proposed by Van Dyk (Van Dyk, 1998) was enhanced in a number of ways to improve its speed of convergence and the quality of the final result. These enhancements include the option to seed the initial generation with solvents that are suspected to perform well, evolving fitness functions and biased gene selection through use of the Robbins chart (Robbins, 1980).

Further evaluation of the method has shown the possibility of further enhancements to this method, in calculation and convergence speed and the quality of the result. These improvements to the original SolvGen algorithm will be discussed in this chapter.

## **3.2 Improving Calculation Speed**

The first step in improving the speed of any computer program should be to determine which parts of the code require the most processor time. In the case of genetic algorithms, a very large part of the processor time is used to generate the pseudorandom numbers used for selection of operators and parent chromosomes, as discussed in chapter 2. In SolvGen, the computer also spent a lot of time calculating activity coefficients. Improving the speed of these two operations could greatly improve the speed of the entire program.

### **3.2.1 Pseudorandom Number Generation**

Almost all compilers available today have built-in pseudorandom number generators. The quality and speed of these generators vary greatly.

Although a faster generator would be beneficial, it is very important that the randomness of the generator, i.e. the cycle length be maintained.

To understand the concept of a cycle length, the manner in which "random" numbers are generated must be considered. A good introductory discussion of pseudorandom numbers may be found in (Parsons, 1995) and a more detailed treatment of the subject is available in (Knuth, 1981).

As computers are inherently deterministic, it is fundamentally impossible to generate truly random numbers using a computer. We therefore have to settle for a sequence of numbers that at least appears to be random. At the very least two consecutive numbers in the series should be uncorrelated.

As the generation of pseudorandom numbers is done using arithmetical methods, we are in the unfortunate position that given the same starting

value, any two sequences will always be identical. If a pseudorandom number generator produces the number 114 and the next number is 87657, then if the number 114 should again be generated, it will again be followed by 87657. This is anything but random. To quote John von Neumann:

*"Anyone who considers arithmetical methods of producing random digits is, of course, in a state of sin."*

The answer to this problem is make the probability of 114 appearing twice in a sequence as small as possible by making the so-called cycle length as long as possible. The cycle-length is the number of pseudorandom numbers that may be generated with a given generator before the sequence starts repeating itself.

### **3.2.1.1 Lehmer's Method**

One of the most common types of pseudorandom number generators is the linear congruential method, or Lehmer's method (Lehmer, 1952). The method uses three constants:

- $a$ : the multiplier
- $m$ : the modulus
- $c$ : the increment

If  $c = 0$ , the method is called the multiplicative congruential method. If  $c \neq 0$ , it is called the mixed congruential method (Parsons, 1995). Pseudorandom numbers are generated according to Equation 3.1

#### **Equation 3.1**

$$x_{n+1} = (ax_n + c) \bmod m$$

With

$x_{n+1}$ : The newly generated pseudorandom number

$x_n$ : The previous pseudorandom number

In order to generate a sequence of numbers, the first number must be specified. This is often called the seed number. Using the same seed number will yield identical sequences. The seed number is usually initialised by the computer's system clock. This makes it very improbable that the same seed number will be used twice.

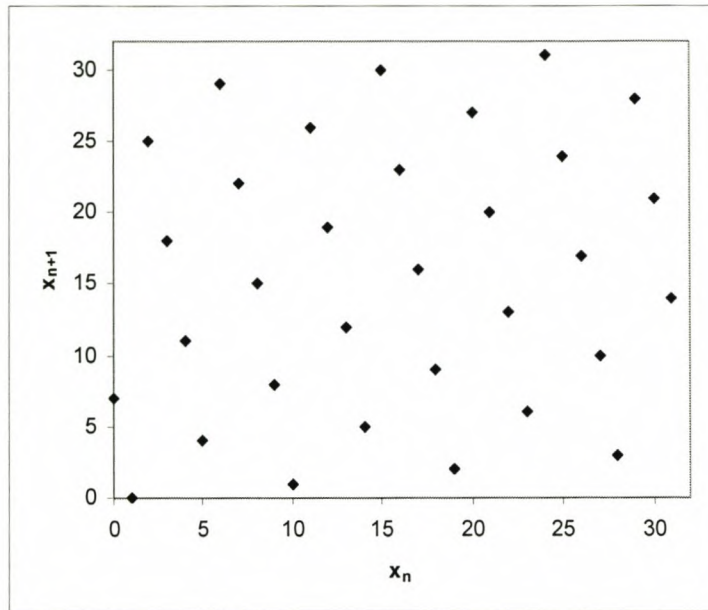
At most  $m$  numbers can be produced before the sequence starts repeating. A generator that succeeds in generating  $m$  numbers before it repeats is called a full-period generator.

### **3.2.1.2 The Lattice Problem**

There is no proof that Lehmer's method will generate good (i.e. very random) pseudorandom numbers. It is in fact very easy to choose values for the three constants that will result in very bad random numbers.

Parsons (Parsons, 1995) gives the following example of a bad generator: Consider the case where  $m = 32$ ,  $a = 25$  and  $c = 7$ . This yields the following sequence: 7, 22, 13, 12, 19, 2, 25, 24, 31, 14, 5, 4, 11, 26, 17, 16, 23, 6, 29, 28, 3, 18, 9, 8, 15, 30, 21, 20, 27, 10, 1, 0, 7...

Although this sequence seems random at first glance, plotting consecutive numbers reveals a different picture:

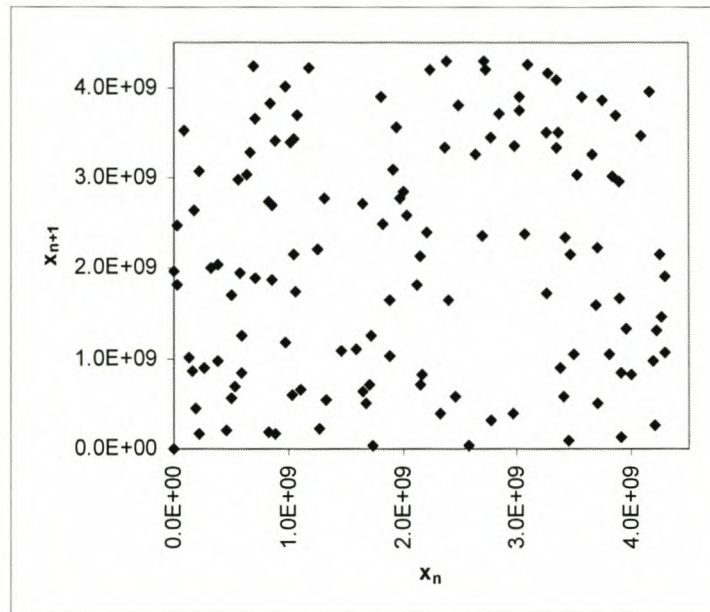


**Figure 3.1 Consecutive Random Numbers with Bad Parameters**

This so-called lattice problem occurs generally with Lehmer generators. Sets of  $k$  consecutive numbers will define points lying on a  $(k - 1)$ -dimensional hyperplane (Parsons, 1995). The generator is then said to be equidistant in  $k$  dimensions. The value of  $k$  is determined by the values of the constants  $a$ ,  $c$  and  $m$ .

The lattice problem may be solved in a somewhat roundabout way by filling a table with pseudorandom numbers before the generator is first called. When the generator is called, the seed is scaled to the length of the table to select an entry. This entry is returned as the pseudorandom number and Lehmer's method is then used to replace this number in the table.

According to Park and Miller good generator may be constructed by setting  $m = 2^{32} - 1$ ,  $a = 16,807$  and  $c = 0$  (Parsons, 1995).



**Figure 3.2 Consecutive Random Numbers with Good Parameters**

Figure 3.2 shows a plot of consecutive pseudorandom numbers when using this parameter set. Two things are immediately clear: the range of random numbers is  $[0; 2^{32} - 2]$  instead of  $[0; 31]$  as with the previous example and the distribution appears random in at least two dimensions, i.e.  $k \geq 2$ . This parameter set also produces a full-period generator.

### **3.2.1.3 Other Pseudorandom Number Generators**

Lehmer's method is popular largely due to its simplicity. Newer methods have been developed in the almost 50 years since Lehmer published his method. Much of the research in pseudorandom numbers has focussed on solving the lattice problem.

Of the pseudorandom number generators available today, the method of Matsumoto and Nishimura (MT19937 or simply the Mersenne Twister) (Matsumoto and Nishimura, 1998) is widely acclaimed to be among the best. The Mersenne Twister is equidistant in 623 dimensions and has a cycle length of  $2^{19937}-1$ !



As the mathematics involved in the Mersenne Twister algorithm can be very complicated, the entire algorithm will not be discussed. Instead, only the core of the method will be very briefly outlined. The algorithm is based on the following linear recurrence (Matsumoto and Nishimura, 1998):

### Equation 3.2

$$\mathbf{x}_{k+n} = \mathbf{x}_{k+m} \oplus \left( \mathbf{x}_k^u \mid \mathbf{x}_{k+1}^l \right) \mathbf{A} \quad (k = 0, 1, \dots)$$

With

- $n$ : The degree of recurrence
- $\mathbf{x}_k$ : The  $k$ -th pseudorandom number in the sequence
- $\mathbf{x}_k^u$ : The upper  $(w - r)$  bit vector of  $\mathbf{x}_k$
- $\mathbf{x}_k^l$ : The lower  $(r)$  bit vector of  $\mathbf{x}_k$
- $w$ : The word size for the computer
- $r$ : An integer constant such that  $0 \leq r \leq w - 1$
- $m$ : An integer constant such that  $1 \leq m \leq n$
- $\mathbf{A}$ : A  $w \times w$  matrix

The random numbers are written as vectors of bits. For example:

### Equation 3.3

$$\mathbf{x} = (x_{w-1}, x_{w-2}, \dots, x_0)$$

With

- $x_i$ : The  $i$ -th bit of  $\mathbf{x}$

With this notation the upper and lower bit vectors of  $\mathbf{x}$ ,  $\mathbf{x}^u$  and  $\mathbf{x}^l$ , are seen to be:

**Equation 3.4**

$$\mathbf{x}^u = (x_{w-1}, x_{w-2}, \dots, x_r)$$

$$\mathbf{x}^l = (x_{r-1}, x_{r-2}, \dots, x_0)$$

The matrix  $\mathbf{A}$ , is chosen for fast multiplication. The following form was selected by Matsumoto and Nishimura (Matsumoto and Nishimura, 1998).

**Equation 3.5**

$$\mathbf{A} = \begin{bmatrix} & & 1 & & & \\ & & & 1 & & \\ & & & & \ddots & \\ & & & & & 1 \\ a_{w-1} & a_{w-2} & a_{w-3} & \cdots & & a_0 \end{bmatrix}$$

With

$$\mathbf{a} = (a_{w-1}, a_{w-2}, \dots, a_0), \text{ a constant}$$

The two operators that are used in Equation 3.2 should also be explained. They are:

- $\oplus$ : 'Bitwise addition modulus two', also called the 'exclusive or' (XOR) operator in Boolean algebra.
- $|$ : A concatenation operator

The pseudorandom numbers are generated as follows:

1.  $\mathbf{x}_0, \mathbf{x}_1, \dots, \mathbf{x}_{n-1}$  are given as seeds.
2.  $\mathbf{x}_n$  is calculated using Equation 3.2 with  $k = 0$ .
3. Further pseudorandom numbers are calculated by setting  $k = 1, 2, \dots$

These pseudorandom numbers are integers. To generate floating point values in the interval  $[0, 1)$ , simply divide the values by the maximum integer that may be stored with 32 bits, i.e.  $2^{32} - 1$ .

The recommended values for the constants (Matsumoto and Nishimura, 1998) are given in Table 3.1.

**Table 3.1 Recommend Constants for MT19937 on 32-bit Processors (Matsumoto and Nishimura, 1998)**

Constant	Value
$n$	624
$m$	397
$r$	31
$a$	9908B0DF <sub>16</sub> (2567483615 in decimal notation)

The Mersenne Twister is much more complicated than Lehmer's method, but it was designed specifically with 32-bit processors in mind and as such, it is very fast indeed.

#### **3.2.1.4A Comparison of the Generators**

The discussion above outlines the criteria for a good (i.e. very random) pseudorandom number generator. Our primary concern with these generators is to find a good method that will be faster than the method used by Borland Delphi, in which the SolvGen program was written.

The built-in generator in Borland Delphi 5.01 was compared with Lehmer's method (with the parameter set used in Figure 3.2) and the Mersenne Twister. The results are listed in Table 3.2 as a percentage of the time taken by the Mersenne Twister to generate random integers.

**Table 3.2 Speed Comparison of Pseudorandom Number Generators**

Generator	Real Numbers	Integer Numbers
Delphi 5.01	138.98	100.19
Lehmer	137.82	101.44
MT19937	107.22	100.00

Although there is very little difference in the speeds of the generators for integer numbers, the Mersenne Twister is almost 40% faster when generating real numbers. This allows a substantial speed increase for the SolvGen program while at the same time decreasing the possibility that the lattice problem will cause cyclic events in the genetic algorithm.

### 3.2.2 Activity Coefficient Calculations

In order to decrease the time spent in the calculation of activity coefficients, the different calculation steps in the UNIFAC model must be considered.

#### Equation 3.6

$$\ln \gamma_i = \ln \gamma_i^C + \ln \gamma_i^R$$

$$\ln \gamma_i^C = 1 - J_i + \ln J_i - 5q_i \left( 1 - \frac{J_i}{L_i} + \ln \frac{J_i}{L_i} \right)$$

$$\ln \gamma_i^R = q_i (1 - \ln L_i) - \sum_k \left( \theta_k \frac{s_{ki}}{\eta_k} - G_{ki} \ln \frac{s_{ki}}{\eta_k} \right)$$

$$r_i = \sum_k v_k^{(i)} R_k$$

$$q_i = \sum_k v_k^{(i)} Q_k$$

$$J_i = \frac{r_i}{\sum_j x_j r_j}$$

$$L_i = \frac{q_i}{\sum_j x_j q_j}$$

$$G_{ki} = v_k^{(i)} Q_k$$

$$\theta_k = \sum_i G_{ki} x_i$$

$$s_{ki} = \sum_m G_{mi} \tau_{mk}$$

$$\eta_k = \sum_i s_{ki} x_i$$

$$\tau_{mk} = \exp \frac{-a_{mk}}{T}$$

With

- $\gamma_i$ : The activity coefficient of component  $i$
- $\gamma_i^C$ : The combinatorial contribution to the activity coefficient
- $\gamma_i^R$ : The residual contribution to the activity coefficient
- $R_k$ : The relative volume of group  $k$
- $Q_k$ : The relative area of group  $k$
- $v_k^{(i)}$ : The number of groups of type  $k$  in molecule  $i$
- $a_{mk}$ : The interaction of main group  $m$  with main group  $k$
- $T$ : The temperature

$$\left. \begin{array}{l} r_i, q_i \\ J_i, L_i \\ G_{ki}, \theta_k \\ s_{ki}, \eta_k \\ \tau_{mk} \end{array} \right\} \text{Auxiliary variables}$$

Subscript  $i$  identifies a species and subscript  $j$  is an index that runs over all species. Subscript  $k$  identifies a UNIFAC subgroup and subscript  $m$  is an index that runs over all subgroups.

The different parts of the calculations can be classified into four classes as is shown in Table 3.3

**Table 3.3 The Classification of the UNIFAC Calculation Steps**

	Calculations dependent on molar fractions	Calculations independent of molar fractions
<b>Calculations not dependent on solvent species</b>		$\left. \begin{aligned} r_i &= \sum_k v_k^{(i)} R_k \\ q_i &= \sum_k v_k^{(i)} Q_k \\ G_{ki} &= v_k^{(i)} Q_k \end{aligned} \right\} \text{for mixture components only}$
<b>Calculations dependent on all components</b>	$J_i = \frac{r_i}{\sum_j x_j r_j}$ $L_i = \frac{q_i}{\sum_j x_j q_j}$ $\theta_k = \sum_i G_{ki} x_i$ $\eta_k = \sum_i s_{ki} x_i$	$\left. \begin{aligned} r_i &= \sum_k v_k^{(i)} R_k \\ q_i &= \sum_k v_k^{(i)} Q_k \\ G_{ki} &= v_k^{(i)} Q_k \end{aligned} \right\} \text{for solvents only}$ $s_{ki} = \sum_m G_{mi} \tau_{mk}$ $\tau_{mk} = \exp \frac{-a_{mk}}{T}$

As the species in the mixture that needs to be separated stay constant throughout the evolution process, the variables that depend on the identity of these species also stay constant. These values need thus be calculated only once, instead of the 100,000 times that the relative volatility is calculated in a typical design run of 10 generations with 10,000 chromosomes. This results in a marked decrease in the time necessary to calculate the fitness of the chromosomes.

When solvents are designed for liquid-liquid extraction (chapter 2) the selectivity and recovery of the solvent is calculated with a liquid-liquid flash calculation. The flash calculation also determines whether or not two immiscible liquid phases form.

The flash calculation is an iterative process in which the compositions of the two liquid phases change in each step until convergence is reached.

As a change in composition will result in a change in activity coefficient, the UNIFAC calculations must be repeated for both liquid phases, for each iteration of the flash calculation. A typical case would require five to ten iterations for the compositions of the two liquid phases to converge to within acceptable tolerances. This implies that the UNIFAC calculations would have to be repeated 500,000 to 1,000,000 times in a ten generation run with 10,000 chromosomes! Any decrease in the time required calculating the selectivity would be greatly magnified through the number of repetitions of the calculations.

Here, it is the separation of the UNIFAC calculations into composition dependent and composition independent parts that allows the improvement in speed. The variables that do not depend on the composition need only be calculated once, at the start of the flash calculation. Only the composition dependant variables need be recalculated at every iteration.

The overall increase in speed is remarkable. To perform the flash calculation 100,000 times with these improvements takes only 19% of the time required without them!

### ***3.3 Improving Convergence***

#### **3.3.1 Gene Selection**

The original SolvGen algorithm used the Robbins chart to bias gene selection in favour of those that contain functional groups that would enhance the selectivity of the solvent.

The Robbins chart is a generalisation of a limited number of experimental observations. It shows the expected deviation from Raoult's law as either a positive or negative deviation or no deviation. The indication is purely qualitative and no indication is given as to the relative values of these

deviations. In order to use the Robbins chart to adjust the selection probability of the genes, an arbitrary increase of the selection probability must be made for every functional group in the gene that would assist the separation. Likewise, an arbitrary decrease must be made for those functional groups that would oppose the separation.

Should a gene contain a functional group that would greatly assist the separation, as well as one that would only slightly counter this effect, the gene as a whole would still assist the separation. Ideally, the selection probability of the gene should be increased. Using the Robbins chart would result in the increase in selection probability due to the first functional group being cancelled by the decrease due to the second group. Clearly, this is not the best method of biasing the selection probabilities.

To solve this problem, a quantitative method was adopted. The activities of the key mixture components are calculated for the case where no solvents are present. Each gene is then added as a solvent on its own and the effect of its presence is calculated by repeating the UNIFAC calculations. This gives a quantitative indication of the effect that this gene as a whole would have on the separation. The adjustment to the selection probability of the gene is then made proportionately to the change in the selectivity it causes. The adjustment is made according to the following formula:

**Equation 3.7**

$$SP^{new} = SP^{old} \left( \frac{\alpha_{gene}}{\alpha_{mixture}} + b \right)$$



With

$SP^{new}$ : The new selection probability

$SP^{old}$ : The old selection probability

$\alpha_{gene}$ : The relative volatility of the key components in the presence of the gene

$\alpha_{mixture}$ : The relative volatility of the key components with no solvents present

$b$ : An adjustable offset

The old selection probabilities,  $SP^{old}$ , have values of either 1 or 0, depending on whether the use of the gene is allowed in the solvent design. The offset is an adjustable value that will determine the extent to which the selection probabilities are biased. Large values of the offset will lessen the effect of the bias and vice versa.

### 3.3.2 Operator Selection

The selection probabilities for the genetic operators were optimised for a test system (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000). Although this set of parameters was found to perform well for many different systems, there can be no claim that it is the optimal set of selection probabilities for each of these systems.

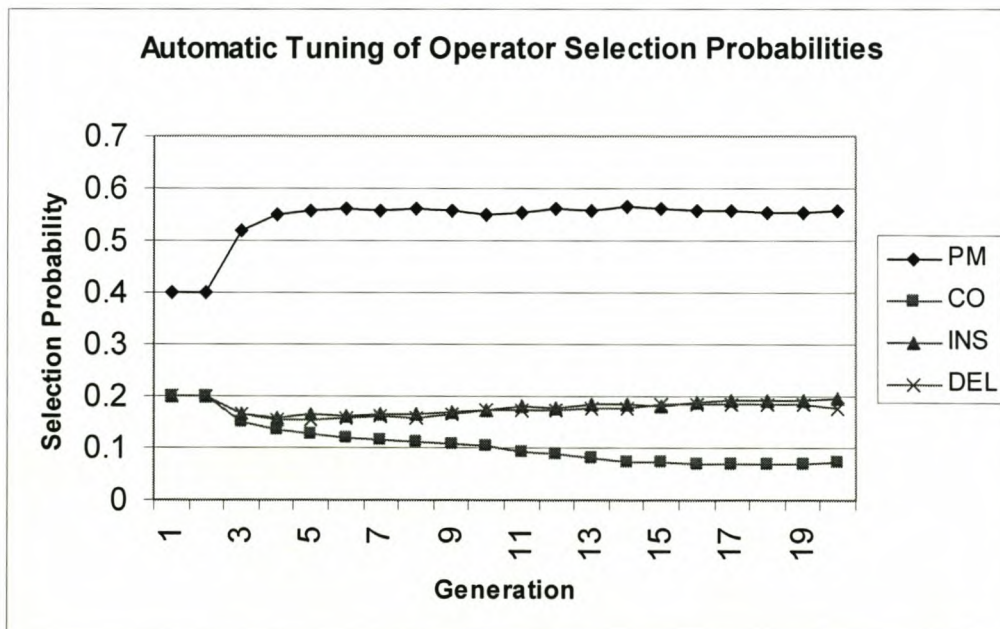
To find the optimal set of selection probabilities for all possible mixtures beforehand is impossible. However, it is possible to find the optimal set while the genetic algorithm is running. This is done through a process called automatic tuning.

Automatic tuning requires that the fitness of each new chromosome be compared with that of its parent chromosome. If the child chromosome has a higher fitness than its parent, the selection probability of the

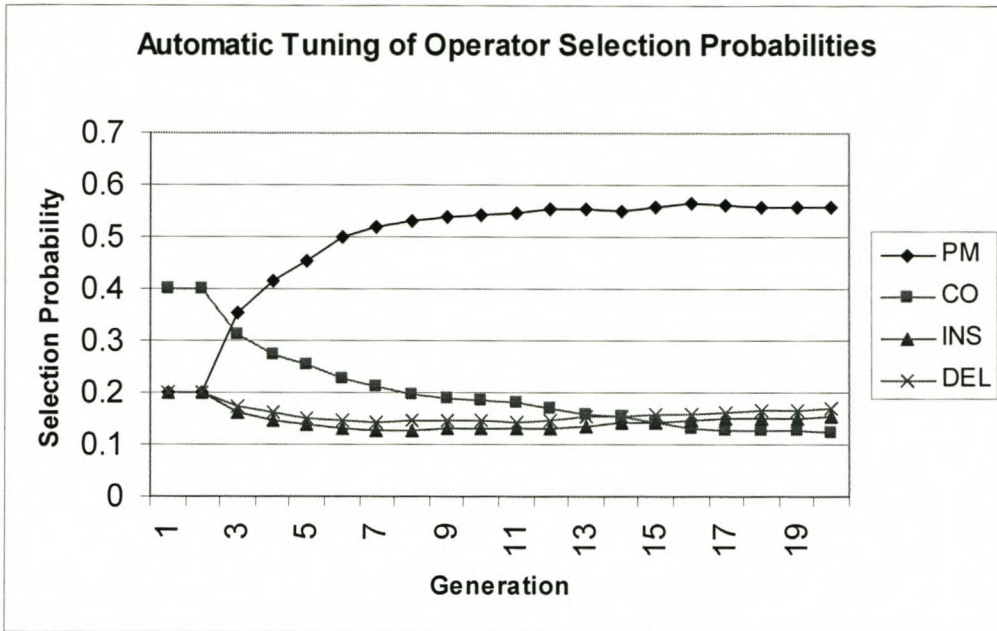
operator that created the child is increased by a small amount; if it is lower, the selection probability is decreased.

This process allows the optimal set of selection probabilities for any mixture to be found within a few generations. As the composition of the chromosome population changes, these optimal values may also change. Through automatic tuning, the genetic algorithm will continue to adapt itself to this change in the population.

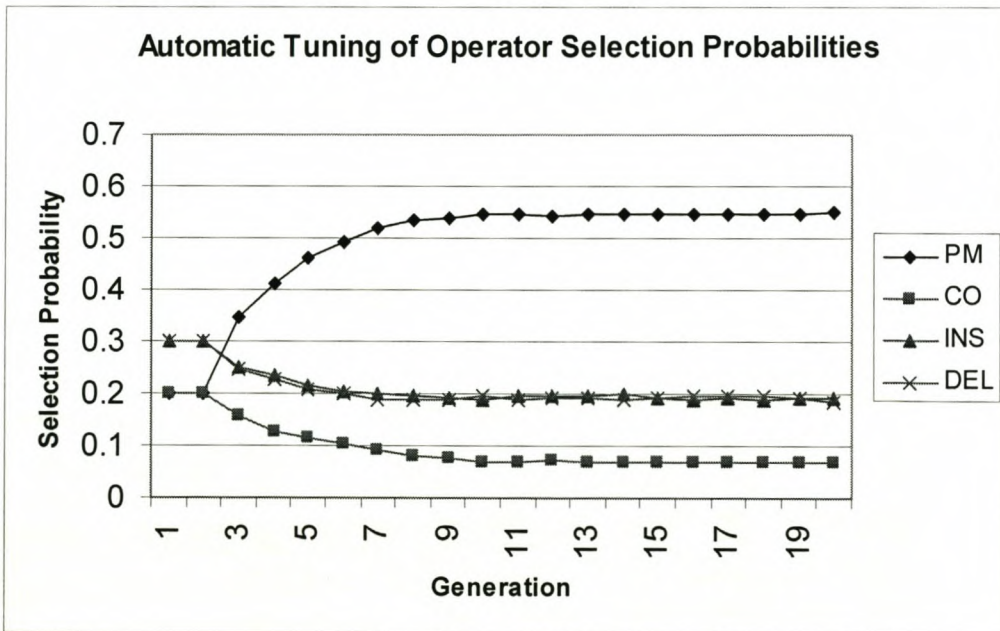
To illustrate the ability of automatic tuning to find the optimal parameter set four runs were done with the same feed composition and requirements, but with different initial values for the selection probabilities of the genetic operators. The values of these selection probabilities during each generation are shown in the following figures.



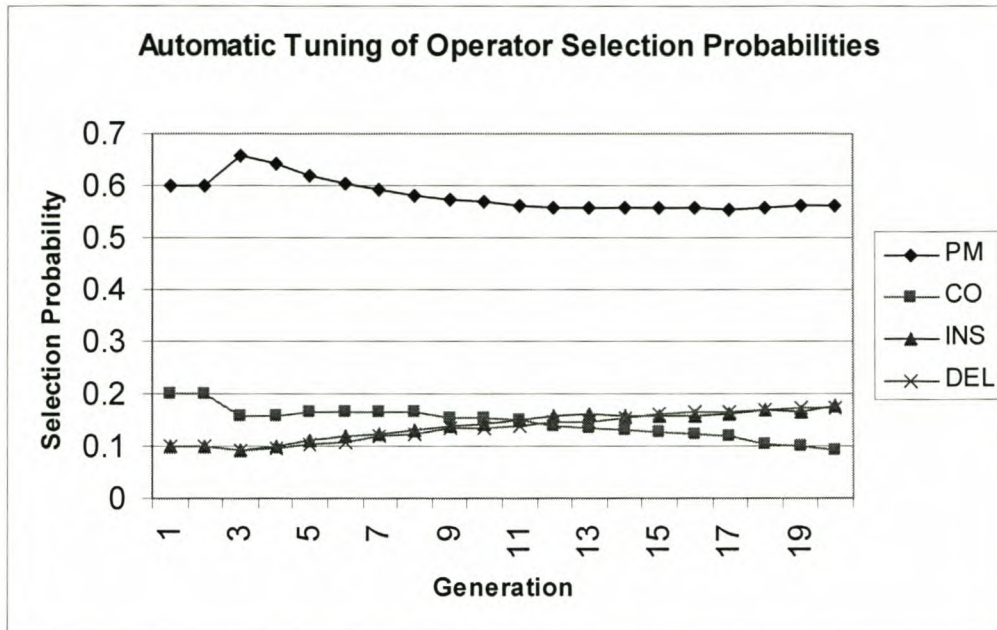
(a)



(b)



(c)



(d)

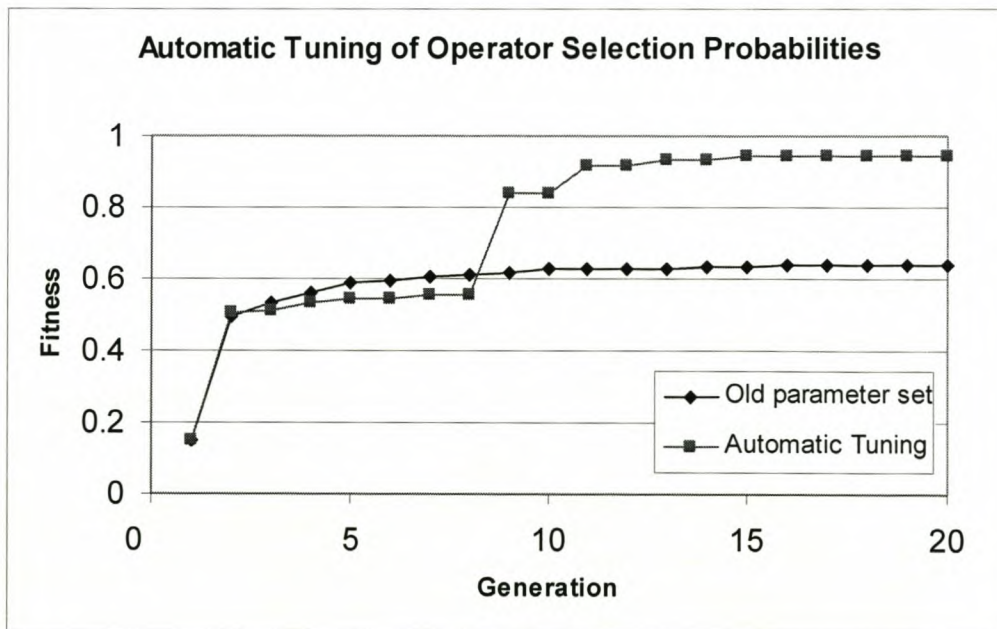
**Figure 3.3 Automatic Tuning of Operator Selection Probabilities**

As can be seen from Figure 3.3, the selection probabilities of the operators quickly converge to approximately the same values, regardless of the starting point. Automatic tuning is only started after the first two generations to allow the system to stabilize first. If this is not done, the point mutation operator will usually completely dominate the other operators. A possible reason for this phenomenon is that the mutated chromosomes of the first few generations greatly outperform those of the initial random generation. This large increase in fitness will then cause a large increase in the selection probability of the operator and a subsequent decrease in the selection probabilities of the other operators.

The effect of this automatic tuning procedure on the performance of the algorithm is illustrated in Figure 3.4. The parameter set (the operator selection probabilities) used by Van Dyk (Van Dyk, 1998) is compared to that achieved through automatic tuning. The value for the fitness of the best individual shown in this graph is the average over five runs of the program.

The old parameter set was also used as the initial values for the operator selection probabilities in Figure 3.3 (b). From Figure 3.3 (b) we can see that the values of these parameters change rapidly until the optimal values are reached after approximately ten generations.

Initially the performance of the algorithm with automatic tuning is similar to that without, as can be seen from first few points in Figure 3.4. However, once the optimal values for the operator selection probabilities have been found, there is a marked improvement in the performance of the algorithm. The rapid increase in the fitness of the best individual after the tenth generation can be attributed to the higher mutation rate achieved at this point. The optimal solvent in this case was found through mutation.



**Figure 3.4 Effect of Automatic Tuning vs. Fixed Selection Probabilities on Algorithm Performance**

### **3.4 Structural Groups and Physical Viability**

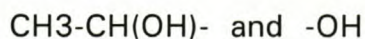
The rules for physical viability used by Gani et al were discussed in the previous chapter. These rules are aimed at producing molecules that satisfy firstly the octet rule and to lesser extent other physical considerations.

On closer study of Table 2.7, some problems become apparent. Consider for example the section dealing with aromatic compounds. In order to construct an aromatic ring at least six groups from class five are required. In all but one of the combinations for aromatic compounds in the table, a limit of five such groups is specified. This does not allow closure of the ring and so it is impossible to form viable molecules in this manner.

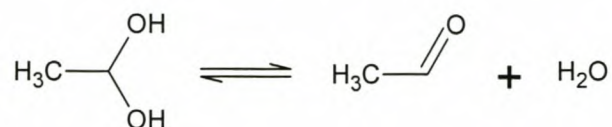
Another problem is discovered when attempting to form cyclic molecules like cyclohexane. In order to construct this molecule we would require six CH<sub>2</sub> groups. Looking at Table 2.7 we find four entries for non-aromatic compounds consisting out of six groups. The highest class of group we require is class two. Unfortunately the entry for this type of molecule limits us to only four groups from this class, making the construction of a simple molecule like cyclohexane impossible.

Clearly these are not insurmountable problems. The addition of more entries into the table would solve both these and other problems. They do however serve to illustrate the complexity of the rules that govern physical feasibility.

The problem of constructing physically viable molecules was to a large extent avoided by the use of pre-constructed genes (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000). There is however still the possibility of combining two genes that cannot form a feasible molecule. For example:



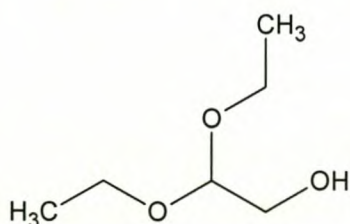
Although this combination would satisfy the octet rule, the resulting molecule would be physically unstable and decompose according to the following reaction:



Van Dyk and Nieuwoudt (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000) attempted to solve this problem by using a subset of the rules developed by Gani et al. Unfortunately the result was not satisfactory, due the problems similar to those discussed above. A more robust method is required.

The type of instability shown in the previous example is the one most often encountered when constructing molecules. It occurs when two heteroatoms (i.e. O, N and S) are bonded to the same carbon atom and at least one is also bonded to a hydrogen atom e.g. hemiacetals. Combinations like these would generally be unstable with some rare exceptions.

If neither of the two heteroatoms were bonded to hydrogen atoms, the combination would be stable. This is evident in the existence of compounds like glycolaldehyde diethyl acetal, as shown in Figure 3.5



**Figure 3.5 Glycolaldehyde Diethyl Acetal (CAS # 621-63-6)**

Another type of bond that, although may be physically viable, should be avoided is that of one heteroatom to another, e.g. peroxides. These compounds are usually highly reactive and would not normally be considered as solvents.

In order to implement this knowledge into a rule for physical viability, the genes are classified according to the atoms with free bonds. This classification is shown in Table 3.4.

**Table 3.4 Free Bond Classification**

Type	Example	Description
I	HO-	Bonding atom is a heteroatom bonded to a hydrogen atom.
II	R-O-	Bonding atom is a heteroatom bonded to a carbon atom.
III	HO-CH <sub>2</sub> -	Bonding atom is a carbon atom bonded to a heteroatom, which is in turn bonded to a hydrogen atom.
IV	R-O-CH <sub>2</sub> -	Bonding atom is a carbon atom bonded to a heteroatom, which is in turn bonded to a carbon atom.
V	R-CH <sub>2</sub>	Bonding atom is a carbon atom bonded to another carbon atom.

The allowed combinations of free bonds are summarised in Table 3.5.



**Table 3.5 Allowed Combinations of Genes**

	I	II	III	IV	V
I	×	×	×	×	✓
II	×	×	×	✓	✓
III	×	×	✓	✓	✓
IV	×	✓	✓	✓	✓
V	✓	✓	✓	✓	✓

The allowable combinations in Table 3.5 can be summarized by a single inequality:

**Equation 3.8**

$$N_5 + N_4 \geq N_2 + N_1$$

With

$N_i$ : The number of genes of type  $i$  in the chromosome

In order to eliminate structures that do not comply with these rules, the penalty system proposed by Van Dyk (Van Dyk, 1998) is used. The penalty is calculated with Equation 3.9 if the structure does not satisfy Equation 3.8.

**Equation 3.9**

$$P = P_v[(N_1 + N_2) - (N_4 + N_5)]$$

With

P: The penalty value

$P_v$ : Penalty contribution for viability test

This simple rule for physical viability, in combination with the pre-constructed genes, allows practically all physically improbable structures to be eliminated. The result is a final generation of candidate solvents that

do not only meet all the requirements in terms of physical properties, but are also physically viable molecules. The quality of the results produced by the SolvGen algorithm is greatly improved in this manner.

### **3.5 Boiling Point Estimations**

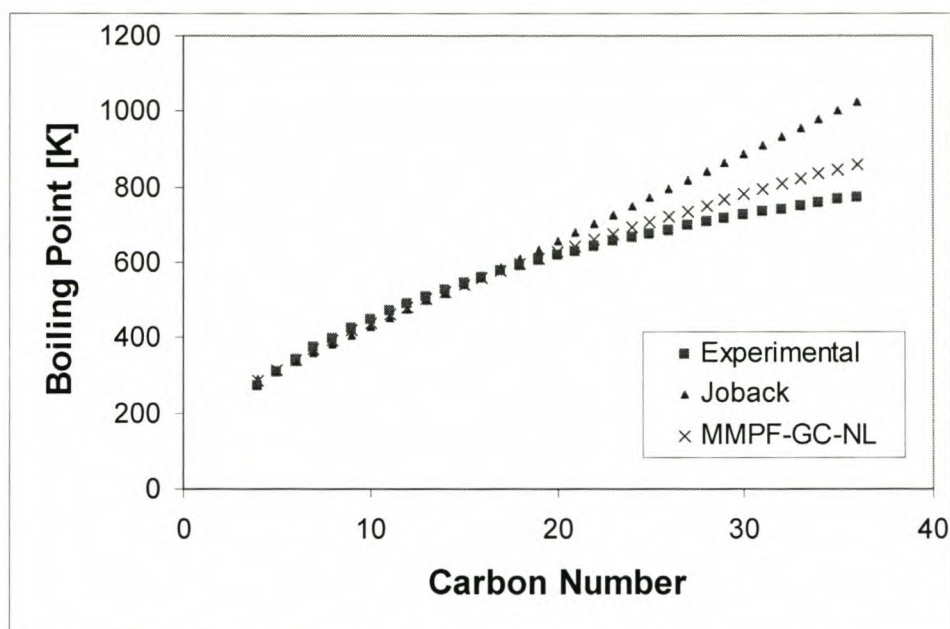
Regardless of the algorithm used to construct molecules, all CAMD methods are completely dependant on the accuracy of the group contribution methods that they employ. If these methods are inaccurate, the CAMD algorithm will produce poor results. In order to increase the reliability of the SolvGen algorithm, the group contribution methods employed by it were investigated.

The boiling point is arguably the most important of the pure component properties used in the design of solvents. Not only does the value of the boiling point help determine whether the solvent is in the correct phase for the separation process, but it is also used to estimate other properties like the vapour pressure and critical temperature.

The method proposed by Joback (Joback and Reid, 1987) is a linear additive method. This linearity is the main cause of inaccuracy, especially when estimating the boiling point of larger molecules. Figure 3.6 shows the estimated boiling points of a number of normal alkanes as well as the experimentally determined values.

The measured data points were extracted from the databank of the Pro/II simulation package produced by SIMSCI. The databank list two references for this data, (API-44, 1948) and (Weast and Astle, 1985). The experimental boiling points beyond tetracosane (C<sub>24</sub>) should be regarded with caution, as decomposition will set in when the normal boiling points of these substances are determined. It is suspected that these data points

may be extrapolations. They are given here only to show the continuing trend in the data.



**Figure 3.6 Comparison of Group Contribution Methods for n-Alkanes**

Clearly, the experimental values do not follow a linear trend. The contribution of each successive methylene group is smaller than that of the preceding methylene group.

Although Joback's method has an acceptable accuracy for low molecular weight compounds, the solvents used in extractive distillation are typically high boiling with relatively high molecular weights. It is precisely for this type of molecule that the inaccuracies in Joback's method are large.

Of the available estimation methods (Lai et al, 1987; Constantinou and Gani, 1994; Simamora and Yalkowsky, 1994; Stein and Brown, 1994; Yalkowsky et al, 1994; Tsibanogiannis et al, 1995; Hall and Story, 1996; Katritzky et al, 1998; Goll and Jurs, 1999; Iwai et al, 1999; Marrero-Morejón and Pardillo-Fontdevila, 1999; Marrero and Gani, 2000; Stanton, 2000), the methods of Marrero-Morejón and Pardillo-Fontdevila (Marrero-

Morejón and Pardillo-Fontdevila, 1999) are of most interest. It is generally applicable (the same sub-molecular groups as in Joback's method are used) and the parameters were fitted to a large database.

These authors developed four different methods for the estimation of boiling points. These methods are:

1. Linear group contribution (MMPF-GC-L)
2. Non-linear group contribution (MMPF-GC-NL)
3. Linear group interaction (MMPF-GI-L)
4. Non-linear group interaction (MMPF-GI-NL)

The functional forms of these models are as follows:

### Equation 3.10

$$\text{Non-linear form} \quad T_b = M^a \sum + b$$

$$\text{Linear form} \quad T_b = a + \sum$$

With

$T_b$ : The boiling point

$M$ : The molar mass of the substance

$a, b$ : Constants

$\sum$ : The total contribution of all the groups (or interactions) in the molecule

It can be seen that the linear methods use the same functional form as Joback and as such will suffer from the same weaknesses. The non-linear methods give significantly better results for small as well as large molecules.

The group-contribution methods are considerably easier to implement than the group interaction methods, without a significant difference in

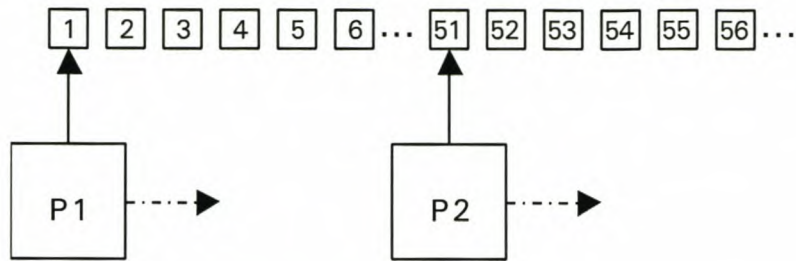
accuracy. These considerations led to the decision to use the second method, i.e. the non-linear group contribution method.

The normal alkane boiling points as estimated using the MMPF-GC-NL method are also shown in Figure 3.6. The error in estimation with this method is clearly much smaller than with Joback's method. For the data points that may be regarded as trustworthy (up to and including tetracosane), there is very good correlation between the predicted and measured values.

For the other pure component properties, e.g. freezing point, no generally applicable methods that are significantly more accurate could be found. This does not represent a great problem, as the importance of these properties is much less than that of the boiling point. To compensate for inaccurate estimations, the weight associated with a specific property may be decreased to lessen its effect on the fitness of the molecules. Should these properties become more important, better methods would have to be found or developed.

### ***3.6 Multi-Processor Architectures***

The current trend towards multi-processor desktop computers may readily be taken advantage of. In order to harness the power of multiple processors, the calculations must be broken up into independent parts that may be done in parallel. As the calculation of the various properties of a chromosome is independent of that of any other chromosome, these calculations are easily divided among the processors. Figure 3.7 shows the case of 100 chromosomes and two processors. Each processor does all of the calculations for one half of the population. This effectively doubles the speed in which the calculations are done.



**Figure 3.7 Making use of Multiple Processors**

The parallel nature of a genetic algorithm makes it very easy to make use of multi-processor architectures. This may not be the case in other CAMD methods. In the mathematical programming methods, for example, most of the calculations must necessarily be sequential. In this case, only limited use can be made of a second processor.

The ability to effectively make use of multi-processor architectures is of increasing importance. While dual processor desktop computers are no longer a rarity, many workstations today have four or more processors. New technology such as Beowulf clusters (commonly implemented on free operating systems like Linux and FreeBSD) gives researchers the ability to build massively parallel computers from standard desktop PC's, at a fraction of the price of large mainframes.

All of this points to a strong future trend towards parallel computing in all aspects of engineering calculations.

### ***3.7 Liquid-Liquid Extraction***

The possibility of extending the SolvGen algorithm to liquid-liquid extraction was discussed by Van Dyk (Van Dyk, 1998). The proposed method was implemented and found to be very computationally intensive.

### 3.7.1 A Faster Flash Algorithm for Liquid-Liquid Extraction

The flash algorithm used in this method calculated the compositions and phase ratios for three phases in equilibrium – two liquid phases and one vapour phase.

A critical evaluation of the algorithm was done and it was found that the three-phase flash algorithm could be replaced by a significantly faster method. The existence of a liquid phase split is the primary concern when designing solvents for liquid-liquid extraction. While the composition of the vapour phase is not necessary for liquid-liquid extraction calculations, it is extremely important for extractive and azeotropic distillation calculations. In order to keep the flash procedure general, the vapour phase composition must also be calculated.

Instead of doing the computationally expensive three-phase flash, a simple liquid-liquid equilibrium calculation may be done to determine whether two liquid phases form. Once the number and compositions of the liquid phases have been determined, finding the composition of the vapour phase becomes a trivial calculation if it is assumed that the system is at its bubble point pressure. As the liquid phases are in equilibrium with each other, it does not matter which of the two liquid phases is used to determine the vapour phase's composition.

The flash calculations are done as follows:

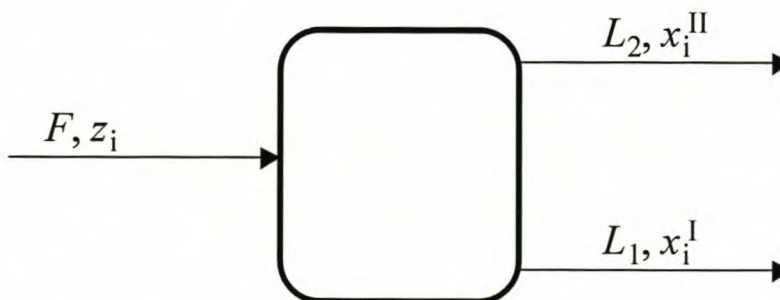


Figure 3.8 The Liquid-Liquid Flash

Consider the system in Figure 3.8. A feed stream with flow rate  $F$  and molar fractions  $z_i$ , separates into two liquid phases with flow rates  $L_1$  and  $L_2$  and molar fractions  $x_i^I$  and  $x_i^{II}$ , respectively. This takes place at a constant temperature.

The equilibrium relationship between these phases can be expressed with

**Equation 3.11**

$$x_i^{II} = K_i x_i^I$$

With

$K_i$ : The equilibrium constant for species  $i$

The equilibrium constants may be calculated with any suitable thermodynamic model, e.g. UNIFAC.

We also define a phase ratio:

**Equation 3.12**

$$\beta \equiv \frac{L_2}{F}$$

A total mass balance and a species mass balance are now combined with the fact that molar fractions sum to unity:

*Total mass balance:*

**Equation 3.13**

$$F = L_1 + L_2$$



*Species mass balance:*

**Equation 3.14**

$$z_i F = x_i^I L_1 + x_i^{II} L_2$$

Thus:

**Equation 3.15**

$$\begin{aligned} z_i &= x_i^I (1 - \beta) + x_i^{II} \beta \\ &= x_i^I [1 - \beta + K_i \beta] \\ x_i^I &= \frac{z_i}{\beta(K_i - 1) + 1} \end{aligned}$$

*The summation requirement*

**Equation 3.16**

$$\sum_i (x_i^{II} - x_i^I) = 0$$

Combining Equation 3.15 with Equation 3.16 gives:

**Equation 3.17**

$$\sum_i \frac{z_i (K_i - 1)}{\beta(K_i - 1) + 1} = 0$$

The following algorithm is used to solve these equations:

1. Estimate values for  $K_i$  and  $\beta$ .
2. For each species, calculate  $x_i$  with Equation 3.15.
3. Use these molar fractions and the thermodynamic model to calculate new values for  $K_i$ .
4. Calculate a new  $\beta$  from Equation 3.17.
5. Repeat steps 2 to 4 until convergence is reached.

To estimate the vapour compositions, first calculate the total pressure with Equation 3.18.

### Equation 3.18

$$P = \sum_i \gamma_i^l x_i^l P_i^{sat} = \sum_i \gamma_i^{II} x_i^{II} P_i^{sat}$$

The vapour phase compositions may then be calculated with Equation 3.19.

### Equation 3.19

$$y_i = \frac{\gamma_i^l x_i^l P_i^{sat}}{P} = \frac{\gamma_i^{II} x_i^{II} P_i^{sat}}{P}$$

The method described here works on the assumption that two liquid phases form. If the phase ratio is determined to be either zero or unity, or the phases are identical, it is clear that only one liquid phase did form.

Methods have also been proposed by various authors (Nelson, 1987; Bunz et al, 1991; Eckert and Kubicek, 1993; Eckert and Kubicek, 1995) that determine the number of liquid phases during the flash calculation. The structure of the calculations is then modified to take advantage of this knowledge. We will discuss the method proposed by Eckert and Kubicek for bubble point calculations.

Eckert and Kubicek write the equilibrium relationship for  $p$  liquid phases and a vapour phase as follows:

*Vapour-Liquid Equilibria***Equation 3.20**

$$0 = y_i - K_i^{(r)} x_i^{(r)} \quad \forall i = 1 \text{ to } n$$

*Liquid-Liquid Equilibria***Equation 3.21**

$$0 = K_i^{(r)} x_i^{(r)} - K_i^{(j)} x_i^{(j)} \quad \forall i = 1 \text{ to } n, j = 1 \text{ to } p, j \neq r$$

With

- $K_i^{(j)}$ : The equilibrium coefficient for component  $i$  in liquid phase  $j$   
 $r$ : The index of the reference liquid phase (arbitrarily chosen)  
 $n$ : The number of components

The summation equations for the liquid phases are:

**Equation 3.22**

$$0 = 1 - \sum_i x_i^{(j)} \quad \forall j = 1 \text{ to } p \quad (\text{a})$$

or

$$0 = \beta^{(j)} \quad (\text{b})$$

With

- $\beta^{(j)}$ : The phase ratio of liquid phase  $j$ , calculated with Equation 3.23

**Equation 3.23**

$$\beta^{(j)} = \frac{L^{(j)}}{F}$$

With

- $L^{(j)}$ : The molar amount of liquid  $i$   
 $F$ : The molar amount of the feed stream

Equation 3.22 (b) is used in cases where the liquid phase  $j$  is known not to exist.

The summation equation for the vapour phase is:

**Equation 3.24**

$$0 = 1 - \sum_y y_i$$

Furthermore, the liquid compositions at the bubble point can be related to the feed composition by:

**Equation 3.25**

$$0 = z_i - \sum_j \beta^{(j)} x_i^{(j)}$$

This gives a system of  $(n + 1)(p + 1)$  equations and variables that must be solved for the pressure, the vapour molar fractions and the molar fractions and phase ratio for each liquid phase (Eckert and Kubicek, 1995).

These equations are solved simultaneously with an iterative method like that of Newton. After every two to three iterations, a correction is done on the number of liquid phases according to the decision diagram in Table 3.6, for one or two liquid phases.

The decision diagram shows conditions for switches from one to two liquid phases and vice versa. Typically, the number of liquid phases is initially assumed to be the maximum possible (Eckert and Kubicek, 1995) and only switches to a lower number of liquid phases should it be necessary.

**Table 3.6 Decision Diagram for Multi-phase Flash (Eckert and Kubicek, 1995)**

From Case	To Case		
	G - L1	G - L2	G - L1 - L2
G - L1	-		$\sum_i x_i^{(2)} \geq 0.99999$ $\mathbf{x}^{(1)} \neq \mathbf{x}^{(2)}$
G - L2		-	$\sum_i x_i^{(1)} \geq 0.99999$ $\mathbf{x}^{(1)} \neq \mathbf{x}^{(2)}$
G - L1 - L2	$\beta^{(2)} \leq 0$ or $\mathbf{x}^{(1)} = \mathbf{x}^{(2)}$	$\beta^{(1)} \leq 0$	-

$\mathbf{x}^{(j)}$  is the vector of molar fractions in liquid phase j

If it is determined that a liquid phase does not exist, the summation equation for that liquid phase changes from Equation 3.22 (a) to (b). The number of unknowns may then be adjusted and the molar fractions for the non-existing liquid are zeroed. If only one liquid phase remains, the bubble point flash becomes a trivial problem and the answer is directly calculated from Equation 3.20 and Equation 3.25. This could result in a considerable saving in computation time for cases where only one liquid phase forms.

The method of Eckert and Kubicek, like that of Nelson and of Bünz et al, uses Newton's method or similar methods for solving simultaneous non-linear equations. This requires that the Jacobian of the system be calculated at every iteration. The speed of the method can be increased by using quasi-Newton methods like that of Broyden, where the Jacobian need not be calculated as often. This still results in a considerable computational overhead. For systems where two liquid phases do form, these methods actually take longer to execute than the direct two-liquid

flash discussed above. As most of the systems in the latter stages of a liquid-liquid extraction solvent design do give two liquid phases, it was decided to use the direct two-liquid method instead of the adaptive simultaneous method, as it would be slightly more efficient.

### **3.7.2 Solvent and Solute Recoveries**

It is not only the selectivity of a solvent that is important, but also its capacity. If the solvent has a low capacity for the solute, a large solvent to feed ratio will be required to recover acceptable amounts of the valuable solute. It is also important that the solvent be as immiscible as possible with the anti-solvent phase. Should significant amounts of solvent dissolve into the anti-solvent phase, this solvent would have to be either recovered or replaced. Neither option is economically attractive. We would therefore like a solvent with not only a high selectivity, but also high recoveries of both the solute and the solvent itself in the solvent phase.

To ensure high solvent and solute recoveries, a penalty function was introduced. The solvent phase is identified as the liquid phase with the highest molar fraction solvent. The percentage of the solvent feed that is recovered in this phase is then determined. If this recovery is less than the required value, a penalty is applied to the fitness of the chromosome.

Similarly, the percentage recoveries of the specified solutes in the solvent phase are determined. Penalties may be applied if these recoveries are either above or below a required value, as determined by the process.

### **3.8 Conclusions**

The modifications to the SolvGen algorithm discussed in this chapter were mostly incremental improvements, aimed at increasing speed and the accuracy of the estimated properties. These improvements, although important in their own right, do not touch on the principal concern – applying the method to more diverse problems of industrial importance.

In the following chapters, the basic algorithm will be extended from the design of simple solvents for extractive distillation to also include blended solvents. The method will also be applied to various other solvent-based separation methods like azeotropic distillation and chromatographic separation.



## 4 Blended Solvents

### *4.1 Introduction*

Case studies in solvent design for extractive distillation (Van Dyk, 1998) have shown that the best solvents for certain separations are sometimes very complex molecules. The complexity of these molecular structures will increase the difficulty of synthesising them and may dramatically increase the cost of these solvents.

The solvent should be seen as a capital expense, the cost of which is countered by the savings due to the smaller columns that can be used to attain a given product purity. However, the overall economic potential of the separation process could be further improved if a simpler, less expensive solvent could be found.

The primary factor that complicates the molecular structure of designer solvents is the number of functional groups that have to be present in order to achieve the required selectivity. If these functional groups could be spread over a number of structural backbones, the complexity of the molecules would be greatly reduced and so should their cost.



As discussed in Chapter 2, some of the existing CAMD algorithms may produce blended solvents instead of the customary single solvent. This will happen when the second part of the algorithm is unable to assemble the functional groups returned by the first part into a single structure.

Unfortunately, the first part of these algorithms works under the assumption that all of the functional groups returned will form part of a single molecule. The group contribution methods are then used to test this hypothetical structure against the property requirements. Should the functional groups be divided into several molecules, properties such as boiling and freezing points or recovery of the solvent will change and may no longer meet the requirements.

In order to overcome this problem, it is necessary to modify the algorithm so that it will design for multiple backbones from the very start.

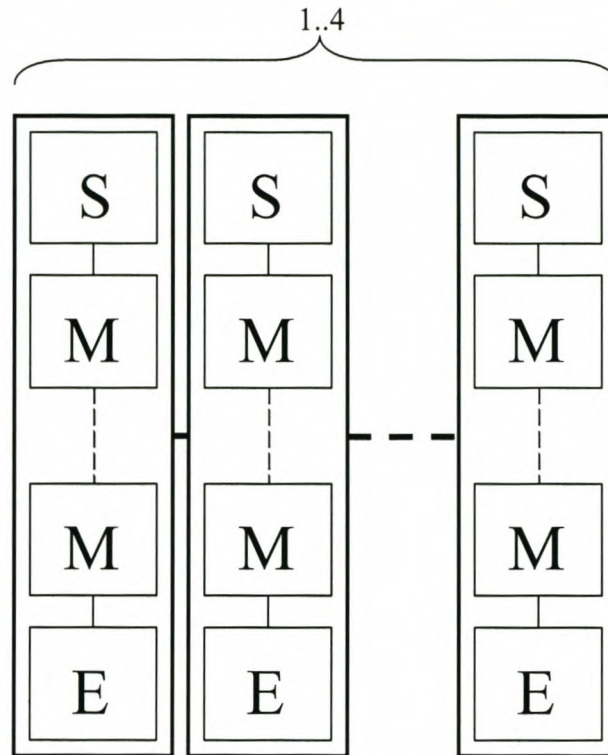
## ***4.2 Extension of the SolvGen Algorithm***

### **4.2.1 Encoding Scheme**

In order to extend the SolvGen algorithm to design blended solvents; new data structures are required. There are a number of requirements for these data structures:

- Like the chromosomes used for single solvent designs, these data structures must be linear in order to be compatible with the genetic operators.
- Each data structure must be able to contain a number of complete molecules.
- It must be possible to evolve the individual molecules, as well as the group as a whole.

A structure that will satisfy all of these requirements is depicted in Figure 4.1.



**Figure 4.1 A Superchromosome**

The superchromosome is similar to the chromosomes used in single solvent design. Instead of being constructed from genes, the superchromosome is constructed from supergenes. Each supergene is in fact a chromosome in itself.

The number of supergenes is allowed to vary between one and a specified maximum. In this study the maximum number of supergenes was arbitrarily set to four. The composition of the blended solvent is taken to be equal parts of each of the individual solvents in the blend. This means that the concentrations of the solvents in the blend may be established in discrete intervals.

## 4.2.2 Reproduction Scheme

In order to satisfy the third requirement above (section 4.2.1), that the blend as a whole, as well as the individual solvents, must be able to evolve, new operators must be defined that operate directly on the superchromosomes. The existing operators (point mutation, crossover, insertion and deletion) will act upon the supergenes/chromosomes that comprise the superchromosome.

These new operators are listed in Table 4.1, along with the normal genetic operators used in the single solvent version of SolvGen.

**Table 4.1 Genetic Operators**

<b>Single Solvent Operator</b>	<b>Description</b>	<b>Blended Solvent Operator</b>	<b>Description</b>
Insertion	Insert a random gene into the chromosome.	Super Insertion	Insert a complete molecule, selected from the entire population of existing molecules, into the superchromosome.
Deletion	Delete a random gene from the chromosome.	Super Deletion	Delete a random molecule from the superchromosome.
Point Mutation	Replace a gene in the chromosome with a randomly selected gene from the pool of available genes.	Super Point Mutation	Replace a complete molecule in the superchromosome with one selected from the entire population of existing molecules.
Crossover	Recombine two parent chromosomes to create two new chromosomes. Each new chromosome consists of half of each parent.	Super Crossover	Recombine two parent superchromosomes to create two new superchromosomes. Each new superchromosome consists of half of each parent.

The selection of operators is done using the same Roulette Wheel method as in the single solvent version of the SolvGen Algorithm (Van Dyk,

1998). The principal change in the algorithm from single to multiple solvents is the initialisation of the first generation of superchromosomes.

Simply initialising four random chromosomes in each superchromosome yielded very poor results. The algorithm repeatedly failed to find solvents that meet the requirements within a reasonable number of generations. This is understandable, as the search space has increased by a power of four, while the number of individuals in the population stayed constant.

Increasing the size of the population to solve this problem is not desirable, as this will slow down the search in direct proportion to the number of extra individuals.

Two different algorithms were implemented in an attempt to solve the problem of initialisation. These are the group assembly and the symbiosis methods.

#### ***4.2.2.1 Group Assembly***

The group assembly method is comprised of two stages. In the first stage a collection of genes is assembled that will result in the required selectivity for the key components in the mixture that is to be separated. In this stage the fitness function of the genetic algorithm is modified so that only selectivity is taken into account. The normal penalty for missing interaction parameters is also included.

Once this set of genes has been found, the genes must be assembled into molecules during the second stage. This places a constraint on the composition of the groups of genes in that there must be an even number of start/end genes in order to satisfy the octet rule during the second stage.

The assembly of the genes into molecules is done by running the genetic algorithm for a second cycle. The genes that must be included in the superchromosome are fixed and thus the only operator that is used is the crossover operator. Crossovers are only allowed between molecules in the same superchromosome. This fixes the genes within a superchromosome and so the selectivity remains constant.

The molecules that are constructed during the second phase must individually fulfil each of the requirements for boiling point, freezing point and physical viability. The mixture must give a liquid-liquid phase split if one is desired and must match the desired recoveries.

These properties depend on the molecular species present in the system and cannot be calculated using a 'solution of groups' approach such as that of UNIFAC. The program is allowed to vary the number of solvents in the blend up to a specified maximum. The number of start/end genes in the collection will determine the minimum number of solvents; the rest will by necessity be cyclic.

This method closely resembles the methods discussed in chapter 1, in the case where it is not possible to construct a single molecule. The problems mentioned in section 4.1 are as valid for this method as for the previous methods.

As the first stage of the method is not concerned with the molecular properties (boiling point, freezing point, recovery etc.), it may result in a selection of genes that cannot be assembled into molecules with the required properties, e.g. a liquid-liquid phase split. In this case, the group assembly method will fail.

#### **4.2.2.2 Symbiosis**

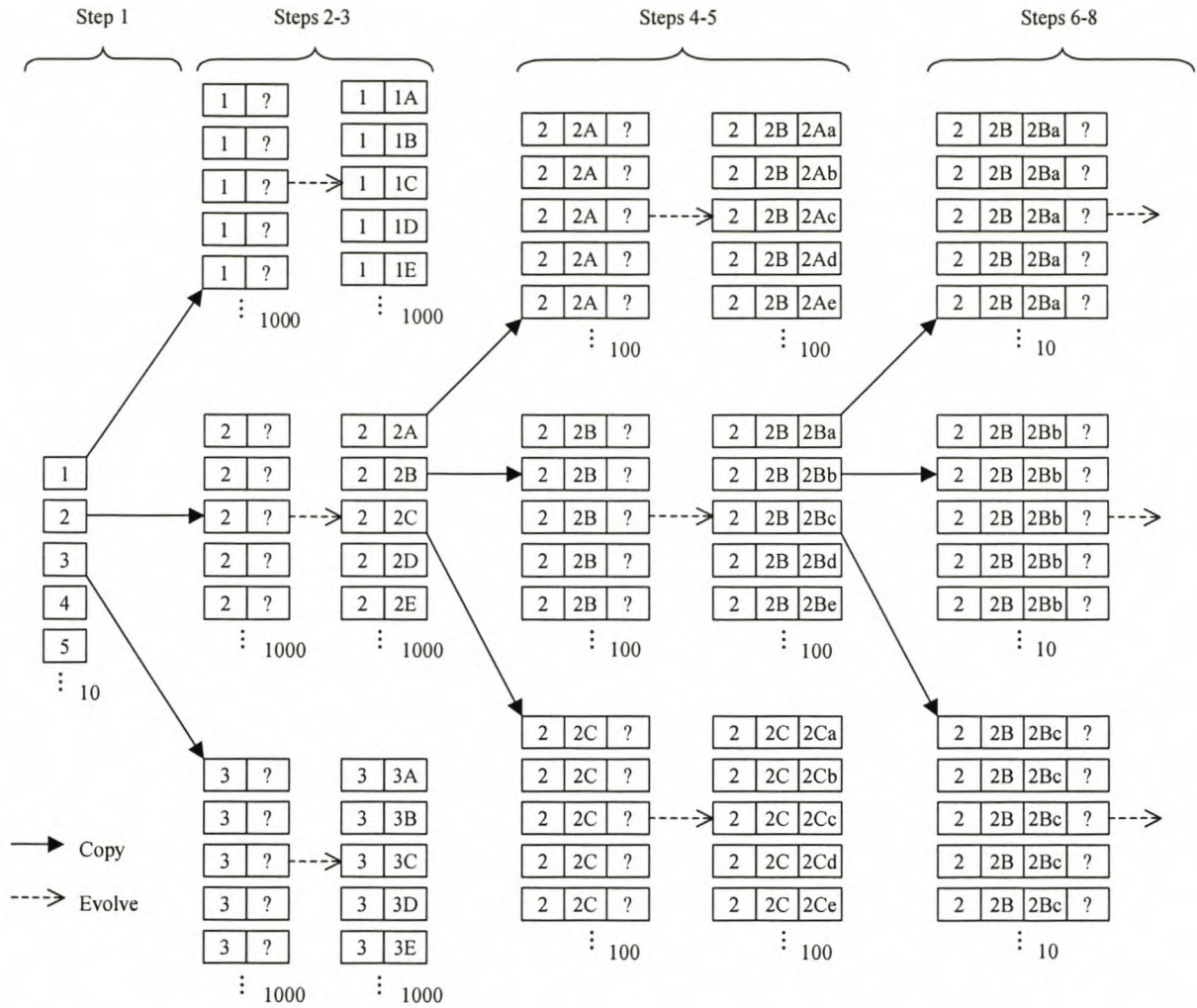
The symbiosis method was designed to overcome the failings of the group assembly method. The individual chromosomes within a superchromosome are evolved as complete molecules from the very first step. Each of these molecules is measured against all of the molecular property requirements (boiling points etc.) while the superchromosome as a whole is measured against the selectivity requirement (and phase split, if required).

Like the group assembly method, the symbiosis method also comprises of two parts: the initialisation stage and the evolution stage. The initialisation stage starts with each superchromosome being initialised to a single random molecule. A number of generations are then allowed for these solvents to evolve.

Molecules are then added one at a time and also allowed a number of generations to evolve until the maximum number of molecules in a blend has been reached. The components that are already present in the blend are kept fixed during these generations. This allows each new solvent that is added to evolve to a structure that will aid the solvents already present. In this stage only the single solvent genetic operators are used.

In the second phase, all the solvents in the blend are allowed to evolve and the entire set of genetic operators listed in Table 4.1 are used.

The method is best explained via an example. Consider the case where a maximum of four solvents is allowed in the blend. The total population size is 10,000 superchromosomes. The process is diagrammatically depicted in Figure 4.2.



**Figure 4.2 The Symbiosis Method**

### Initialisation Stage

#### Step 1

A single solvent design is run for a specified number of generations. Upon completion, the 10 best unique solvents from the population of 10,000 are selected.

#### Step 2

Copies of the solvents selected in step 1 are paired up with 1000 new, randomly generated solvents each. This results in a population of 10,000 binary mixtures in 10 groups of 1000 each. Every individual in a specific group has the same first solvent.

### *Step 3*

The first solvent in each of the mixtures created in step 2 is kept fixed while the second solvents are allowed to evolve for a number of generations. Upon completion, the ten best unique mixtures from each of the ten groups created in step 2 are selected.

### *Step 4*

Copies of the binary mixtures selected in step 3 are now combined with 100 randomly generated solvents each. This results in a population of 10,000 ternary mixtures in 100 groups of 100 each. Each member of a specific group has the same first and second solvents.

### *Step 5*

The first and second solvents in each mixture are kept fixed while the third solvents are allowed to evolve. Upon completion, the ten best unique mixtures from each of the 100 groups created in step 4 are selected.

### *Step 6*

Copies of the ternary mixtures selected in step 5 are combined with 10 randomly generated solvents each. This results in a population of 10,000 quaternary mixtures, divided into 1000 groups of ten each. Each member of a group has the same first, second and third solvents.

### *Step 7*

The first three solvents in each blend are kept fixed while the newly added fourth solvents are allowed to evolve for a number of generations.

## **Evolution Stage**

### *Step 8*

After completion of step 7 above, all of the solvents in each blend are allowed to evolve freely. All of the operators in Table 1 are used and so



the number of solvents in each blend may vary due to the super insert and super delete operations.

As the symbiosis method works with complete molecules, the fitness is always measured against all of the required properties. This avoids the problems encountered in the second stage of the group assembly method.

### **4.2.3 Evaluation Scheme**

As mentioned in the previous section, each molecule in the blend must meet the requirements for the boiling point and freezing point. The blend as a whole must meet the requirement for selectivity and recovery (and phase split, if required).

The fitness of the blend is calculated using the sigmoidal property fitness functions proposed by Van Dyk (Van Dyk, 1998). The weighted sum of these property fitness values is then assigned to the superchromosome. For properties like boiling and freezing points, the property fitness of the blend is taken to be the average of the individual property fitness values of the molecules in the blend.

The solvent recovery is calculated for the blend as a whole. This implies that the different components of the solvent blend are treated as a single species to calculate the total molar recovery of the blend. This method works well in the single stage calculations that are used to rate the candidate solvents, but care should be taken that the composition of the blend does not alter over the multiple stages of a real separation process. Whether such a separation occurs can only be determined through a multi-stage calculation and is best done during the simulation stage of the design process. Although such a multi-stage calculation could be incorporated into the molecular design algorithm, its computational cost would be prohibitive.

### **4.3 Conclusions**

The ability to design blended solvents gives the engineer much more flexibility in designing a separation process. Optimal selectivity may be achieved without the added cost of a complicated, difficult to synthesise solvent. The symbiosis method can also be combined with the seeding method discussed in (Van Dyk, 1998) to make use of co-solvent and/or anti-solvent effects in liquid-liquid extraction.

# 5

## **5 Entrainers for Heterogeneous Azeotropic Distillation**

### ***5.1 Introduction***

Many azeotropic mixtures of industrial importance are separated through heterogeneous azeotropic distillation (Widagdo and Seider, 1996). An important example of this type of process is the dehydration of alcohols, most notably ethanol, (through addition of benzene) and isopropanol (through the addition of isopropyl ether). Other separations include the dehydration of chloroform through addition of mesityl oxide and the dehydration of formic and acetic acids through the addition of toluene. The possibility of improving such processes through the design of improved entrainers is very enticing.

In order to understand the properties that such an entrainer must possess, a study of the phenomenon of azeotropism is required.

## 5.2 Azeotropism

At low to moderate pressures, the relationship between the compositions of a liquid and a vapour phase in equilibrium can be expressed by Equation 5.1.

### Equation 5.1

$$y_i P = \gamma_i x_i P_i^{sat}$$

With

- $y_i$ : The molar fraction of component  $i$  in the vapour
- $x_i$ : The molar fraction of component  $i$  in the liquid
- $\gamma_i$ : The activity coefficient of component  $i$
- $P$ : The total pressure
- $P_i^{sat}$ : The vapour pressure of component  $i$

In the case of an ideal system, the activity coefficient,  $\gamma$ , is equal to unity and Equation 5.1 reduces to Raoult's Law. For values of  $\gamma > 1$ , the system is said to exhibit a positive deviation from Raoult's Law and for values of  $\gamma < 1$ , a negative deviation.

In certain cases this deviation may be large enough that the system exhibits extrema on its temperature-composition and pressure-composition phase diagrams. These maxima and minima are called constant boiling mixtures, or azeotropes, because the liquid and vapour compositions at these points are identical (Seader et al, 1997). At this point, the relative volatility, as defined by Equation 5.2 becomes equal to unity and separation of the mixture through simple distillation is impossible.

### Equation 5.2

$$\alpha_{ij} = \frac{y_i/x_i}{y_j/x_j}$$

With

$\alpha_{ij}$ : The relative volatility of components i and j

The formation of azeotropes is not limited to highly non-ideal mixtures. By substituting Equation 5.1 into Equation 5.2 the following relationship is found:

### Equation 5.3

$$\alpha_{ij} = \frac{y_i/x_i}{y_j/x_j} = \frac{\gamma_i P_i^{sat}}{\gamma_j P_j^{sat}}$$

The relative volatility will equal unity when the ratio of activity coefficients,  $\gamma_i / \gamma_j$  equals the ratio of vapour pressures  $P_j^{sat} / P_i^{sat}$ . In the case of an ideal mixture, the activity coefficients are equal to unity and an azeotrope will be formed whenever the vapour pressures of the two components are equal. This is a so-called Bancroft point (Gmehling et al, 1994).

From the above equations it can be seen that azeotropes may be observed in homogeneous binary systems when one of the following conditions are met (Gmehling et al, 1994):

1. For a positive deviation from Raoult's Law (Pressure maximum azeotropes):

$$\ln \gamma_2^\infty > \ln \left( \frac{P_1^{sat}}{P_2^{sat}} \right) > -\ln \gamma_1^\infty$$

2. For a negative deviation from Raoult's Law (Pressure minimum azeotropes):

$$\ln \gamma_2^\infty < \ln \left( \frac{P_1^{sat}}{P_2^{sat}} \right) < -\ln \gamma_1^\infty$$

Where  $\gamma_i^\infty$  is the infinite dilution activity coefficient of component i.

From these conditions it is clear that even mixtures with large differences in vapour pressure may form azeotropes, given strong deviations from ideal behaviour.

These conditions are valid when the curves of activity coefficient versus composition do not show maxima or minima. Should either a maximum or minimum occur and these conditions be met, two azeotropic points may exist (Gmehling et al, 1994). This has been observed in the case of benzene-hexafluorobenzene (Gmehling et al, 1977) as well as for acetic acid-isobutyl acetate (Christensen and Olson, 1992). In the latter case this was due to strong non-ideality in the vapour phase (Gmehling et al, 1994).

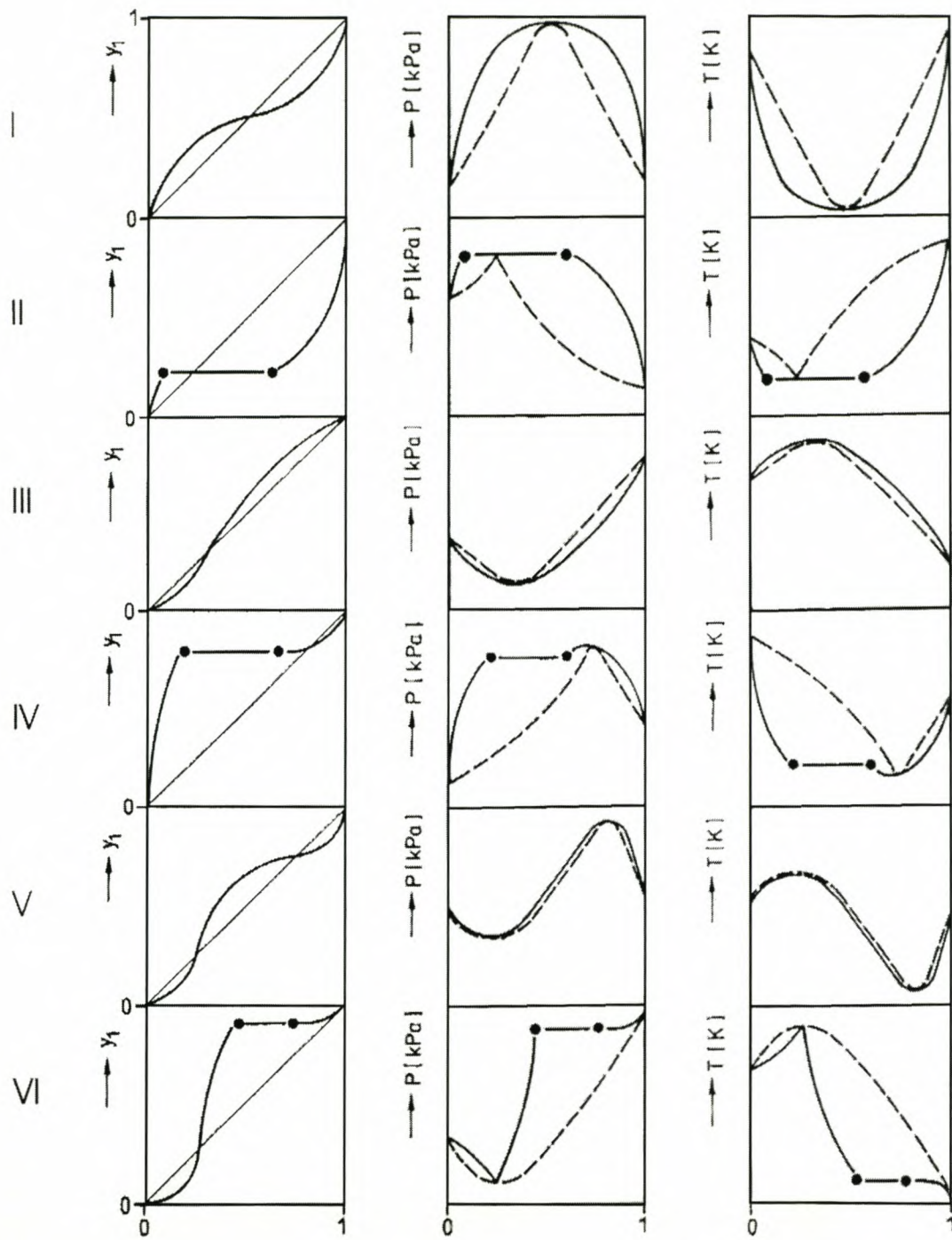
Large deviations from ideality may also lead to the formation of immiscible liquid phases. Should an azeotrope form in such a system, it will in most cases be a heterogeneous azeotrope, i.e. the phase split occurs at the azeotropic composition. In some binary systems however, homogeneous azeotropes and miscibility gaps are found at the same temperature, but different compositions (Gmehling et al, 1994; Seader et al, 1997).

For heterogeneous azeotropes, the vapour composition is equal to the overall liquid composition. Since strong positive deviations from Raoult's law are required for a liquid-liquid phase split, pressure minimum azeotropes are never heterogeneous (Gmehling et al, 1994; Seader et al, 1997).

The different types of binary azeotropes are summarised in Table 5.1 and Figure 5.1.

**Table 5.1 Different Types of Binary Azeotropes (Gmehling et al, 1994)**

	Type	System
<b>I</b>	Homogeneous Pressure Maximum	1-propanol – water ethanol – benzene ethanol – 1,4-dioxane
<b>II</b>	Heterogeneous Pressure Maximum	1-butanol – water benzene – water methanol – cyclohexane
<b>III</b>	Homogeneous Pressure Minimum	trichloromethane – ethyl acetate trichloromethane – 2-butanone
<b>IV</b>	Homogeneous Pressure Maximum In system with miscibility gap	2-butanone – water 2-butanol – water methyl acetate – water
<b>V</b>	Double Azeotrope	benzene – hexafluorobenzene methyl acetate – 1,2-epoxy butane diethyl amine – methanol
<b>VI</b>	Homogeneous Pressure Minimum In system with miscibility gap	triethyl amine – acetic acid hydrogen chloride – water hydrogen bromide – water

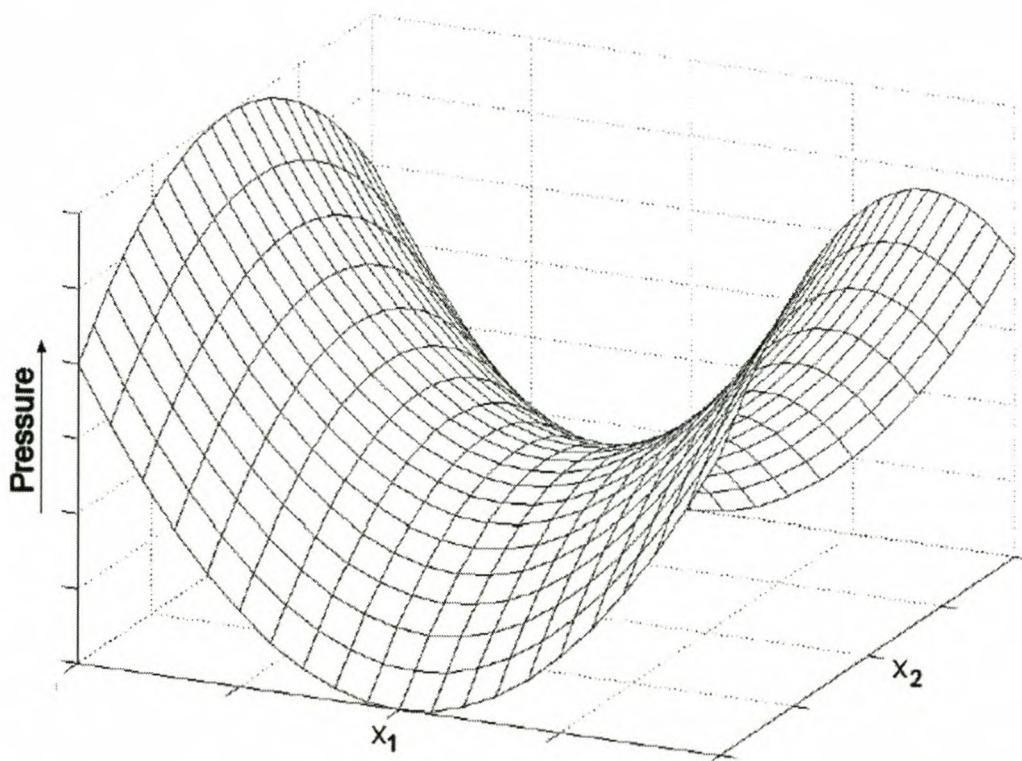


**Figure 5.1 Different Types of Binary Azeotropes.  $y$ - $x$ ,  $P$ - $x$  and  $T$ - $x$  Behaviour. (Gmehling et al, 1994)**

The existence of ternary and quaternary azeotropes is much less probable, as the condition that all the relative volatilities should be unity, becomes harder to satisfy as more components are added. The very existence of quinary azeotropes is a matter of dispute (Gmehling et al, 1994).



As with binary azeotropes, different types of multi-component azeotropes have been observed. In addition to pressure maximum and pressure minimum azeotropes so-called minimum-maximum or saddle point azeotropes can occur. At these points the pressure forms a minimum on one axis and a maximum on another, as illustrate in Figure 5.2. The axes of the saddle need not be parallel to the composition axes as is show by the example in Figure 5.4.



**Figure 5.2 A Saddle Point Azeotrope**

The different types of ternary azeotropes are summarised in Table 5.2.

**Table 5.2 Different Types of Ternary Azeotropes (Gmehling et al, 1994)**

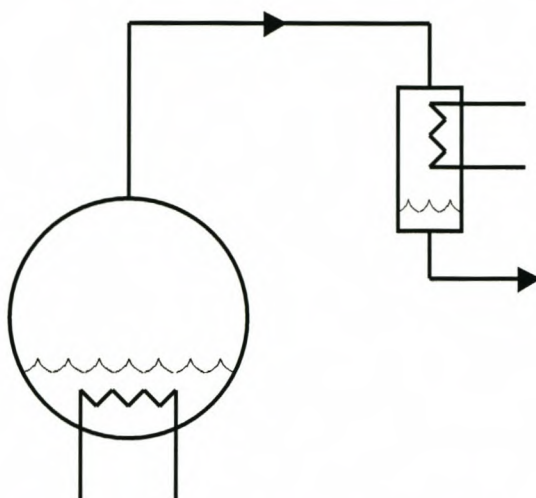
	Type	System
I	Homogeneous Pressure Maximum	trichloromethane – ethanol – hexane 2-propanone – methanol – methyl acetate benzene – cyclohexane – 2-propanol
II	Homogeneous Pressure Minimum	hydrogen fluoride – hexafluorosilicic acid -water
III	Homogeneous Saddle Point	2-propanone – trichloromethane – methanol 2-propanone – trichloromethane – hexane water – formic acid – acetic acid
IV	Heterogeneous Pressure Maximum	2-propanol – water – benzene ethanol – water – cyclohexane 1,2-dichloroethane – water – formic acid
V	Homogeneous Pressure Maximum In system with miscibility gap	ethanol – ethyl acetate – water 2-propanone – methanol – cyclohexane ( < 323K) 2-propanol – water – nitromethane

Just as the binary azeotropic point cannot be crossed by simple distillation, ternary systems are divided into distillation regions by boundary lines and quaternary systems by boundary planes (Seader and Henley, 1998).

### **5.3 Distillation Regions in Ternary Systems**

In order to understand how distillation regions are formed, we must consider the possible changes in composition that a mixture may undergo during distillation.

### 5.3.1 Residue Curves



**Figure 5.3 Differential Distillation (Seader and Henley, 1998)**

Figure 5.3 shows an apparatus for simple Rayleigh batch or differential distillation. No trays or packing is used and there is no reflux. An amount,  $W$ , of a ternary mixture is fed into the still pot, with liquid phase molar fractions  $x_i$ . The molar fractions in the vapour phase are indicated by  $y_i$ . If we assume that the liquid is perfectly mixed and maintained at its bubble point temperature, the following material balance can be written for any component (Seader and Henley, 1998):

#### Equation 5.4

$$\frac{dx_i}{dt} = (y_i - x_i) \frac{dW}{dt}$$

As  $W$  decreases with time, it is possible to combine the amount of liquid in the still ( $W$ ) with the time ( $t$ ) according to the method of Doherty and Perkins (Doherty and Perkins, 1978) into the variable  $\xi$  as defined by Equation 5.5.

**Equation 5.5**

$$\frac{dx_i}{d\xi} = x_i - y_i$$

Combining these two equations yields:

**Equation 5.6**

$$\frac{d\xi}{dt} = -\frac{1}{W} \frac{dW}{dt}$$

Given the starting value of  $W = W_0$  at  $t = 0$ , then Equation 5.6 can be solved to give  $\xi$  as a function of time.

**Equation 5.7**

$$\xi(t) = \ln \left[ \frac{W_0}{W(t)} \right]$$

As  $W$  is a monotonically decreasing function of time,  $\xi$  must be a monotonically increasing function of time. It can be seen as a warped, dimensionless time (Seader and Henley, 1998). This interpretation allows the simple distillation or the batch distillation process of a ternary mixture to be modelled by the following system of equations:

**Equation 5.8**

$$\frac{dx_i}{d\xi} = x_i - y_i, \quad i = 1, 2 \quad (a)$$

$$\sum_{i=1}^3 x_i = 1 \quad (b)$$

$$y_i = K_i x_i \quad (c)$$

$$\sum_{i=1}^3 y_i = 1 \quad (d)$$

The equilibrium ratios,  $K_i$ , are calculated with a thermodynamic model, as per usual.

At a fixed pressure, the temperature and composition can be written as functions of the dimensionless time,  $\xi$ . Given an initial value, the changing liquid composition can be plotted to yield a residue-curve map such as Figure 5.4. Circles indicate the three binary azeotropes and one ternary azeotrope. The arrows indicate the composition change in the liquid phase with  $\xi$ .

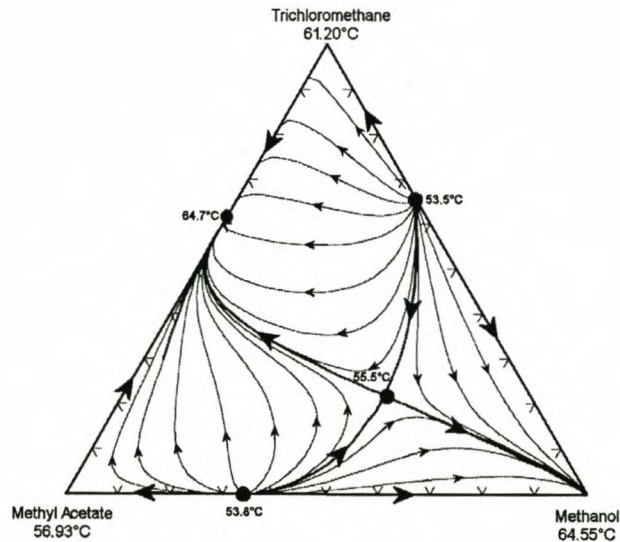


Figure 5.4 A Residue Curve Map. Adapted from (Gmehling et al, 1994).

At azeotropes and pure components, the derivative  $\frac{dx_i}{d\xi} = 0$  and these are thus singular points in the residue curves.

### 5.3.2 Distillation Lines

Distillation lines are similar to residue curves, but where residue curves are the operating lines at zero reflux, the distillation lines are the operating

lines at total reflux. Under these conditions, the liquid stream leaving tray  $n$  in the column,  $x_n$  is identical to the vapour stream entering the tray,  $y_{n+1}$ .

If the vapour leaving the tray is in equilibrium with the liquid on the tray, we may write the following expression:

**Equation 5.9**

$$y_{n+1} = \mathfrak{F}(x_{n+1})$$

With

$\mathfrak{F}$ : A function that maps  $x_{n+1}$  onto  $y_{n+1}$ , e.g. Equation 5.1

At total reflux,  $y_{n+1} = x_n$ , which gives:

**Equation 5.10**

$$x_n = \mathfrak{F}(x_{n+1})$$

This may be expanded to

**Equation 5.11**

$$x_{n+1} = \bar{\mathfrak{F}}(x_n) = \bar{\mathfrak{F}}^2(x_{n-1}) = \dots = \bar{\mathfrak{F}}^n(x_0)$$

With

$\bar{\mathfrak{F}}$ : The inverse of function  $\mathfrak{F}$ .

The points  $x_0$  to  $x_n$  form the distillation line, which has been defined as the locus of liquid compositions whose vapour compositions at equilibrium lie on the same line (Widagdo and Seider, 1996), i.e. the operating lines at total reflux.

The distillation lines may be plotted to form a distillation line map, similar to the residue curve map shown in Figure 5.4.

For an infinite number of stages, the limit  $\lim_{n \rightarrow \infty} \mathfrak{F}^n(x_o) = \hat{x}$ , the limiting composition. This is a stationary point in the distillation line. Pure components and azeotropes may form such stationary points (Widagdo and Seider, 1996).

### 5.3.3 Residue Curves as an Approximation of Distillation Lines

Van Dongen and Doherty (Van Dongen and Doherty, 1985) considered the case of a distillation column under reflux. With the assumption of constant molar overflow, the following species balances may be written (Widagdo and Seider, 1996):

*Rectifying section:*

**Equation 5.12**

$$\mathbf{y}_{m+1}^r = \frac{r}{r+1} \mathbf{x}_m^r + \frac{1}{r+1} \mathbf{x}_D \quad \forall m = 0, 1, \dots, M$$

$$\mathbf{x}_0^r = \mathbf{x}_D$$

*Stripping section*

**Equation 5.13**

$$\mathbf{x}_{n+1}^s = \frac{s}{s+1} \mathbf{y}_n^s + \frac{1}{s+1} \mathbf{x}_B \quad \forall n = 0, 1, \dots, N$$

$$\mathbf{x}_0^s = \mathbf{x}_B$$

With

- $M$ : The number of stages in the rectifying section
- $N$ : The number of stages in the stripping section
- $r$ : The reflux ratio in the rectifying section
- $s$ : The reflux ration in the stripping section
- $\mathbf{y}_m^r$ : A vector of vapour mole fractions on stage  $m$  in the rectifying section
- $\mathbf{x}_n^s$ : A vector of liquid mole fractions on stage  $n$  in the stripping section
- $\mathbf{x}_D$ : The vector of mole fractions in the distillate
- $\mathbf{x}_B$ : The vector of mole fractions in the bottoms-product

The stages in the rectifying section are counted downwards, while those in the stripping section are counted upwards.

Equation 5.12 and Equation 5.13 define the operating lines of the column. They are a set of difference equations that, when combined with an equilibrium relation like Equation 5.1, may be solved to yield a set of discrete points. These difference equations may also be approximated by the following ODE's (Ordinary Differential Equations) with continuous variables  $\hat{\mathbf{x}}^r, \hat{\mathbf{y}}^r, \hat{\mathbf{x}}^s$  and  $\hat{\mathbf{y}}^s$  (Widagdo and Seider, 1996):

### *Rectifying section*

#### **Equation 5.14**

$$\frac{d\hat{\mathbf{x}}^r}{dh_r} \approx \hat{\mathbf{x}}_r - \frac{r}{r+1} \hat{\mathbf{y}}_D + \frac{1}{r} \mathbf{y}_D \quad (\text{a})$$

$$\hat{\mathbf{x}}^r(h_r = 0) = \mathbf{x}_D \quad (\text{b})$$



### Stripping section

#### Equation 5.15

$$\frac{d\hat{\mathbf{x}}^s}{dh_s} \approx \frac{s}{s+1} \hat{\mathbf{y}}^s + \frac{1}{s+1} \mathbf{x}_B - \hat{\mathbf{x}}^s \quad (\text{a})$$

$$\hat{\mathbf{x}}^s(h_s = 0) = \mathbf{x}_B \quad (\text{b})$$

With

$h_r$ : The elevation in the rectifying section relative to the condenser ( $h_r = 0$ )

$h_s$ : The elevation in the rectifying section relative to the reboiler ( $h_s = 0$ )

At total reflux and total reboil, Equation 5.14 and Equation 5.15 reduce to (Van Dongen and Doherty, 1985):

#### Equation 5.16

$$\frac{d\hat{\mathbf{x}}^r}{dh_r} \approx \hat{\mathbf{x}}^r - \hat{\mathbf{y}}^r \quad (\text{a})$$

$$\frac{d\hat{\mathbf{x}}^s}{dh_s} \approx \hat{\mathbf{y}}^s - \hat{\mathbf{x}}^s \quad (\text{b})$$

These equations have similar forms to Equation 5.8 (a), which defines the residue curves. This has led to the residue curves also being interpreted as approximate models of a column under total reflux (Widagdo and Seider, 1996), and thus of the distillation lines.

The distillation lines and residue curves are thus expected to lie close together, as is the case (Widagdo and Seider, 1996). It has also been shown that distillation lines and residue curves have identical properties in the vicinity of stationary points (Zharov, 1969). In areas of high curvature though, the difference between the residue curves and distillation lines may be significant.

### 5.3.4 Approximate Sketches of Residue Curves and Distillation Lines

The pure components and azeotropes are all singular points in the residue curves and the distillation lines.

The singular points of a residue curve may be classified according to the eigenvalues of the Jacobian of Equation 5.8 (a). There are three possibilities:

1. Both eigenvalues are negative: The singular point is a stable node and the residue curves point towards it. This point will be the highest boiling node in a distillation region.
2. Both eigenvalues are positive: The singular point is an unstable node and the residue curves point away from it. This point will be the lowest boiling point in a distillation region.
3. One eigenvalue is positive and one negative: The singular point is a saddle and residue curves will point both towards and away from it. All nodes in a distillation region that are intermediate in boiling point between the stable and unstable nodes are saddles (Seader and Henley, 1998).

It has been shown by Zharov that this classification is also valid for distillation lines (Widagdo and Seider, 1996).

Residue curve and distillation line maps with multiple stationary points may be divided into regions by simple distillation boundaries (residue curve maps) or distillation line boundaries (distillation line maps). Each of the regions will have a distinct start and end point for all the residue curves or distillation lines in that region – the unstable and stable nodes. The important difference between simple distillation boundaries and

distillation line boundaries, is that the operating lines of a simple distillation column cannot cross distillation line boundaries, whereas simple distillation boundaries may be crossed in certain cases, usually in areas of high curvature, where they lie furthest from the distillation lines (Stichlmair et al, 1989; Rev, 1992; Widagdo and Seider, 1996).

The classification of nodes given above was used by Foucher et al (Foucher et al, 1991), to develop a system of rapidly approximating the residue curve or maps for ternary systems. As the residue curves and distillation lines usually lie close together, this method may also be used to sketch distillation line maps.

The method developed by Foucher et al is based on the following:

Ternary systems, with very few exceptions, will have at most three binary azeotropes and one ternary azeotrope. Therefore, the following restrictions are applicable (Foucher et al, 1991):

**Equation 5.17**

$$N_1 + S_1 = 3 \quad (a)$$

$$N_2 + S_2 = B \leq 3 \quad (b)$$

$$N_3 + S_3 = 1 \text{ or } 0 \quad (c)$$

In these equations, N is the number of stable and unstable nodes and S the number of saddles. The subscript indicates the number of components, thus  $S_1$  will be the number of pure component saddles etc. B is the number of binary azeotropes.

Doherty and Perkins (Doherty and Perkins, 1979) also developed the following relationship:

**Equation 5.18**

$$2N_3 - 2S_3 + 2N_2 - B + N_1 = 2$$

These relationships may be used in a nine-step method to draw approximate residue curve maps (Foucher et al, 1991).

**Step 0:** Mark the azeotropes on the ternary diagram and label the pure components and azeotropes with their boiling points. The pure components should be arranged in ascending order according to boiling point, starting at the topmost vertex and proceeding in an anticlockwise direction.

Determine the value of B, the number of binary azeotropes.

**Step 1:** Draw arrows on the edges of the triangle in the direction of increasing temperature.

**Step 2:** Determine the type of node at each pure component vertex. Pure components with two arrows pointing inwards are stable nodes; those with two arrows pointing outwards are unstable nodes; vertices with one arrow pointing inwards and one pointing outwards are saddles. This determines the values of  $N_1$  and  $S_1$ .

**Step 3:** (For a ternary azeotrope.) Determine the type of singular point at the ternary azeotrope. The point will be a node under the following conditions:

(a)  $N_1 + B < 4$  and / or

(b) Excluding the pure component saddles, the ternary azeotrope has the highest, second highest, lowest

or second lowest boiling point of all the singular points.

If neither of these conditions is met, the point will be a saddle.

**Step 4:** (For a ternary saddle.) If the ternary azeotrope is determined to be a saddle (in step 3), connect the ternary azeotrope to all binary azeotropes and to all pure component nodes (but not saddles).

Draw arrows on these connecting lines in the direction of increasing boiling point.

Determine the type of singular point at the binary azeotropes. Azeotropes with all arrows pointing inward are stable nodes; those with all arrows pointing outward are unstable nodes and those with arrows pointing both inward and outward are saddles. This determines the values of  $N_2$  and  $S_2$ . These values should be checked against Equation 5.17 and Equation 5.18. Should these equations not be satisfied, one or more boiling points may be in error.

In the special case where  $N_1 + B = 6$ , there are more candidate connections than can be made to the saddle and the boiling point combinations of the stationary points will decide which connections are made, as described in (Foucher et al, 1991).

The residue curve map is now complete.

**Step 5:** (For a ternary node or systems without a ternary azeotrope.) Determine the number of binary nodes and saddles from

Equation 5.17 (b) and Equation 5.18 by solving for  $N_2$  and  $S_2$ .

**Step 6:** Determine the value of  $B_{ib}$ , the number of binary azeotropes that are intermediate boiling. Check this value for consistency against the following:

$$(a) B - B_{ib} = N_2$$

$$(b) S_2 \leq B_{ib}$$

If these tests are not satisfied, one or more of the boiling points may be incorrect.

**Step 7:** If  $S_2 \neq B_{ib}$  no unique residue curve map can be determined with this method and Equation 5.8 must be used instead. If  $S_2 = B$ , there is a unique structure which will be determined in the next step.

**Step 8:** The number of separatrices equals the number of binary saddles,  $S_2$ . Each of these binary saddles must be connected to a node.

A ternary node must be connected to at least one binary saddle. This implies that a pure component node cannot be connected to a ternary node and an unstable node cannot be connected to a stable node.

The connections for the binary saddles are determined according to the following rules:

- (a) A minimum boiling binary saddle must be connected to an unstable node with a lower boiling point.
- (b) A maximum boiling binary saddle must be connected to a stable node that boils at a higher temperature

At this point the two binary saddles have not been formally identified. Although this may be done through the eigenvalues criteria outlined above, considering the connections to the ternary azeotrope may also identify the saddles.

To help explain the method, the hypothetical ternary mixture depicted in Figure 5.5 will be used as an example. The three components are identified as H (the high boiling component), I (intermediate boiling) and L (low boiling). There are two minimum boiling binary azeotropes (HL and HI) and one maximum boiling binary azeotrope (IL), as well as a ternary azeotrope.

The boiling points of the pure components and azeotropes are indicated on the first ternary diagram in Figure 5.5. As there are three binary azeotropes,  $B = 3$ .

The next step requires the direction of increasing boiling point to be drawn in on the edges of the ternary diagram. This is shown on the second diagram in Figure 5.5.

The arrows drawn in step 1 allow the determination of the type of stationary point at each vertex. In this case, pure component H forms a stable node, while both I and L form saddle points, thus  $N_1 = 1$  and  $S_1 = 2$ .

The type of stationary point at the ternary azeotrope must now be determined. As  $N_1 + B = 1 + 3 = 4$ , the system fails the first test for being a node, but as the ternary azeotrope has the second lowest boiling point when excluding the saddles L and I, it is indeed a node.

Equation 5.18 can be solved for  $N_2$ :

$$\begin{aligned} N_2 &= \frac{2 + B - N_1 + 2S_3 - 2N_3}{2} \\ &= \frac{2 + 3 - 1 + 2(0) - 2(1)}{2} \\ &= 1 \end{aligned}$$

From Equation 5.17 (b) it then follows that  $S_2 = 2$ .

Binary azeotrope HL is the lowest boiling stationary point in the system and pure component H the highest boiling. This implies that there are two intermediate boiling azeotropes, HI and IL, thus  $B_{ib} = 2$ . This must be checked for consistency:  $B - B_{ib} = 3 - 2 = 1 = N_2$ , so the first test is passed. Furthermore,  $S_2 = 2 = B_{ib}$ , thus the second check is also satisfied.

As  $S_2 = B_{ib}$ , as seen in the previous step, this system will indeed have a unique residue curve map, which we can now construct.

As there are two binary saddles, there will be two separatrices. Each of these lines will run from a binary saddle to a node. To construct these lines we must first identify the binary saddles. This will be done by considering the allowed connections with the ternary azeotrope.

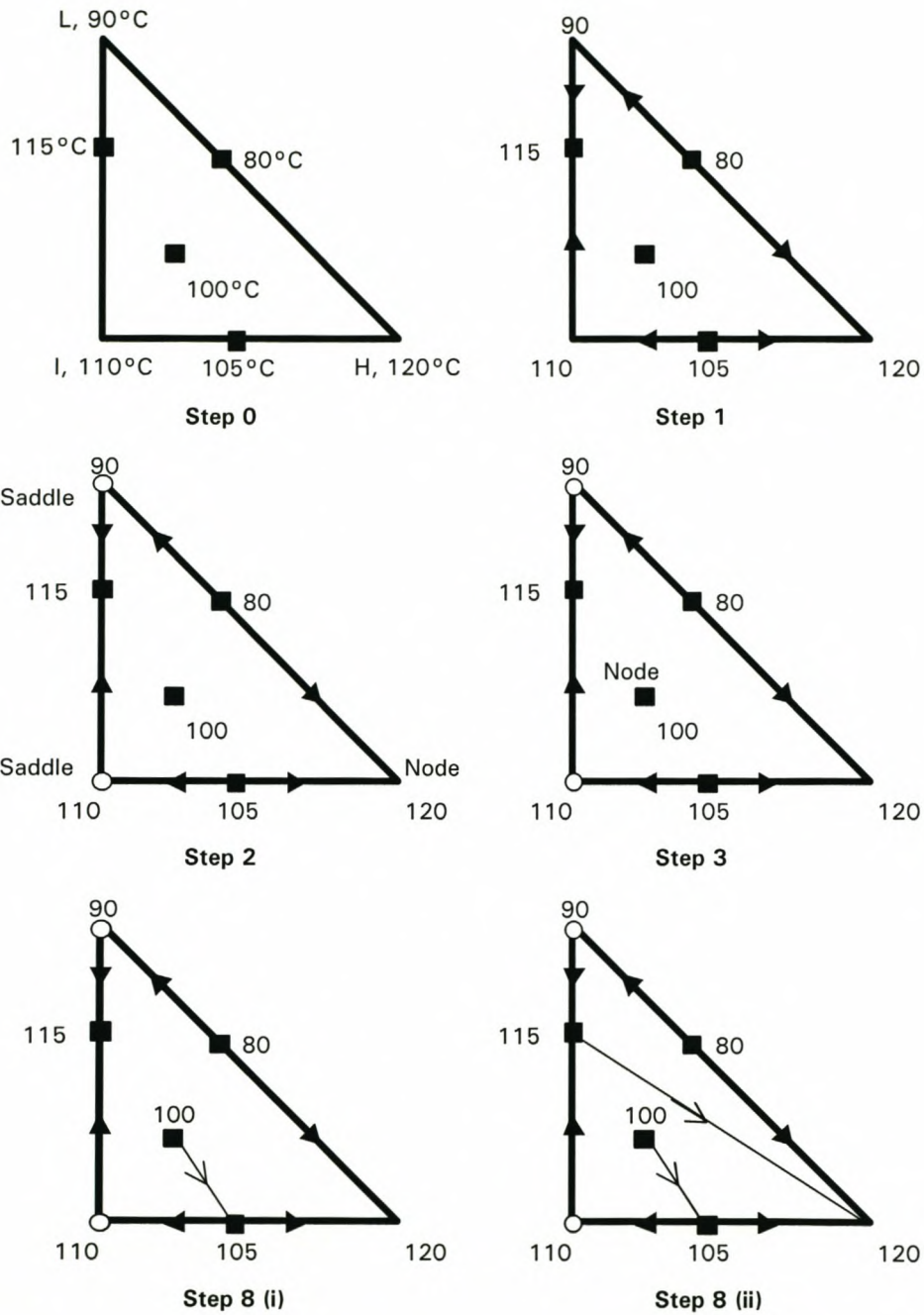
Consider first the HL azeotrope. Should the ternary node be connected to this azeotrope, HL would be an unstable node and thus the ternary azeotrope would be a stable node. This connection is not allowed, as



stable and unstable nodes may not be connected. Similarly, the ternary node cannot be connected to the IL azeotrope. In this case, IL would be a stable node and the ternary an unstable node. This leaves only the HI azeotrope. The connection is shown in Figure 5.5 as step 8 (i). The ternary azeotrope is an unstable node in this case.

One more connection is required and as all the possible connections to the ternary azeotrope have been considered, this connection must be between a binary azeotrope and a pure component. The second binary saddle must also be identified.

HL is a minimum boiling azeotrope and as such must be connected to an unstable node with a lower boiling point. As HL is the lowest boiling stationary point in the system, no such connection is possible. This leaves only IL. IL is a maximum boiling azeotrope, which should be connected to a stable node with a higher boiling point. Connecting IL to H would satisfy this requirement. The outline of residue curve map is thus completed, as shown in Figure 5.5 as step 8 (ii).



**Figure 5.5 Determination of a Residue Curve Map**

The existence of a miscibility gap complicates the construction of the residue curve map. The above method has been extended to partially miscible systems by Pham and Doherty (Pham and Doherty, 1990; Pham and Doherty, 1990; Pham and Doherty, 1990). The residue curve maps for heterogeneous systems are similar to those of homogeneous systems in that they are divided into regions by simple distillation boundaries

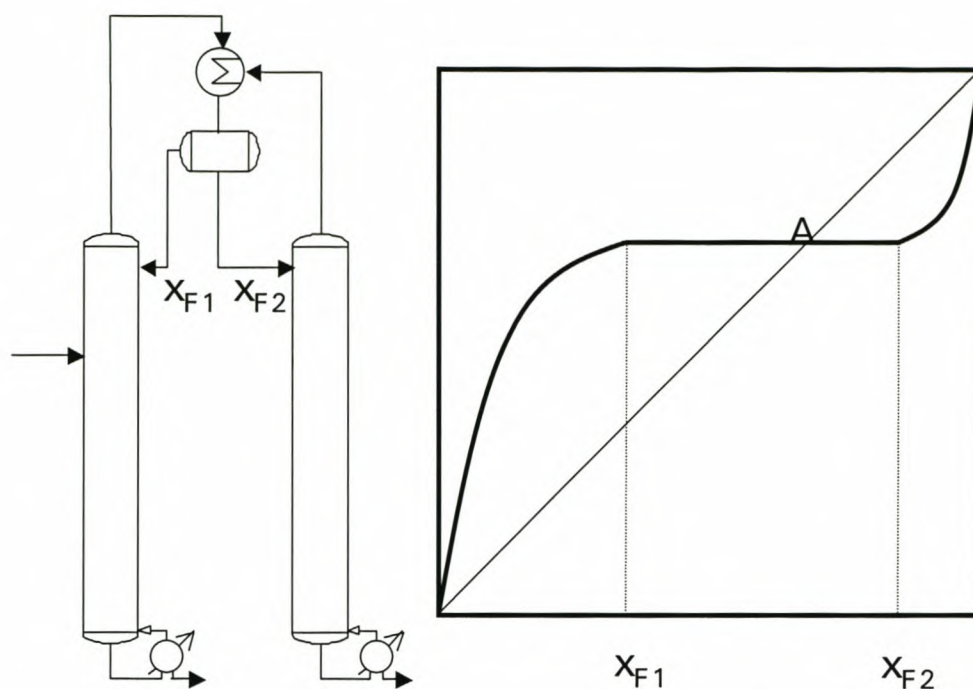
(Widagdo and Seider, 1996). They are however more restricted as heterogeneous azeotropes can only be saddles or unstable nodes (they cannot be high boiling).

The existence of distillation line boundaries can considerably complicate separation processes. The feed composition will determine the distillation region that the process must operate in, as the distillation line boundaries cannot be crossed by means of simple distillation. The feasible products will be restricted to the stable and unstable nodes of the specific distillation region.

In order to cross the distillation line boundaries imposed by azeotropes, enhanced distillation methods are used. These may include processes like extractive distillation, where an extractive agent or solvent is added in order to break the azeotrope. It is also possible to cross distillation boundaries using phenomena like liquid phase immiscibility. This is the basis of heterogeneous azeotropic distillation.

#### ***5.4 Heterogeneous Azeotropic Distillation – A Short Review***

A detailed discussion of heterogeneous azeotropic distillation falls outside the scope of this work. It would however be beneficial to briefly review some of the more important aspects. An excellent review of the subject is available in (Widagdo and Seider, 1996).



**Figure 5.6 Binary Heterogeneous Azeotropic Distillation. Adapted from (Sattler, 1995)**

Figure 5.6 illustrates the case of binary heterogeneous azeotropic distillation. A similar configuration is used for ternary heterogeneous azeotropic distillation.

The mixture is fed into the first column and distilled to near the azeotropic point (A on the phase diagram). When the distillate is condensed, it separates into two liquid phases of composition  $x_{F1}$  and  $x_{F2}$ .

The liquid phase that is rich in the less volatile component is fed back into the column as reflux, while the other phase is fed to a second column, run in stripping mode. The overhead product of this column is also fed into the condenser. The products are withdrawn in the bottoms of the two columns. The less volatile component is withdrawn from the first column and the more volatile component from the second column.

In the case of ternary azeotropic distillation, the overhead product of the second column will usually be mostly entrainer and should be fed into the first column instead of the recycle drum. The entrainer is continuously recycled in the system and only a small make-up stream is required.

The key to the success of this process is that the system must have a wide enough miscibility gap around the azeotrope. The wider this miscibility gap is, the easier the separation will be. If a binary azeotropic system does not exhibit such a miscibility gap, adding a third component may induce it. This component, the entrainer, must be chosen such that a low boiling heterogeneous azeotrope forms with as wide a miscibility gap as possible. This may be a ternary azeotrope as is commonly the case, or a binary heterogeneous azeotrope formed with one of the mixture components, as is used in the separation of water and acetic acid through azeotropic distillation. The entrainer in this case, ethyl acetate, forms a heterogeneous binary azeotrope with water.

The azeotrope must be a negative node, so that it may be recovered in the distillate, where the two liquid phases may be separated.

In order to select an appropriate entrainer for the separation of a binary system, a method must be found with which to predict the existence of heterogeneous azeotropes. A number of such methods have been proposed and some of these will be considered here.

### ***5.5 Methods for Finding Azeotropes***

A number of authors have attempted to find all azeotropes in a system simultaneously by solving a system of non-linear equations. The main difference between their approaches lies in the methods used to solve this system of equations.

Fidkowski et al (Fidkowski et al, 1993) used a homotopy continuation method while Harding and Floudas (Harding et al, 1997; Harding and Floudas, 2000) preferred a global optimisation method based on convex underestimators and a branch and bound strategy developed by Maranas and Floudas (Maranas and Floudas, 1995).

A third group of researchers under Stadherr used an Interval-Newton method (Maier et al, 1988; Maier et al, 1999) developed by Kearfott (Kearfott and III, 1991).

As will be seen, these methods were developed for mathematical robustness, not computational efficiency. In order to be able to find suitable heterogeneous azeotropes in the systems of interest, two new methods were developed. These are a grid search method and a residue curve tracing method. These methods will also be discussed in detail.

### 5.5.1 Homotopy Continuation Method

Fidkowski's method (Fidkowski et al, 1993) starts with the fact that the liquid and vapour compositions are identical at an azeotropic point:

#### Equation 5.19

$$f_i(\mathbf{x}) \equiv y_i(\mathbf{x}) - x_i = 0 \quad \forall i = 1 \text{ to } N_s - 1$$

With

- $\mathbf{x}$ : The vector of liquid mole fractions
- $N_s$ : The number of species present

A suitable thermodynamic model supplies the functional relation between  $y_i$  and  $x_i$  at equilibrium. To find the azeotropes present in a system, all of the roots of Equation 5.19 must be found, subject to the following constraints:

### Equation 5.20

$$\begin{aligned}\sum_i x_i &= 1 \\ \sum_i y_i &= 1 \\ 0 \leq x_i \leq 1 \quad \forall i = 1 \text{ to } N_s\end{aligned}$$

Conventional root-finding methods cannot be used with certainty, as the system is non-linear, constrained and has multiple roots. There are the trivial solutions at the pure component compositions as well as an additional root for each azeotrope.

The behaviour of the system is also influenced by the value of the pressure that is specified, as was first discovered in 1859 by Roscoe and Ditmar (Fidkowski et al, 1993). Azeotropes may even appear or disappear as the pressure is changed. This presents the possibility of tracking the solutions of Equation 5.19 with changing pressure from some initial condition. Unfortunately, a suitable starting pressure, where no azeotropes are present, cannot easily be determined beforehand. Instead, Fidkowski et al developed a method, by which the equilibrium surface itself is gradually deformed, starting from Raoult's law.

A homotopy parameter,  $t$ , is introduced into the equilibrium model, such that the result is Raoult's law at  $t = 0$  and the appropriate physical model at  $t = 1$ .

With Equation 5.1 as our starting point, the extended equilibrium relationship becomes:

### Equation 5.21

$$\tilde{y}_i = \left[ (1-t) + t\gamma_i \right] \frac{x_i P_i^{sat}}{P} \quad \forall i = 1 \text{ to } N_s - 1$$

With

$\tilde{y}_i$ : The molar fraction of component  $i$  in the vapour, calculated with the homotopy method

$t$ : The homotopy parameter

Now a homotopy continuation method may be used to find the root of the following system:

### Equation 5.22

$$h_i(\mathbf{x}, t) \equiv \tilde{y}_i(\mathbf{x}, t) - x_i = 0 \quad \forall i = 1 \text{ to } N_s - 1$$

As starting point for tracking the solutions, the pure components are used as these would be the roots of Equation 5.22 at  $t = 0$  when there are no azeotropes in the ideal mixture. Should such azeotropes exist (at Bancroft points), the homotopy would have to be expanded to include the vapour pressures.

As  $t$  increases, cascade bifurcations (branching) occur. At each bifurcation a new solution branch occurs. Near  $t = 0$ , there are  $N_s$  branches – one for each pure species. With increasing  $t$ , these branches bifurcate to form branches for each of the binary azeotropes. These branches then bifurcate in turn to branches for ternary azeotropes and so the process continues.

The type of each azeotrope must be determined from the eigenvalues of the Jacobian of the residue curve map (Equation 5.8 (a)), which is equivalent to the negative of the Jacobian of Equation 5.22 at  $t = 1$ .



The method, though efficient and fairly reliable (Widagdo and Seider, 1996), has not yet been extended to partially miscible systems, rendering it useless for finding heterogeneous azeotropes.

### 5.5.2 Convex Underestimator Method

Harding et al (Harding et al, 1997) attempted to find all the homogeneous azeotropes in a mixture by solving the azeotropic existence equations with a global optimisation algorithm. The method was later extended by Harding and Floudas (Harding and Floudas, 2000) to include heterogeneous and reactive azeotropes.

For homogeneous azeotropes, the composition equality may be written as

#### Equation 5.23

$$y_i = x_i \quad \forall i = 1 \text{ to } N_s \quad (\text{a})$$

$$\sum_i x_i = \sum_i y_i = 1 \quad (\text{b})$$

$$0 \leq x_i, y_i \leq 1 \quad (\text{c})$$

This is essentially the same formulation as used by Fidkowski. The vapour composition,  $y_i$ , can be calculated with Equation 5.1 and a suitable thermodynamic model.

In the case of heterogeneous azeotropes, the existence of an azeotrope requires that the vapour composition be identical to the overall liquid composition. Equation 5.23 (a) thus changes to

#### Equation 5.24

$$y_i = \sum_{j \in P^L} m^{L_j} x_i^{L_j} \quad \forall i = 1 \text{ to } N_s$$

With

$P^L$ : The set of liquid phases

$m^{Lj}$ : The fraction of the total liquid made up by liquid phase  $j$

$x_i^{Lj}$ : The molar fraction of component  $i$  in liquid phase  $j$

The optimisation method used to solve this system of equations was developed by Maranas and Floudas (Maranas and Floudas, 1995). In this method, each non-linear equation is replaced by two inequalities and a single slack variable,  $s$ , is introduced.

Equation 5.1 may be rewritten for each liquid phase into the following (Harding and Floudas, 2000):

#### Equation 5.25

$$y_i P = \gamma_i^{Lj} x_i^{Lj} P_i^{sat} \quad \forall i \in P^L \quad (a)$$

$$\therefore \ln P + \ln y_i - \ln P_i^{sat} - \ln \gamma_i^{Lj} - \ln x_i^{Lj} = 0 \quad \forall i = 1 \text{ to } N_s \quad \forall j \in P^L \quad (b)$$

This allows the entire set of equations consisting of Equation 5.23 (b) and (c), Equation 5.24 and Equation 5.25 (b) to be formulated into the following optimisation problem (Harding and Floudas, 2000):

### Equation 5.26

$$\min_{x,y,T,s} s$$

subject to

$$\ln P + \ln y_i - \ln P_i^{sat} - \ln \gamma_i^{L_j} - \ln x_i^{L_j} - s \leq 0 \quad \forall i = 1 \text{ to } N_s \quad \forall j \in P^L$$

$$-\ln P - \ln y_i + \ln P_i^{sat} + \ln \gamma_i^{L_j} + \ln x_i^{L_j} - s \leq 0 \quad \forall i = 1 \text{ to } N_s \quad \forall j \in P^L$$

$$y_i - \sum_{j \in P^L} m^{L_j} x_i^{L_j} - s \leq 0 \quad \forall i = 1 \text{ to } N_s$$

$$-y_i + \sum_{j \in P^L} m^{L_j} x_i^{L_j} - s \leq 0 \quad \forall i = 1 \text{ to } N_s$$

$$\sum_i y_i = 1$$

$$\sum_i x_i^{L_j} = 1 \quad \forall j \in P^L$$

$$\sum_{j \in P^L} m^{L_j} = 1$$

$$s \geq 0$$

$$0 \leq y_i \leq 1 \quad \forall i = 1 \text{ to } N_s$$

$$0 \leq x_i^{L_j} \leq 1 \quad \forall i = 1 \text{ to } N_s \quad \forall j \in P^L$$

$$0 \leq m^{L_j} \leq 1 \quad \forall j \in P^L$$

$$T^L \leq T \leq T^U$$

With

$T$ : The temperature

$T^L$ : The lower bound for the temperature

$T^U$ : The upper bound for the temperature

$s$ : The slack variable

As several of the constraints are nonconvex, there may be multiple global optima (were the solution,  $s^* = 0$ ), each corresponding to an azeotrope. (Harding and Floudas, 2000). A local optimisation method is likely to miss some of these solutions.

The approach followed by Harding et al, is to replace each nonconvex constraint with a convex underestimator and then use a commercially available non-linear solver to find the global minimum of this convex problem. These underestimators will always have values lower than that of their associated functions in the same domain.

Suitable underestimating functions were developed for the Antoine equation as well as a number of activity coefficient models, including Wilson, NRTL, UNIQUAC and UNIFAC. (Harding et al, 1997; Harding and Floudas, 2000).

A branch and bound strategy is used to enclose all of the solutions to the original problem. Once the global minimum of the convex related problem is found within a search region (or box), there are two possibilities:

1. The convex problem is strictly positive, in which case the original problem has no roots within the box, as the convex problem is an underestimator. The search region may be discarded.
2. The convex problem has a minimum that is zero or negative. In this case the original problem may or may not have a root in the box. The search region is now subdivided and the procedure is repeated for each new box.

As the size of the search region decreases, the estimating functions come closer to the original constraints (Harding et al, 1997). By tightening the bounds around the solutions to the convex problem, these points will more accurately represent the solutions to the original problem. This method is theoretically guaranteed to find all of the azeotropes predicted by the selected thermodynamic model (Harding et al, 1997), but floating-point rounding errors may lead to this guarantee being lost (Maier et al, 1988).

### 5.5.3 Interval Newton Method

The method used by Maier, Brennecke and Stadtherr is in many respects similar to that used by Harding et al.

The composition equality for homogeneous azeotropes is the same as used by Harding, i.e. Equation 5.23. The vapour phase molar fractions may be eliminated through use of Equation 5.1. This gives:

#### Equation 5.27

$$x_i(P - \gamma_i P_i^{sat}) = 0 \quad \forall i = 1 \text{ to } N_s \quad (\text{a})$$

$$\sum_i x_i = 1 \quad (\text{b})$$

$$0 \leq x_i \leq 1 \quad (\text{c})$$

As the vapour pressure and activity coefficient models are usually found in logarithmic form, it is convenient to follow the practice of Harding and Floudas (Harding and Floudas, 2000) and rewrite Equation 5.27 (a) as follows:

#### Equation 5.28

$$x_i [\ln P - \ln P_i^{sat}(T) - \ln \gamma_i(T)] = 0 \quad \forall i = 1 \text{ to } N_s$$

Equation 5.27 (b) and Equation 5.28 combine to form a set of  $N_s + 1$  non-linear equations and  $N_s + 1$  variables. In this case, the temperature is the  $(N_s + 1)^{\text{th}}$  variable and the pressure is fixed, but the reverse is equally possible.

Form Equation 5.28 it is clear that the system will have trivial roots at the pure components. This is the same formulation as used by Fidkowski

(Fidkowski et al, 1993), where these trivial roots were the starting points of the solutions tracking method. If we assume that there are no components for which the molar fraction is zero at the azeotrope, Equation 5.28 may be simplified by eliminating the trivial roots:

**Equation 5.29**

$$\ln P - \ln P_i^{sat} - \ln \gamma_i = 0 \quad \forall i = 1 \text{ to } N_s$$

This formulation will result in a system with  $k + 1$  equations and  $k + 1$  variables with roots at all the azeotropes with  $k$  components that are present in the mixture.

A similar process is followed for heterogeneous azeotropes. In this case the vapour phase composition is identical to the overall liquid composition and Equation 5.24 together with Equation 5.23 (b) and (c) should be used. The complete derivations of the required system of equations for both the temperature explicit and the pressure explicit cases with two liquid phases are given in Appendix A.

The system of non-linear equations is now solved using an Interval-Newton / Generalised Bisection (INTBIS) method proposed by Kearfott (Kearfott, 1987; Kearfott and Ill, 1991; Kearfott, 1992; Kearfott, 1996) and based on the work by Hansen (Hansen, 1968; Hansen and Sengupta, 1981; Hansen and Greenburg, 1983). This method is mathematically and computationally guaranteed to find all the roots of a system of equations (Schnepper and Stadherr, 1996). Unlike the method of Maranas and Floudas (Maranas and Floudas, 1995) that was used by Harding et al (Harding et al, 1997; Harding and Floudas, 2000), rounding errors do not affect this guarantee.

The INTBIS method has been applied to a vast number of chemical engineering related problems by many authors. Some of these applications are reviewed by Balaji et al (Balaji et al, 1995) and Kearfott (Kearfott, 1996). The details of the method are summarised by Schnepfer and Stadherr (Schnepfer and Stadherr, 1996) and will be briefly discussed here.

### **5.5.3.1 Interval arithmetic**

Before the interval Newton can be understood, the basic concepts of interval arithmetic should be reviewed. For a detailed discussion of interval analysis, refer to (Moore, 1966).

#### **Definitions**

A real interval number,  $X$  is defined as

#### **Equation 5.30**

$$X = [a, b] = \{x \in \mathfrak{R} \mid a \leq x \leq b\} \text{ with } a, b \in \mathfrak{R} \text{ and } a \leq b$$

In the case where  $a = b$ , the interval is said to be degenerate. Real numbers,  $x \in \mathfrak{R}$ , could be seen as degenerate intervals,  $X = [x, x]$ . The set of real intervals is  $\underline{\mathfrak{R}}$ .

Interval vectors and matrices are similar to their real counterparts, e.g.:

#### **Equation 5.31**

$$X = (X_1, X_2, \dots, X_n)^T \in \underline{\mathfrak{R}}^n, X_i \in \underline{\mathfrak{R}}$$

and

$$\underline{\mathbf{X}} = \begin{bmatrix} X_{11} & X_{12} & \dots & X_{1n} \\ X_{21} & X_{22} & \dots & X_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ X_{m1} & X_{m2} & \dots & X_{mn} \end{bmatrix} \in \underline{\mathfrak{R}}^{m \times n}, X_{ij} \in \underline{\mathfrak{R}}$$

An interval vector may be interpreted as an n-dimensional rectangle, and is generally referred to as a box.

The midpoint of interval  $X = [a, b]$  is  $\bar{x} \in \mathfrak{R}$  and it may be calculated as follows:

**Equation 5.32**

$$\bar{x} = \frac{a+b}{2}$$

The midpoint of a box,  $\bar{x} \in \mathfrak{R}^n$ , is a real vector. Similarly an interval matrix will have a real midpoint matrix of which each entry is the midpoint of the corresponding interval in the interval matrix.

The width, or diameter, of an interval  $X = [a, b]$ , may be calculated with Equation 5.33.

**Equation 5.33**

$$w(X) = b - a$$

The width of a box  $X = (X_i)$ , is defined as follows:

**Equation 5.34**

$$w(\mathbf{X}) = \max_i w(X_i)$$



Further definitions include the absolute value of an interval:

**Equation 5.35**

$$|X| = \max\{|a|, |b|\}$$

Analogously, the norm of a box is defined as:

**Equation 5.36**

$$\|\mathbf{X}\| = \max_i |X_i|$$

The final definition that is required is the volume of a box, which may be calculated as follows:

**Equation 5.37**

$$V(\mathbf{X}) = \prod_i w(X_i)$$

**Interval Operations**

Given the intervals  $X = [a, b]$  and  $Y = [c, d]$ , the four basic arithmetic operations are defined as follows:

**Equation 5.38**

$$X + Y = [a + c, b + d] \quad \text{(a)}$$

$$X - Y = [a - d, b - c] \quad \text{(b)}$$

$$X \times Y = [\min(ac, ad, bc, bd), \max(ac, ad, bc, bd)] \quad \text{(c)}$$

$$X/Y = [a, b] \times [1/d, 1/c], \quad 0 \notin [c, d] \quad \text{(d)}$$

For interval division where  $0 \in [c, d]$ , an extended interval arithmetic must be used (Moore, 1966; Hansen, 1968).

### Arithmetic

In order to counter errors due to rounding of floating point numbers, so-called rounded-interval arithmetic is used. This entails that the lower bounds of intervals are rounded down to the largest number less than or equal to its value, which can be accurately represented by a computer. Similarly, the upper bound is rounded upwards. In this manner the interval stored in the computer memory will always include the actual answer.

A key feature of interval methods is that, if the real values in a function are replaced with interval equivalents, the resulting interval value will be an *inclusion monotone interval extension* of the function (Moore, 1966), (Schnepper and Stadherr, 1996). The implication is that all possible values that may be assumed by the function (its range) within the region defined by the input intervals (its domain) will be elements of the interval result calculated in this way. For example:

$$f(x, y, z) = x(y - z)$$

In interval form this becomes:

$$F(X, Y, Z) = X(Y - Z)$$

The extreme values that the real version of this function can assume in the range  $1 \leq x \leq 2$ ,  $1 \leq y \leq 2$ ,  $1 \leq z \leq 2$ , may be found by inspection to be  $-2$  (minimum) and  $2$  (maximum). Setting  $X = Y = Z = [1, 2]$  in the interval version of the function yields:

$$\begin{aligned}
 F(X, Y, Z) &= [1, 2] \times ([1, 2] - [1, 2]) \\
 &= [1, 2] \times [-1, 1] \\
 &= [-2, 2]
 \end{aligned}$$

So we find that the interval extension of the function exactly enclosed all the values of  $f(x, y, z)$  within the given domain. This is not always the case. The example function could also be written as:

$$f(x, y, z) = xy - xz$$

For real values, this would yield identical values to the previous form. In the interval case we find the following:

$$\begin{aligned}
 F(X, Y, Z) &= X \times Y - X \times Z \\
 &= [1, 2] \times [1, 2] - [1, 2] \times [1, 2] \\
 &= [1, 4] - [1, 4] \\
 &= [-3, 3]
 \end{aligned}$$

This result is an overestimate of the range of  $f(x, y, z)$ . This is the so-called dependence problem (Schnepper and Stadherr, 1996), which is encountered when a single interval variable occurs more than once in a function. The interval arithmetic operations will treat these occurrences as separate intervals and not recognise their dependence. The resulting value will always include the true range of the function (Moore, 1966; Schnepper and Stadherr, 1996).

Interval arithmetic may also be found in systems of equations. Consider for example:

**Equation 5.39**

$$\underline{A}\mathbf{x} = \underline{B}, \underline{A} \in \mathfrak{R}^{n \times n}, \mathbf{x} \in \mathfrak{R}^n, \underline{B} \in \mathfrak{R}^n$$

If  $\hat{A} \in \mathbb{R}^{n \times n}$  and  $b \in \mathbb{R}^n$ , then the solution to this system of interval equations is the set:

**Equation 5.40**

$$S = \{x \mid \hat{A}x = b, \hat{A} \in \underline{A}, b \in B\}$$

This set is in general not an interval box and may have very complicated geometry (Schnepper and Stadherr, 1996). In order to solve Equation 5.39, one would rather seek a box containing  $S$ . Various techniques have been developed to do this (Neumaier, 1990).

**5.5.3.2 The Interval Newton Method**

In order to find all the solutions to the system of non-linear real equations,  $f(x) = 0$  within a specified box, we may employ Newton's method, extended to intervals:

**Equation 5.41**

$$\underline{F}'(X^{(k)})(N^{(k)} - x^{(k)}) = -f(x^{(k)})$$

With

- $k$ : An iteration counter
- $X^{(k)}$ : The current box
- $\underline{F}'(X^{(k)})$ : A suitable interval extension of the real Jacobian  $J(x)$  of  $f(x)$  over the current box  $X^{(k)}$
- $x^{(k)}$ : A point in the interior of  $X^{(k)}$ , usually the midpoint
- $f(x^{(k)})$ : The system of non-linear equations

The basic idea is to solve Equation 5.41 for  $N^{(k)}$ , as any root,  $x^* \in X^{(k)}$ , of  $f(x)$  will also lie within the interior of  $N^{(k)}$  (Moore, 1966). Once the box  $N^{(k)}$  has been found, it may be used in the following iteration:

### Equation 5.42

$$X^{(k+1)} = X^{(k)} \cap N^{(k)}$$

Various methods of solving for  $N^{(k)}$  have been proposed (Schnepper and Stadherr, 1996). These methods differ in the tightness with which  $N^{(k)}$  encloses the solution of Equation 5.41. Clearly a tighter enclosure will lead to faster convergence of the iterations in Equation 5.42.

As for systems of real equations, Equation 5.41 may be solved through an interval version of Gaussian elimination, but is more often solved with a Gauss-Seidel procedure (Schnepper and Stadherr, 1996). The Gauss-Seidel procedure computes  $N^{(k)}$  on a component-by-component basis. After each component is calculated, it may be used in the iteration process described with Equation 5.42 and the result used to calculate the subsequent components of  $N^{(k)}$ . This strategy, while not enclosing the complete solution set of Equation 5.41, will enclose the part necessary for the interval Newton iteration (Schnepper and Stadherr, 1996). The procedure is as follows (Hansen and Greenburg, 1983):

1. First precondition Equation 5.41 with a real matrix  $Y^{(k)}$ . The system then becomes:

### Equation 5.43

$$Y^{(k)} \underline{F}'(X^{(k)}) (N^{(k)} - x^{(k)}) = -Y^{(k)} f(x^{(k)})$$

$Y^{(k)}$  is chosen to be the inverse of the midpoint matrix of  $\underline{F}'(X^{(k)})$  (Kearfott et al, 1991; Schnepper and Stadherr, 1996).

2. Solve for  $N^{(k)}$  by executing the steps in Equation 5.44 once for each of its components.

**Equation 5.44**

$$\underline{M} = Y^{(k)} \underline{F}'(\underline{X}^k) \quad (a)$$

$$\underline{b} = Y^{(k)} \underline{f}(\underline{x}^{(k)}) \quad (b)$$

$$N_i^{(k)} = x_i^{(k)} - \frac{b_i + \sum_{j=1}^{i-1} M_{ij} (X_j^{(k+1)} - x_j^{(k+1)}) + \sum_{j=i+1}^n M_{ij} (X_j^{(k)} - x_j^{(k)})}{M_{ii}} \quad (c)$$

$$X_i^{(k+1)} = N_i^{(k)} \cap X_i^{(k)} \quad (d)$$

With

$N_i^{(k)}$ : The  $i$ 'th component of  $N^{(k)}$ , an interval

$x_i^{(k)}$ : The  $i$ 'th component of  $\underline{x}^{(k)}$ , a real value

$X_i^{(k)}$ : The  $i$ 'th component of  $\underline{X}^{(k)}$ , an interval

$b_i$ : The  $i$ 'th component of  $\underline{b}$ , a real value

$M_{ij}$ : The entry in  $\underline{M}$  in row  $i$  and column  $j$ , an interval

3. If  $0 \in M_{ii}$  for any  $N_i^{(k)}$ , extended interval arithmetic should be used.

If  $X^{(k+1)} = X^{(k)} \cap N^{(k)} = \emptyset$ , there is no solution of  $f(\underline{x})$  in  $X^{(k)}$ , since this solution would also have been enclosed in  $N^{(k)}$ . It has also been proven for several techniques for finding  $N^{(k)}$ , that if  $N^{(k)} \subset X^{(k)}$ , there is a unique zero of  $f(\underline{x})$  in  $X^{(k)}$  and that Newton's method for real values will converge to this root from any starting point inside  $X^{(k)}$  (Neumaier, 1990).

These two facts can be used as an existence and uniqueness test for roots. This can be used in the same manner as Harding et al (Harding et al, 1997; Harding and Floudas, 2000) used the value of the solution of the convex related problem to test for the existence of a root of the real problem. The added benefit of a uniqueness test makes this method much more powerful.

The basic algorithm proceeds as follows:

1. Set the initial search box,  $X^{(k)}$ , to the entire search space.
2. Calculate  $N^{(k)}$ , using the method of Hansen et al described above.
3. If  $X^{(k)} \cap N^{(k)} = \emptyset$ , there is no root in  $X^{(k)}$  and the box may be discarded.  
If  $N^{(k)} \subset X^{(k)}$ , there is an unique root in  $X^{(k)}$  and it may be found with Newton's method for real arithmetic.
4. If neither of the conditions in step 3 is met, the iteration process described in Equation 5.42 may be repeated, or the box may be bisected. Schnepper and Stadherr (Schnepper and Stadherr, 1996) suggest that the box be bisected if the ratio of the volumes of the boxes,  $V(X^{(k+1)}) / V(X^{(k)}) > 0.6$ .
5. If the box is bisected, the process is repeated for each of the new boxes.

#### 5.5.4 Comments on Simultaneous Methods

The branch and bound strategy used by Maier et al (Maier et al, 1988; Maier et al, 1999) is in essence the same as that used by Harding (Harding et al, 1997; Harding and Floudas, 2000). Both of these methods are theoretically guaranteed to find all the azeotropes predicted by the thermodynamic model that is used. Unfortunately, these methods are not very fast.

For the system Acetone / Methyl Acetate / Ethyl Formate, Maier et al (Maier et al, 1988) report a processor time of 2.72 sec. on a Sun Ultra 1/140 workstation. The processor times for other ternary systems vary between 1.32 sec. and 3.72 sec. Harding reports a processor time of 8.66 sec. on a Hewlett Packard 9000/730 workstation to find all of the azeotropes for the Acetone / Methyl Acetate / Methanol system.

Even if these processor times could be reduced to only one second per ternary system, it would take almost 28 hours for the 100 000 systems

that would have to be tested in a standard 10 generation design with 10 000 chromosomes in the population. This renders these methods practically useless for any molecular design application.

They should however not be written off completely. Moore's Law states that the number of transistors in a standard computer's processor should double every 18 months. Not only has this "law" been obeyed since its formulation by Gordon Moore (co-founder of Intel) in 1965, the rate of increase is itself increasing! (Harrow, 2001) Within the foreseeable future standard desktop computers may become fast enough so that the methods described above will not take seconds to execute, but only fractions of a second. Until then however, other methods must be found.

The first step in increasing the speed of a search algorithm is to divide the problem into separate searches for binary and multi-component azeotropes. Binary azeotropes are easily found by locating the extrema of the bubble or dew point pressure curves. Once these binary azeotropes have been located, an efficient method for locating higher azeotropes, especially ternary azeotropes, is required.

Two such methods were developed and will be discussed in the following sections.



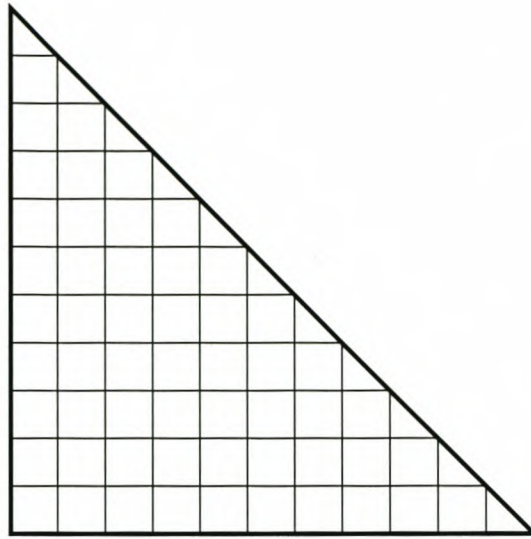
### 5.5.5 Grid Search Method

As stated above, we are interested in finding heterogeneous ternary azeotropes. As all heterogeneous azeotropes are low boiling (Gmehling et al, 1998; Seader and Henley, 1998), such an azeotrope may be found by locating the point of maximum pressure within the region of partial miscibility.

Although a gradient-based method would be very efficient in finding such a pressure maximum, these methods often fail to find the ternary azeotrope. This may be attributed to the complexity of the bubble point pressure surface projected onto the composition space. Various authors have reported the existence of ridges and valleys on this surface. It has also been shown that these ridges and valleys do not start or end at pure components or azeotropes (Rev, 1992; Widagdo and Seider, 1996).

In order for a gradient-based method to find the ternary azeotrope, a starting point close to the azeotrope must be used. To find such a point a grid search is executed.

A grid may be superimposed on the ternary diagram as shown in Figure 5.7. At each internal grid point a liquid-liquid equilibrium calculation is done in order to establish the boundaries of the miscibility gap. The grid point within the two-liquid region, at which the maximum bubble point pressure is calculated, is used as the starting point for the gradient method. Coarsening the grid can reduce the number of calculations that must be performed and so increase the speed of the method. Too coarse a grid however, may cause the method to fail, as the starting point may be too far from the azeotrope.



**Figure 5.7 The Search Grid**

With a well-executed flash algorithm, this method is surprisingly efficient when compared to the simultaneous methods described in previous sections. The search typically executes in less than 0.1 seconds on an Intel Pentium III 933MHz desktop PC, when using UNIFAC as the thermodynamic model.

Once the azeotrope has been located, an eigenvalue test will determine whether it is a saddle or negative node. If both eigenvalues of the Jacobian of Equation 5.8 (a) are positive, the azeotrope will be a negative node. If one eigenvalue is positive and the other negative, the azeotrope will be a saddle point.

Alternatively, the pressure may be calculated at a number of points surrounding the azeotrope. The pressure profile found in this manner may then be compared to that of a local maximum and a saddle point (Figure 5.2) to determine the type of azeotrope.

This search method may be directly extended to quaternary or higher systems. As higher azeotropes are very rare (Gmehling et al, 1994), the

search would typically be for ternary azeotropes formed by the components of the multi-component mixture. Not all triplets need be tested. It has been proven by Doherty and Perkins (Doherty and Perkins, 1979) that ternary azeotropes cannot form in systems with no binary azeotropes. This means that only those combinations where at least one binary azeotrope forms need be considered.

As we would like to use the azeotrope to effect a separation, the effect of the components that do not form part of the azeotrope (the non-azeotrope components) should be investigated. The interactions of a non-azeotrope component with one or more of the azeotrope components may 'break' the azeotrope. This is the case in the separation of azeotropic mixtures with extractive distillation, where the solvents are chosen specifically to break any azeotropes formed by the key components. Should the azeotrope not exist in the presence of one or more of the non-azeotrope components, the azeotrope would not be suitable for heterogeneous azeotropic distillation.

The effect of the non-azeotrope components may be investigated by doing a series of bubble-point flash calculations. The components that do not form part of the azeotrope are added in various ratios to the azeotropic composition to make up the feed streams for each flash calculation.

The vapour and liquid compositions calculated in the flash are then compared on a non-azeotrope component free basis. If they are identical, the azeotrope was not affected by the presence of the extra components and should be suitable to effect the desired separation. If these vapour and liquid compositions differ, the azeotrope may have been broken by one or more of the non-azeotrope components.

If the azeotrope is not affected by the extra components present in the feed, the entrainer should be suitable to affect the desired separation, if not, another entrainer must be found.

### **5.5.6 Residue Curve Tracing Method**

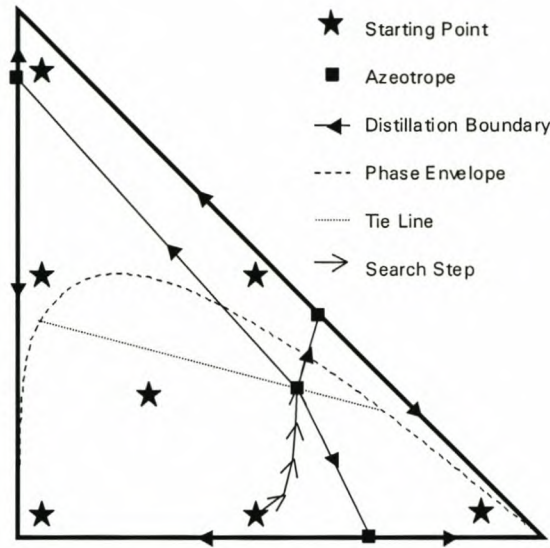
As an alternative to the grid search method described above, we may make use of the fact that we wish to find a negative node. As all residue curve lines originate in negative nodes, we need only trace these lines back to their origin to find any suitable heterogeneous azeotrope present, provided that we start within the correct distillation region.

As binary azeotropes may also form negative nodes, this method will locate both binary and ternary heterogeneous azeotropes that are the lowest boiling species in their distillation regions. Should a heterogeneous binary azeotrope form that boils at a lower temperature than any other pure component or azeotrope, it may also be used to affect the desired separation, provided it forms between the entrainer and one of the key components.

The process consists of a series of liquid-liquid flashes and bubble point calculations to find the vapour composition and pressure. The vapour composition calculated in such a flash is then used as the feed composition to the next flash. In this manner the residue curves are traced back to their origin. The azeotrope is found within a specified tolerance by doing a convergence check on the vapour composition calculated in each step.

To ensure that lowest boiling azeotrope is found, several starting points may be used as shown in Figure 5.8. Should the residue curve map be divided by distillation boundaries, at least one of these starting points should be in the correct distillation region to terminate at the lowest

boiling azeotrope. Figure 5.8 also shows the stepwise progression from one of these starting points to the azeotrope.



**Figure 5.8 The Residue Curve Tracing Method**

The speed of the method for locating ternary azeotropes may be further increased by making use of the fact that in ternary systems, the ternary azeotrope must be connected by a distillation boundary to a binary saddle. Instead of the seven starting point shown in Figure 5.8, one need only start at the binary azeotropes. This typically gives a maximum of three starting points instead of seven.

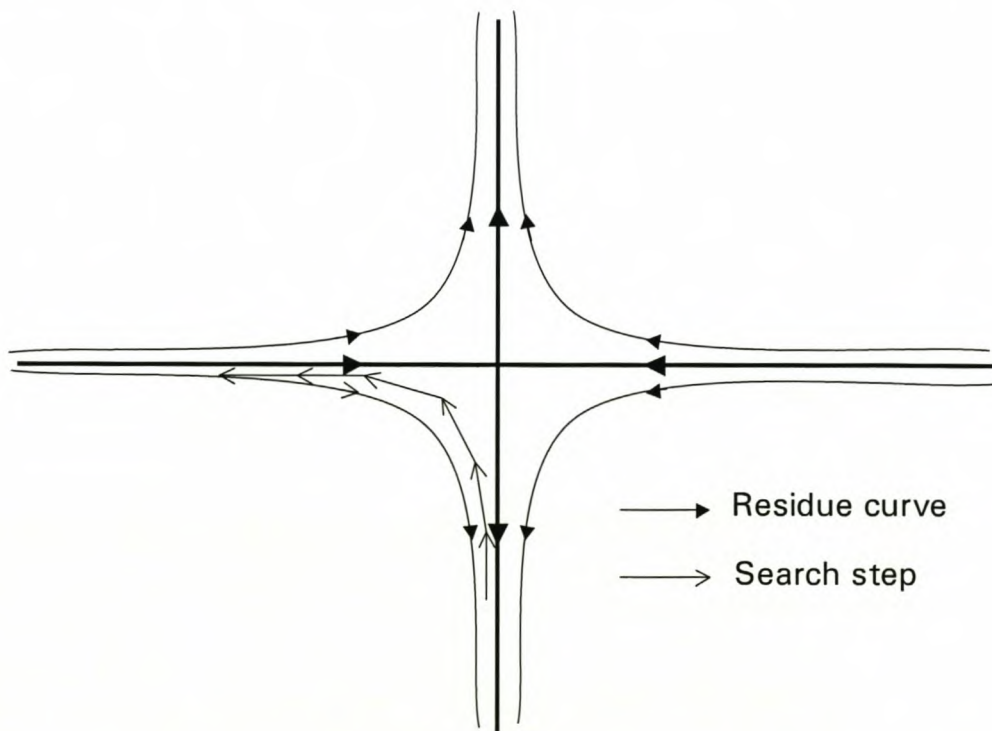
The method may also be applied to quaternary and higher mixtures. The search may be done in the multi-component composition space, but as quaternary azeotropes are exceedingly rare and the very existence of quinary azeotropes a point of debate (Gmehling et al, 1994), this search need in practice only be done for the various component triplets.

A similar approach as with the grid search method is followed in these cases. Component triplets that do not form binary azeotropes may be discarded, as they cannot form ternary azeotropes. All other triplets are

then investigated for suitable heterogeneous ternary azeotropes. As with the grid search method, the effect of the non-azeotrope components on the azeotrope should be investigated in each case.

The search method should not normally terminate at saddle azeotropes unless a search step ends at exactly the azeotropic composition. Because residue curves both start and end at saddle points, the tracing algorithm should change course near a saddle azeotrope to follow residue curves that do not terminate at the saddle. This is illustrated in Figure 5.9.

If the presence of a saddle point azeotrope is suspected, the multiple starting point method discussed above should be used. If the binary azeotropes are used as starting points, the tracing algorithm may run along a residue curve that terminates at the ternary saddle.



**Figure 5.9 The Residue Curve Tracing Method Near Saddle Azeotropes**

As heterogeneous azeotropes can only be saddles or negative nodes (Gmehling et al, 1994; Widagdo and Seider, 1996; Seader and Henley,

1998), this method should always locate a suitable azeotrope if one is present in the system. However, as the ternary azeotrope, if one is present, will not necessarily be the only negative node present in the system, the end-point of each search should be evaluated to ensure that it is indeed a suitable azeotrope.

The method is extremely efficient. Typically only 25 – 30% of the number of calculations done in the grid search method is needed. The specific number of iterations required will depend on the system under consideration.

## ***5.6 A Fitness Function for Entrainers***

The first step in assigning a fitness value to a candidate entrainer is to determine whether a suitable heterogeneous azeotrope is formed by the addition of the entrainer. This azeotrope may be ternary, as is the case when benzene is added to a mixture of water and ethanol, or it may be binary as is found when ethyl acetate is added to a mixture of water and acetic acid.

When more than one suitable azeotrope is formed, and both are negative nodes in their respective distillation regions, the composition of the feed will determine which azeotrope will form the distillate. If it is possible to manipulate the feed composition to fall into the more beneficial distillation region, the azeotrope that forms the negative node in that region may be considered.

When there are components present in the feed that do not form part of the azeotrope, the effect of their presence on the azeotrope should be determined as was discussed above.

Once it has been determined that a suitable heterogeneous azeotrope is formed by the addition of the entrainer and that this azeotrope is a negative node, a relative fitness must be allocated to the chromosome. As stated previously, we would like the miscibility gap at the azeotropic point to be as wide as possible to increase the ease of separation. As such, the liquid-liquid separation factor at the ternary azeotrope may serve as an indication of the suitability of the entrainer.

The separation factor,  $\beta_{ij}$ , is similar to the relative volatility,  $\alpha_{ij}$ , but defined for liquid-liquid systems, instead of vapour-liquid systems. The definition of the separation factor is given in Equation 5.45.

**Equation 5.45**

$$\beta_{ij} = \frac{x_i^I / x_i^{II}}{x_j^I / x_j^{II}}$$

With

- $\beta_{ij}$ : The separation factor of components i and j
- $x_i^I$ : The mole fraction of component i in liquid phase I
- $x_i^{II}$ : The mole fraction of component i in liquid phase II

The separation factor is used in the fitness function in the place of the relative volatility. The penalty function used to help force a liquid-liquid split in the design of solvents for liquid-liquid extraction (Van Dyk, 1998) (Van Dyk and Nieuwoudt, 2001), may also be used.

The fitness function developed here may be improved in one more manner. It may well be possible that an azeotrope forms that consists of mostly entrainer. Although such an entrainer may have a very high selectivity, it will not be an economically attractive choice, due to the large amount of entrainer that would have to be evaporated and



subsequently condensed. The algorithm may be encouraged to find more suitable entrainers by including a penalty based on the amount of entrainer present in the azeotrope.

To implement this penalty system, the selectivity is multiplied by a scaling factor, as shown in Equation 5.46.

#### Equation 5.46

$$\beta_{12}^* = \beta_{12} \frac{c_1}{1 + c_2 \exp(x_E - 0.5)}$$

With

$\beta_{12}^*$ : The scaled selectivity

$x_E$ : The mole fraction entrainer in the azeotrope

$c_1, c_2$ : Constants

The effect of the scaling factor is illustrated in Figure 5.10, with both the constants,  $c_1$  and  $c_2$  set to 4, as is used in SolvGen.

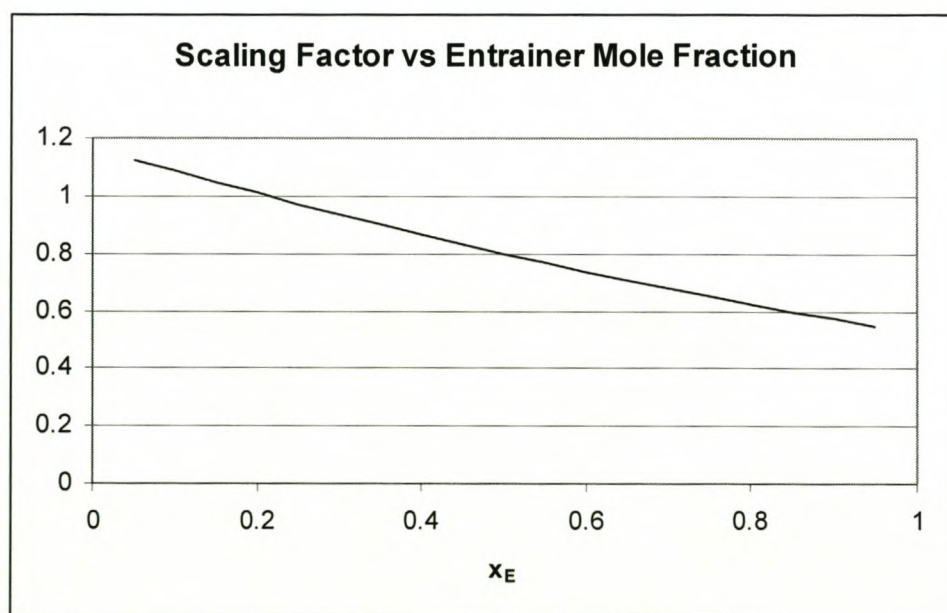


Figure 5.10 The Scaling Factor for Azeotrope Selectivities

The severity of the penalty may be adjusted by modifying the constants. The scaling factor also rewards entrainers with small molar fractions in the azeotrope.

With the inclusion of this scaling factor, the search algorithm will not only find highly selective entrainers, but also those with high capacities, i.e. entrainers that make up a smaller part of the azeotropic composition. This should lead to less expensive separations processes, increasing the profitability of the entire plant.

## **5.7 Conclusions**

With the fitness function and heterogeneous azeotrope location methods developed in this chapter, it is now possible to design entrainers for the heterogeneous azeotropic distillation of binary mixtures. The grid search and residue curve tracing methods may be extended to multi-component mixtures, but as quaternary and higher azeotropes are much more rare than binary and ternary azeotropes, the effort of searching for higher azeotropes is not justified at this point. Rather, binary or ternary azeotropes formed between the entrainer and some of the mixture components should be located. In this case the effect of the non-azeotrope components should be investigated, as discussed.

Unlike simple and extractive distillation, the extent of separation that can be achieved with azeotropic distillation is partly determined by the feed composition, as this determines which distillation regions will be operated in (Widagdo and Seider, 1996). By varying the ratio of entrainer to feed, or the feed composition, it may be possible for the process to operate in a more beneficial distillation region. As the algorithms for finding azeotropes that were developed in this work are relatively fast, entrainer searches may be carried out at various ratios in a reasonable time.

# 6

## 6 Chromatographic Separations

### 6.1 Introduction

Chromatography was first discovered by Mikhail Tswett, a Russian-Polish botanist, in 1903. Although there are differing reports, it is generally accepted that while attempting to separate plant pigments by passing them through a column packed with chalk, he noticed that the different pigments passed through the column at different rates, forming visible colour bands. Based on this observation, he named the phenomenon chromatography – *chroma* (colour) + *graphy* (writing). Tswett first used this name in two papers published by him in 1906 (Christian and O'Reilly, 1986; Lightfoot, 1999).

In 1941 Martin and Synge developed liquid-liquid (or partition) chromatography (LLC). They used a stationary liquid phase, spread over the surface of an inert support. This stationary phase is selected to be immiscible with the mobile liquid phase in which the mixture components are dissolved. These solutes then partition themselves between the liquid phases, influencing the speed with which they move through the column and causing them to separate. In 1952 they were awarded the Nobel Prize in chemistry for their work.

The following are extracts from the presentation speech made by Professor A. Tiselius at the award ceremony (Nobel Institute, 1970):

*"The method of Martin and Synge, in different forms, has already found extensive application in all branches of chemistry and important discoveries have been made with it. New and interesting substances have been traced and isolated with its help. Metabolic pathways in the organism can be studied and formerly unknown intermediary products identified."*

*"Partition chromatography has had other extremely important applications when it has been used as a means of studying the structure of giant molecules."*

*"The young English chemist Sanger has recently succeeded in putting together an unusually difficult puzzle of this sort; from the mixtures which were separated by Martin and Synge's method, among others, he has been able to get an almost complete picture of the structure of the insulin molecule - a result which perhaps more than any other shows the method's great scope and principal significance."*

Sanger was himself awarded with the Nobel Prize in chemistry in 1958 for his work in proteins in general, but specifically for the isolation of insulin.

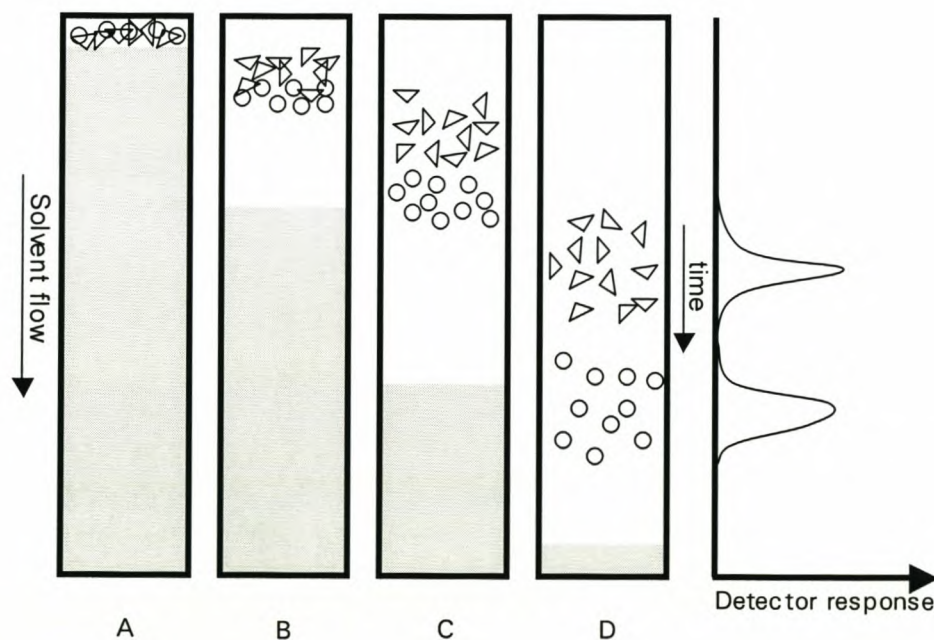
From this, the importance of chromatographic techniques, not just as a method of chemical analysis, but also in the isolation of pharmaceuticals and naturaceuticals (pharmaceutically active compounds of natural origin) may be clearly seen. This is not a past trend - chromatography is still the method of choice for isolating these types of compounds (Cramer and Jayaraman, 1993; Lightfoot, 1999). There are also continuous

developments in the field of process chromatography, where chromatographic separation is applied to larger scale separations in the biotechnology field (Lightfoot, 1999).

## 6.2 The Basic Principles of Chromatography

### 6.2.1 Liquid-Liquid and Gas-Liquid Chromatography

Consider a mixture of two hypothetical components, A and B. This mixture is to be separated via liquid-liquid chromatography. A small sample of the mixture is dissolved in a carrier solvent, the mobile phase, and introduced at the top of the chromatographic column, as seen in Figure 6.1 A



**Figure 6.1 Separation of a Binary Mixture with LC**

The column is packed with a porous support, coated with the stationary phase. The void fraction of the column is taken up by solvent of the mobile phase already present in the column. This solvent is indicated in

Figure 6.1 by the shaded area. As more of the mobile phase is fed into the column, the solvent already present is gradually displaced.

As the solutes are transported through the column, they move at different speeds as a result of interactions with the stationary liquid phase coated on the support and are eventually separated. The progression of this separation is shown in Figure 6.1 A – D. As the solutes pass through the column exit, they are detected by a sensor apparatus and the response of this detector is plotted against time. Such a plot is called a chromatogram, an example of which is also shown in Figure 6.1.

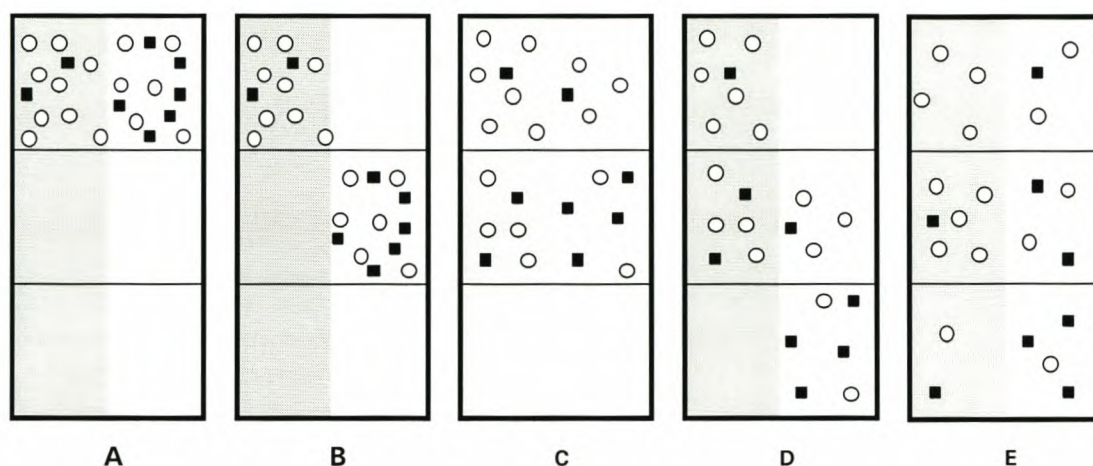
This is the basic method of liquid-liquid chromatography. Gas-liquid chromatography differs from this process only in that the mobile phase is a gas instead of a liquid.

### **6.2.2 A Cell Model for Chromatography**

The mechanism of the separation process may be better understood if the two liquid phases are seen as a series of cells. As the mobile phase flows through the column, the solutes will partition themselves between the two immiscible liquids (or the liquid and gas) in opposite cells until equilibrium is reached. This is the state the system is in, in Figure 6.2 A.

After this local equilibrium has been reached, the mobile phase advances one cell and carries the solute with it. Figure 6.2 B shows the system directly after this has happened. As the concentrations in opposite cells now differ from their equilibrium values, the solute again partitions itself between these phases until equilibrium is reached. Figure 6.2 C shows the system again at equilibrium. The mobile phase now again moves one cell down (Figure 6.2 D) and equilibrium is again reached (Figure 6.2 E).

The two mixture components have different equilibrium concentrations in the stationary phase. The higher the concentration of a solute in the stationary phase cells, the slower it will be carried through the column. This can be seen from the differing mobile phase concentrations of the two species in Figure 6.2 A – E. The greater the difference in the rates at which the solutes are transported through the column, the easier the separation will be.



**Figure 6.2 A Cell Model of the Separation Process**

This model gives a qualitative picture of the separation process. However, if we are to design mobile or stationary phases for chromatographic separations, a quantitative measure is required.

### 6.2.3 Selectivity Measurements

As illustrated with the somewhat crude cell model, the separation in a chromatographic column is a function of the equilibrium concentrations of the solutes in the mobile and stationary phases. The process may be written as follows:



With

$X_s$ : The solute species in the stationary phase

$X_m$ : The solute species in the mobile phase

The distribution coefficient of component X is given by (Christian and O'Reilly, 1986):

### Equation 6.1

$$C_X = \frac{[X]_s}{[X]_m}$$

With

$C_X$ : The distribution coefficient of component X

$[X]_s$ : The concentration of X in the stationary phase [mol/cm<sup>3</sup>]

$[X]_m$ : The concentration of X in the mobile phase [mol/cm<sup>3</sup>]

As the sample that is fed into the column is typically very small compared to the amount of stationary and mobile phase solvents, we may safely assume that the solutes will be infinitely diluted. The relationship for liquid-liquid equilibrium thus becomes:

### Equation 6.2

$$\gamma_s^\infty x_s = \gamma_m^\infty x_m$$

With

$\gamma_s^\infty$ : The infinite dilution activity coefficient of the solute in the stationary phase.

$\gamma_m^\infty$ : The infinite dilution activity coefficient of the solute in the mobile phase.

$x_s$ : The molar fraction of the solute in the stationary phase

$x_m$ : The molar fraction of the solute in the mobile phase



As an infinitely diluted solute will have negligible effect on the volume of the solution, we may make the assumption that the volumes of the mobile and stationary phases will be those of the two solvents. This gives us an expression for the concentrations used in Equation 6.1.

### Equation 6.3

$$[X]_s = \frac{x_s}{v_s}$$

$$[X]_m = \frac{x_m}{v_m}$$

With

$v_s$ : The molar volume of the stationary phase solvent [cm<sup>3</sup>/mol]

$v_m$ : The molar volume of the mobile phase solvent [cm<sup>3</sup>/mol]

Combining Equation 6.3 with Equation 6.1 and Equation 6.2 gives:

### Equation 6.4

$$C_X = \frac{v_m \gamma_m^\infty}{v_s \gamma_s^\infty}$$

This is the same result published by Park et al (Park et al, 1991; Park et al, 1993) for liquid-liquid chromatography. Gas-liquid chromatography may be treated similarly. In this case the equilibrium relationship is:

### Equation 6.5

$$y_m P = x_s \gamma_s^\infty P_x^{sat}$$

With

$y_m$ : The molar fraction of the solute in the mobile (gas) phase

P: The total pressure

$x_s$ : The molar fraction of the solute in the stationary phase

$P_x^{sat}$ : The vapour pressure of the pure solute

In Equation 6.5 the assumption of an ideal vapour phase has been made. We may further eliminate the pressure by using the ideal gas law. This result in:

**Equation 6.6**

$$\frac{x_s}{y_m} = \frac{RT}{v_m \gamma_s^\infty P_x^{sat}}$$

Combining the equation with Equation 6.1 and Equation 6.3 yields an equation for the distribution coefficient:

**Equation 6.7**

$$C_X = \frac{RT}{v_s \gamma_s^\infty P_x^{sat}}$$

This result is again the same as that published by Park et al (Park et al, 1991).

According to Christian and O'Reilly (Christian and O'Reilly, 1986), a more practical measurement is the so-called capacity factor, defined by Equation 6.8.

**Equation 6.8**

$$K_X = \frac{\text{Total moles of } X \text{ in stationary phase}}{\text{Total moles of } X \text{ in mobile phase}} = \frac{V_s [X]_s}{V_m [X]_m} = \frac{V_s}{V_m} C_X$$

With

- $V_m$ : The volume of the mobile phase in the column (also called the dead volume)
- $V_s$ : The volume of the stationary phase in the column
- $K_X$ : The capacity factor of solute X

This value can be directly determined from a chromatogram by means of Equation 6.9 (Christian and O'Reilly, 1986).

### Equation 6.9

$$V_r = V_m(1 + K_X) = V_m + V_s C_X$$

With

$V_r$ : The retention volume for the solute

The retention volume is the volume of mobile phase that must flow through the column before solute  $X$  exists. For a constant flow system, this is directly proportional to the retention time of the solute, which leads to the following relationship between capacity factor and retention time:

### Equation 6.10

$$K_X = \frac{t_r - t_0}{t_0}$$

With

$t_r$ : The retention time

$t_0$ : The column dead time

The column dead time is the time required to displace the mobile phase present in the column at the start of the process.

The ratio of retention times for two solutes will thus be proportional to the ratio of their capacity factors. By combining this concept and Equation 6.8 with Equation 6.4 for liquid-liquid chromatography and Equation 6.7 for gas-liquid chromatography, the following may be found:

For liquid-liquid chromatography:

**Equation 6.11**

$$\delta_{12} = \frac{\gamma_{1,m}^{\infty} \gamma_{2,s}^{\infty}}{\gamma_{1,s}^{\infty} \gamma_{2,m}^{\infty}}$$

With

$\delta_{12}$ : The relative selectivity of the column

$\gamma_{j,s}^{\infty}$ : The infinite dilution activity coefficient of component j in the stationary phase

$\gamma_{j,m}^{\infty}$ : The infinite dilution activity coefficient of component j in the stationary phase

For gas-liquid chromatography:

**Equation 6.12**

$$\delta_{12} = \frac{\gamma_{2,s}^{\infty} P_2^{sat}}{\gamma_{1,2}^{\infty} P_1^{sat}}$$

We now have a direct relationship between the infinite dilution activity coefficients of the solutes and their relative retention times in the column. This may be used as a measure of the selectivity of the column for each solute.

### **6.3 A Fitness Function for Chromatographic Separation**

The infinite dilution activity coefficients may be estimated with UNIFAC. It has been proven by Park et al (Park et al, 1991; Park et al, 1993) that UNIFAC is accurate enough for at least qualitative predictions of retention times and to show the relative merit of one solvent phase over another.

As the UNIFAC interaction parameters are continuously updated and improved by the work of Gmehling and others (Hansen et al, 1991; Gmehling et al, 1998), the ability of UNIFAC to quantitatively predict retention time will improve.

The estimated selectivity must now be transformed into a measure of the fitness of a chromosome. Due to the similarity of liquid-liquid chromatography to liquid-liquid extraction, the functional form of the fitness function used for this process (Equation 2.7) may be employed directly. The selectivity estimated with the equations derived in this chapter, simply replaces the selectivity calculated for the liquid extraction process.

The same penalty function to enforce a liquid-liquid split is also used to ensure that the stationary and mobile phases will be immiscible.

Similarly, the fitness function used for extractive distillation may be employed in the case of gas-liquid chromatography. This is similar in form to that of liquid-liquid extraction, but now phase-split is neither required, nor desired. Again the selectivity estimated from this work is used.

## **6.4 Conclusions**

Once a fitness function has been developed, it is possible to use the SolvGen algorithm to design either stationary or mobile phases for chromatographic separations.

These two solvents may be designed together, using the algorithms for blended solvents developed earlier. The requirements for solvent recovery must however differ from that which would be used for liquid-liquid extraction. In liquid-liquid extraction processes, it is desirable for the components in the solvent mixture to remain in the same liquid phase,

whereas for this design the components are required to separate into two liquid phases.

The design may also be limited to one of the solvents, by using a pure solvent algorithm and specifying either the stationary or mobile phase solvent.

To avoid mixing of the two phases, the mobile phase is selected to have an opposite polarity than the stationary phase. In normal operations the stationary phase will be the non-polar solvent. If a polar stationary phase is used, the process is called reverse-phase chromatography (Christian and O'Reilly, 1986; Park et al, 1993).

Traditionally the stationary phase is considered to be responsible for determining the selectivity of a column. This may well be the case in gas-liquid chromatography, but the effect of the mobile phase should not be disregarded in liquid-liquid chromatography.

It is unfortunate that the UNIFAC model is not yet accurate enough to make quantitative predictions for complex macromolecules, although the free volume modifications of UNIFAC have been successfully applied to polymer systems. The model is however undergoing constant improvement and may in the foreseeable future reach the required level of accuracy. Work is currently underway at the Computer-Aided Process Engineering Centre at the University of Denmark, under Prof. Rafiqul Gani and others, to extend the free volume modification of UNIFAC to accurately predict the solubilities of proteins and other complex macromolecules (CAPEC, 2001).

In this and the previous chapters, the SolvGen algorithm has been improved and extended to processes like heterogeneous azeotropic distillation and chromatographic separations. To test the effectiveness of

these modifications a number of separation problems with industrial relevance will be considered.

These case studies will include extractive distillation, liquid-liquid extraction, heterogeneous azeotropic distillation and chromatographic separations. In each case the SolvGen algorithm will be employed to find solvents or entrainers that will perform better than those that are currently used in industry.

# 7

## **7 Case Studies in Computer-Aided Molecular Design**

### ***7.1 Introduction***

In this chapter, the SolvGen algorithm will be applied to various solvent design problems. In each case the results will be compared with solvents that are currently in use in industry, if any are available.

### ***7.2 Extractive Distillation Problems***

#### **7.2.1 Binary Systems**

The simplest test for the algorithm's ability to find good solvents for extractive distillation is the separation of binary mixtures. There are many such examples in industry and the literature. Three systems were selected and solvents were designed to enable the separation of these mixtures by means of extractive distillation. The systems are listed in Table 7.1.



**Table 7.1 Test Systems for Solvent Design**

Components	Industrial Solvent
Methanol / Acetone	Ethylene Glycol, Water
Cyclohexane / Benzene	Aniline
C <sub>7</sub> + C <sub>8</sub> Isomers / Toluene	Aniline, Phenol

It was proposed to find solvents that would outperform those that are currently in use. As a measure of comparison, the relative volatilities attained with a solvent at 350K and the mixture's bubble-point pressure was used. Equation 7.1 was used to calculate these values. For all of these tests a solvent to feed ratio of 4:1 (molar) was used. The feed stream in all cases was an equimolar mixture of the two components.

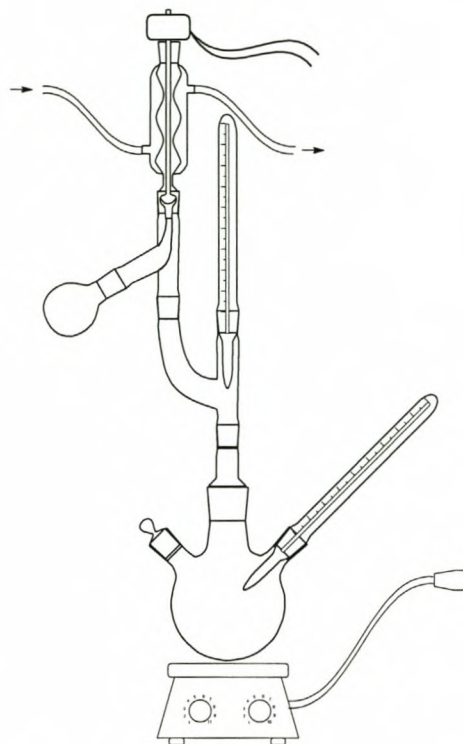
**Equation 7.1**

$$\alpha_{ij} = \frac{y_i/x_i}{y_j/x_j}$$

As the design algorithm can only function within the search space provided by the group-contribution methods, the relative volatilities and boiling points listed here are those estimated by the Modified UNIFAC (Dortmund) method (Gmehling et al, 1998) and the MMPF-GC-NL method (Marrero-Morejón and Pardillo-Fontdevila, 1999). The only exception is when 1-methyl-2-pyrrolidone (NMP) was used as solvent. This molecule is not currently supported as an individual molecule by the version of the Modified UNIFAC (Dortmund) model available in the literature. In these cases standard UNIFAC (Hansen et al, 1991) was used.

Comparing the predicted relative volatilities of the proposed and industrial solvents gives us a fair indication as to the success of the algorithm in finding better solvents. Predictive models should however always be

verified. The proposed solvents were tested in a simple equilibrium still (Figure 7.1) at 0.95 barA. The measured relative volatilities are indicated where available.



**Figure 7.1 A Simple Equilibrium Still**

### ***Methanol / Acetone***

Acetone and methanol are among the most widely used solvents in industry. The methanol / acetone system forms a homogeneous azeotrope that makes the system a very good candidate for separation by extractive distillation. Two solvents are commonly used to separate this system (Seader et al, 1997) – water and ethylene glycol.

Alternative solvents were also previously designed with SolvGen for this separation (Van Dyk and Nieuwoudt, 2000). Some of the proposed solvents are listed in Table 7.2.

**Table 7.2 Solvents for the Acetone (1) / Methanol (2) System**

Proposed Solvents	Predicted $\alpha_{12}$	Measured $\alpha_{12}$ [Solvent : Feed]	$T_b$ [K]
<chem>CNCCN</chem> N,N'- dimethylethylenediamine	4.71	7.73 [1.08 : 1]	405.9
<b>Industrial Solvents</b>			
H <sub>2</sub> O Water	3.12	-	373.2
<chem>OCCO</chem> Ethylene glycol	3.50	-	470.4

Clearly the N,N'-dimethylethylenediamine performs much better than either water or ethylene glycol in this separation. This prediction was experimentally verified.

In this design, primary amines were not allowed, as these compounds would react with the acetone. This is achieved by setting the selection probabilities of all genes with primary amine groups to zero.

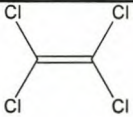

The increase in relative volatility attained with N,N'-dimethylethylene will allow smaller columns to be used to attain the same purity of product, resulting in a capital saving. If an existing column is used, a higher purity may be reached with the improved solvent.

Both of the commercial solvents cause acetone to be recovered in the distillate. The ability to recover either component in the distillate would give added flexibility when designing the separation process. This is especially so if the feed consists of mainly acetone that must be purified. Should acetone be recovered in the distillate, all of the acetone must be

evaporated and then condensed, increasing the cost of utilities. In these cases it would be preferable to recover methanol in the distillate.

It was therefore proposed to design a solvent that would allow the recovery of methanol in the distillate, instead of the more volatile acetone. The results are listed in Table 7.3.

**Table 7.3 Solvents for the Methanol (1) / Acetone (2) System**

Proposed Solvents	Predicted $\alpha_{12}$	Measured $\alpha_{12}$ [Solvent : Feed]	$T_b$ [K]
 Tetrachloroethylene	5.44	2.57 [5.21 : 1]	394.0
 1,4-Dibromobutane	3.93	6.12 [1.66 : 1]	402.9

The proposed solvents performed well, but are unfortunately either chlorinated or brominated compounds and would as such not be popular choices. These solvents also illustrate the unfortunate inaccuracies that are sometimes encountered when using UNIFAC. In both cases the predicted relative volatilities were incorrect by a considerable margin. The importance of testing the predictions of any group-contribution method cannot be overemphasised.

As chlorinated and brominated compounds are generally unpopular due to environmental and health reasons, genes containing chlorine and bromine were deactivated and a second design run was done. The result for this run is shown in Table 7.4.

**Table 7.4 More Solvents for the Methanol (1) / Acetone (2) System**

Proposed Solvents	Predicted $\alpha_{12}$	Measured $\alpha_{12}$ [Solvent : Feed]	$T_b$ [K]
$\text{CH}_3(\text{CH}_2)_{10}\text{CH}_3$ Dodecane	2.44	1.56 [3.27 : 1]	500.7

Although dodecane did not cause as large a relative volatility as the chlorinated and brominated compounds, it is not toxic nor harmful. A higher solvent to feed ratio will increase the relative volatility of the methanol over acetone and lead to a better separation.

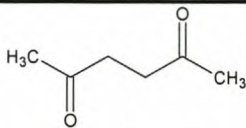
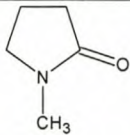
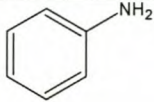
This last example illustrates the power of CAMD when applied to common separation problems. An easily available, inexpensive solvent has been identified that allows the natural relative volatility of the acetone / methanol system to be reversed. If a large proportion of the feed stream is acetone, the ability to recover methanol in the distillate will result in considerable savings in utilities costs. This is because all of the acetone need not be evaporated and subsequently condensed.

### ***Cyclohexane / Benzene***

Benzene and cyclohexane may be co-produced, as in the new benzene and cyclohexane production facility at Al Jubail (Saudi Arabia), co-owned by Chevron and Saudi Industrial Venture Capital Group (Technology, 2001). Benzene may also be converted to cyclohexane to lower the benzene content in petrol/gasoline in order to meet new EU regulations that came into effect on January 1<sup>st</sup> 2000.(BRC, 2001). In both these processes, the separation of benzene from cyclohexane becomes a necessary step - in the former case, to purify the products, in the latter, to recover benzene in order to recycle it to the reactor.

Benzene and cyclohexane form a minimum boiling azeotrope and may be separated by means of extractive distillation with aniline as solvent (Seader et al, 1997). Cyclohexane will be recovered in the distillate. Alternative solvents were designed for this separation; the results are given in Table 7.5.

**Table 7.5 Solvents for the Cyclohexane (1) / Benzene (2) System**

Proposed Solvents	Predicted $\alpha_{12}$	Measured $\alpha_{12}$ [Solvent : Feed]	$T_b$ [K]
 Acetylacetone	2.89	4.87 [1.89 : 1]	439.0
 1-Methyl-2-Pyrrolidone (NMP)	4.16*	6.00 [3.68 : 1]	475.2
<b>Industrial Solvents</b>			
 Aniline	2.12*	-	417.1

\*  $\alpha_{12}$ -value from UNIFAC (Hansen et al, 1991)

The two proposed solvents, acetylacetone and NMP are both classified as non-toxic (Sigma-Aldrich, 2001). Aniline, which is commercially used for this separation is classified as toxic and highly carcinogenic (Sigma-Aldrich, 2001). Not only are the proposed solvents safer, they also promise a much-improved separation. This prediction was experimentally tested and found to hold true. In both cases, the solvents performed better than predicted.

Again, through the application of CAMD techniques, it was possible to find improved solvents for an industrially important separation process. The use of these solvents may lead to the use of smaller columns to affect the same degree of separation. Should an existing process be converted to the new solvents, higher purities may be attained. In either case there will be a definite impact of the profitability of the process.

### ***C7 + C8 Isomers / Toluene***

The separation of aliphatics and aromatics of similar molecular weight and/or boiling point is of definite industrial importance. The petrol/gasoline produced by fractionation of crude oils contains mostly unbranched hydrocarbons with a very low octane rating. In order to improve the anti-knock characteristics of the fuel, refineries often reform these compounds into aromatics. (Key, 2001). This is the main source of benzene, toluene and xylenes (BTX) in petrol/gasoline. In order to recycle the unreacted aliphatics back to the reformer, it must be separated from the aromatic products.

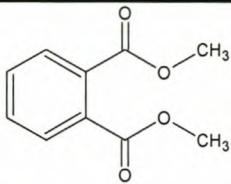
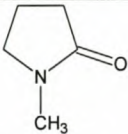
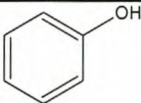
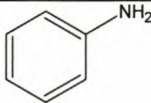
With new regulations on the amount of aromatics allowed in petrol/gasoline (BRC, 2001), less BTX will be produced by reforming and aromatics may even be removed from the fuel in future (SRI Consulting, 2001). In either case the separation of close boiling aromatics and aliphatics remain an important industrial process.

As representative compounds of the relevant aliphatics, a mixture of heptane and octane isomers was used. Toluene was used to represent the BTX compounds.

Aniline and Phenol are currently used to separate heptane isomers from toluene (Seader et al, 1997). The difficulty of the separation is increased by the requirement that the octane isomers be recovered in the distillate.

A solvent was designed to enable this separation. The results are listed in Table 7.6.

**Table 7.6 Solvents for the C<sub>7</sub> + C<sub>8</sub> Isomers (1) / Toluene (2) System**

Proposed Solvents	Predicted $\alpha_{12}$	Measured $\alpha_{12}$ [Solvent : Feed]	T <sub>b</sub> [K]
 Dimethyl Phthalate	5.33	6.89 [3.63 : 1]	545.1
 1-Methyl-2-Pyrrolidone (NMP)	6.06*	6.36 [3.79 : 1]	475.2
<b>Industrial Solvents</b>			
 Phenol	4.27	-	420.9
 Aniline	4.72	-	417.1

\*  $\alpha_{12}$ -value from UNIFAC (Hansen et al, 1991)

The two solvents that are currently used in industry are classified as toxic (phenol) and both toxic and carcinogenic (aniline). In contrast to this, the proposed solvents are both non-toxic (Sigma-Aldrich, 2001). Not only are dimethyl phthalate and NMP safer to use, but they are also predicted to perform better than the currently used solvents. These predictions were verified experimentally.



Again it was possible to improve on an industrially important separation process through the use of CAMD.

### 7.2.2 Blended Solvents for Extractive Distillation

In the examples above, binary mixtures were used to test the algorithm's ability to design effective pure solvents. A similar approach will be followed to examine the design of blended solvents.

Blended solvents allow the distribution of the active functional groups that cause the increase in relative volatility to be spread over a number of molecular backbones. If these functional groups were to be contained by a single molecule, the complexity of the structure would potentially make the solvent difficult to synthesise and thus expensive. There is also the potential that the solvent blends may affect a better separation than their component solvents, due to synergistic effects in the blend.

Three test systems were chosen; they are listed in Table 7.7

**Table 7.7 Test Systems for Blended Solvent Design**

Components	Industrial Solvent
Acetone / Methanol	Ethylene Glycol, Water
Ethanol / Ethyl Acetate	Trimethylbenzene
Methanol / Methyl Acetate	2-Methoxyethanol

As before, all solvent designs were done for an equimolar feed at 350K, with a solvent to feed ratio of 4:1. The blended solvents are in all cases equimolar mixtures of the components.

All selectivities given are as predicted by the Modified UNIFAC (Dortmund) method (Gmehling et al, 1998), except where stated

otherwise. The boiling points were estimated with the MMPF-GC-NL method (Marrero-Morejón and Pardillo-Fontdevila, 1999).

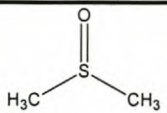
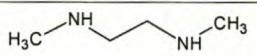
### **Acetone / Methanol**

As stated above, two solvents are currently used to separate this system by means of extractive distillation. These are ethylene glycol and water, both of which will allow the recovery of acetone in the distillate.

Improved solvents have been generated for this system previously (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000) and in this work. The ability of blended solvents to outperform the pure solvents was also investigated.

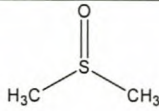
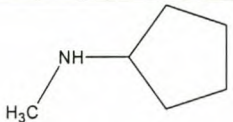
Two solvent blends were designed (Table 7.8). The relative volatilities attained with the individual solvents are also listed for comparison.

**Table 7.8 Blended Solvents for the Acetone (1) / Methanol (2) System**

Pure solvents			Blended Solvents	
Solvent	$\alpha_{12}$	$T_b$ [K]	Solvent	$\alpha_{12}$
 Dimethyl sulfoxide (DMSO)	2.98*	464.1	DMSO + DMEDA	8.14*
 N,N'-dimethylethylenediamine (DMEDA)	5.81	405.9		

\*  $\alpha_{12}$ -value from UNIFAC (Hansen et al, 1991)

Table 7.8 (Continued)

Pure solvents			Blended Solvents	
Solvent	$\alpha_{12}$	$T_b$ [K]	Solvent	$\alpha_{12}$
 Dimethyl sulfoxide (DMSO)	2.98*	464.1	DMSO + N,N-Methylcyclopentylamine	5.96*
 N,N-Methylcyclopentylamine	3.74	432.1		

\*  $\alpha_{12}$ -value from UNIFAC (Hansen et al, 1991)

As can be seen from the listed relative volatilities, the blended solvents perform better than their individual components. This may be due to a synergistic effect in the blend. The accuracy of these predictions, and thus the existence of this synergy, must still be verified experimentally.

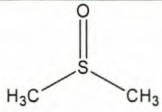
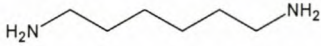
In both cases the blend was made up from DMSO and a secondary amine. Primary amines were not allowed, as these will react with the acetone.

### ***Methyl Acetate / Methanol***

This system also forms a minimum boiling azeotrope, which may be separated using ethylene glycol monomethyl ether (2-methoxyethanol) as solvent (Seader et al, 1997). The estimated relative volatility with this solvent is 2.21 (UNIFAC) with methyl acetate in the distillate. As with the previous system, improved solvents have been designed for this system (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000). In this work, the focus was moved to solvent blends.

The solvent blend proposed for this system is given in Table 7.9. The effects of the individual components are again listed for comparison.

**Table 7.9 Blended Solvents for the Methyl Acetate (1) / Methanol System**

Pure solvents			Blended Solvents	
Solvent	$\alpha_{12}$	$T_b$ [K]	Solvent	$\alpha_{12}$
 Dimethyl sulfoxide (DMSO)	3.55 *	464.2	DMSO + Hexamethylenediamine	7.83 *
 Hexamethylenediamine	2.80	472.8		

\*  $\alpha_{12}$ -value from UNIFAC (Hansen et al, 1991)

The synergistic effect of the blend is again evident in these results. The blended solvent attains a much higher relative volatility than was the case with the individual components. Again, this prediction should be verified experimentally.

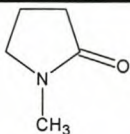
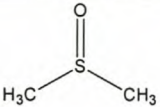
### ***Ethyl Acetate / Ethanol***

The third system is that of ethanol and ethyl acetate. This system forms a low boiling azeotrope. Aromatics, like trimethylbenzene, have been proposed as solvents for separating this system with extractive distillation (Seader et al, 1997), resulting in ethanol being recovered in the distillate. The predicted relative volatility for this separation is 3.27 (UNIFAC). Improved pure solvents for this separation have also been designed previously (Van Dyk, 1998; Van Dyk and Nieuwoudt, 2000).

The ability to manipulate which component is recovered in the distillate will give greater flexibility in the design of separation systems. It was therefore proposed to find a blended solvent that would allow the recovery of ethyl acetate in the distillate. The designed solvents are given in Table 7.10. The relative volatilities were estimated with standard UNIFAC (Hansen et al, 1991).

**Table 7.10 Blended Solvents for the Ethyl Acetate (1) / Ethanol (2)**

**System**

Pure solvents			Blended Solvents	
Solvent	$\alpha_{12}$	$T_b$ [K]	Solvent	$\alpha_{12}$
 1-Methyl-2-pyrrolidone (NMP)	3.53 *	475.2	NMP + DMSO	5.92 *
 Dimethyl sulfoxide (DMSO)	4.56 *	464.2		

\*  $\alpha_{12}$ -value from UNIFAC (Hansen et al, 1991)

Both of the individual solvents are able to reverse the relative volatility of the system. Using them together results in an even higher relative volatility, due to a synergistic interaction. This prediction should be verified experimentally.

In the three systems for which blended solvents were designed, it was possible in each case to find a solvent blend that outperformed its individual components. This is not always the case. Much more often the relative volatility attained by the blend is approximately the average of

that of the individual components. When the requirement for the relative volatility was increased in these cases, the algorithm converged to a single solvent.

### 7.2.3 The Purification of Alpha-Olefins

The extractive design problems that were investigated so far are relatively simple problems. In this section a much more complicated problem will be considered.

Normal alpha-olefins have a myriad of possible applications. They can be used in polymerisation as homo- or comonomers. They may be used in the production of surfactants like AOS (alpha olefin sulfonate) or detergent alcohols ( $C_{13} - C_{15}$ ). Synthetic base fluids for high-performance lubricants can be prepared by oligomerising normal alpha olefins (particularly  $C_{10}$ ). They may also be used in the production of plasticiser alcohols ( $C_8 - C_{10}$ ) and many other products (CPChem, 2001).

The ability to produce high purity alpha-olefins is very important. Impurities may react to form unwanted by-products or poison the catalyst used in the reactor. This may raise the cost of the process or lower the price of the final product. It will also lessen the demand for (and eventually cause a drop in the price of) the impure alpha-olefins.

Two types of impurities are expected in normal alpha-olefin product streams (La Grange et al, 2001):

1. Close-boiling olefins. These may include branched or cyclic structures and may be polyunsaturated (dienes and trienes).
2. Oxygenates, like ketones and aldehydes. These may be remnants of the manufacturing process.

These impurities may only be present in very low concentrations, but can still cause problems, especially the dienes and trienes. These compounds often lead to cross-polymerisation and need only be present in very low concentrations to be a significant problem.

The purification of the normal alpha-olefins is usually done with extractive distillation. 1-Methyl-2-pyrrolidone (NMP) has been used as a solvent in such a process. Even after a number of extractive distillation stages, the impurities may still be present in unacceptable concentrations. It is thus proposed to find a suitable solvent to be used in conjunction with NMP in order to improve the product.

Adding co-solvents to the NMP has the benefit that the viscosity and heat of vaporisation of the solvent blend will not differ as greatly from that of NMP as would be the case if NMP was simply replaced. This will make it easier to switch from NMP to a blend in an existing plant.

1-Octene was chosen as a representative alpha-olefin. Due to the large number of possible contaminants, various solvent designs were done. In each run a different contaminant was used. Some of the compounds that were used as representative contaminants are listed in Table 7.11.

The solvents found in this manner were analysed in an attempt to identify significant functional groups that aid the separation. The main types of solvents identified in this manner were phenolics and aliphatic and aromatic sulfoxides, sulfones, nitriles and amides. A number of solvents from each of these groups were tested in the laboratory to verify their predicted selectivity.

A commercial 1-octene product sample was obtained and fed into a continuously recirculating equilibrium cell as shown in Figure 7.2. The candidate solvents were mixed with an equal amount of NMP. This

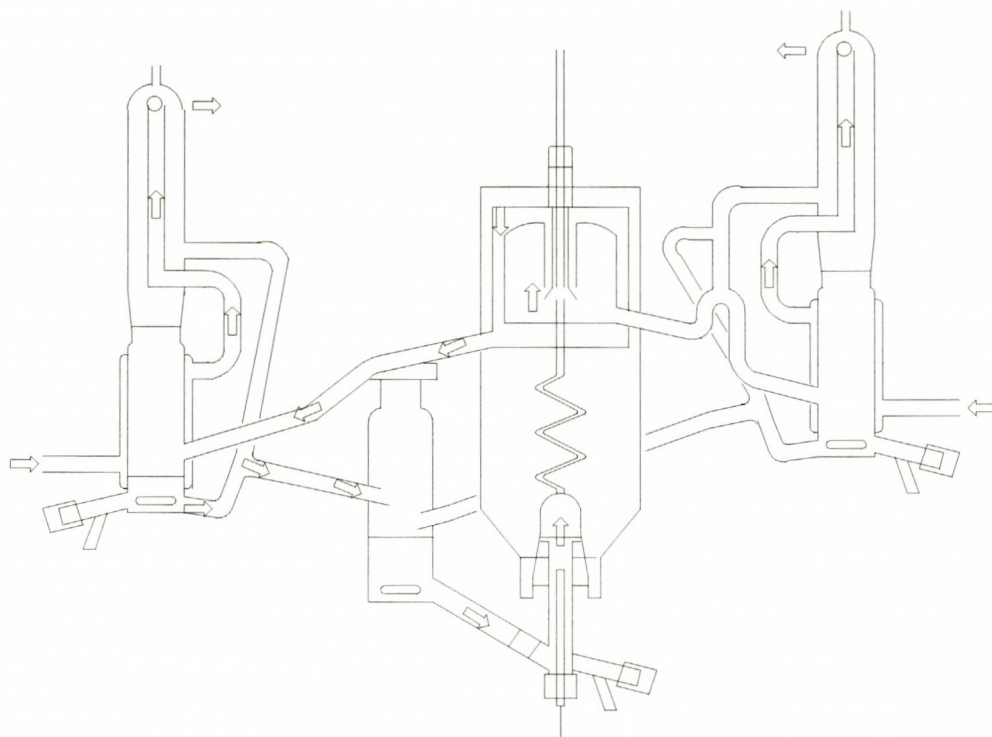
solvent mixture was then fed into the equilibrium cell in a 4:1 mass ratio with the octene.

The relative volatilities that were obtained with each solvent are listed in Table 7.12. As there were a large number of impurities present in the octene, all of these were lumped together as a pseudo-component. The relative volatility was determined between the octene and this pseudo-component.

An additional run was done with just NMP, to serve as a benchmark, resulting in a relative volatility of 1.02. To test the effectiveness of NMP itself, a run was also done with just the octene and no solvents. In this last case, a relative volatility of only 1.01 was measured. It is clear that the impurities in the octene are extremely difficult to remove.

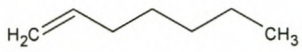

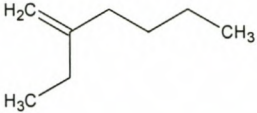
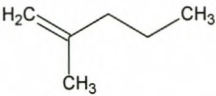
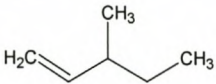
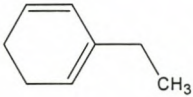

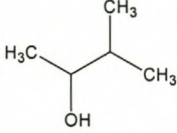
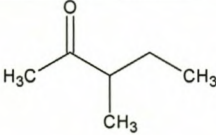
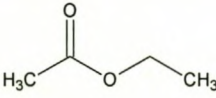
The still was operated under isobaric conditions with the pressure set at 0.95 barA. The temperatures measured at equilibrium varied between 130°C and 145°C, with the higher temperatures being recorded for the higher boiling solvents.





**Figure 7.2 A Continuously Circulating Equilibrium Still**

**Table 7.11 Some Representative Contaminants in 1-Octene**

1-Heptene	
1-Nonene	
2-Ethyl-1-Hexene	
2-Methyl-1-Pentene	
2-Methyl-2-Pentene	
1,5-Ethylcyclohexadiene	
1,5-Cyclooctadiene	
3-Methyl-2-Butanol	
3-Methyl-2-Pentanone	
Ethyl acetate	

**Table 7.12 Some of the Co-solvents (with NMP) Tested**

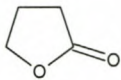
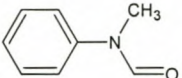
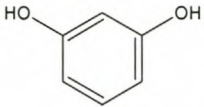

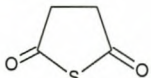
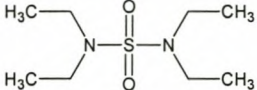
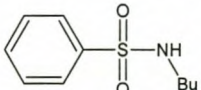
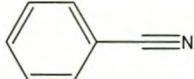

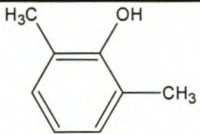
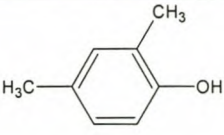
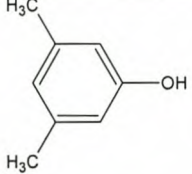
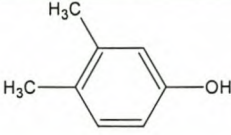
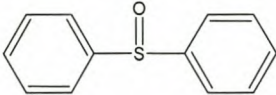
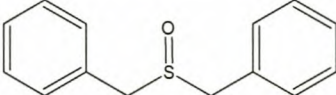
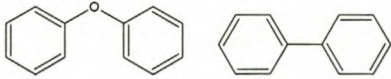

Solvent	$\alpha_{12}$
$\gamma$ -Butyrolactone 	1.05
N-methylformanilide 	1.05
Resorcinol 	1.05
Hydroquinone 	1.05
Sulfolane 	1.07
N,N,N',N'-Tetraethylsulfamide 	1.06
N-butylbenzenesulfonamide 	1.06
Benzonitrile 	1.06
Adiponitrile 	1.13

Table 7.12 (Continued)

Solvent	$\alpha_{12}$
2,6-Xylenol 	1.09
2,4-Xylenol 	1.11
3,5-Xylenol 	1.06
3,4-Xylenol 	1.10
Diphenyl Sulfoxide 	1.15
Benzyl Sulfoxide 	1.04
Dowtherm A (Eutectic mixture of Biphenyl and Diphenyloxide) 	1.05
m-Cresol 	1.06

The co-solvents that performed best were adiponitrile, the xylenols and diphenyl sulfoxide. As a mixture of the different xylenols should be cheaper to obtain than the pure components, such a mixture was also tested. 2,4-Xylenol and 2,5-xylenol were mixed in a 2 : 1 ratio. The result for this test was a relative volatility of 1.08, approximately the average of

that attained with all the individual xylenols. However, when the ratio of mixed xylenols to NMP was increased to 9 : 1, the relative volatility dropped to 1.048. This can be seen as experimental evidence of the synergy effects in the blended solvents.

Looking at these results, one immediately notices the very low relative volatilities. This is an indication of the extreme difficulty posed by this separation. In practice a final purification step would be done in superfractionation columns (La Grange et al, 2001), with a very large number of theoretical stages. A small increase in the selectivity of the solvent will have a substantial effect on the final product purity.

We may estimate the number of plates required at total reflux, using Fenske's method (Coulson and Richardson, 1991). We will make the following assumptions:

- The feed is 99.9% octene
- The distillate is 99.99% octene
- The bottoms flow rate is 10% of the feed rate
- The relative volatility remains constant

Fenske give the minimum number of stages as follows:

**Equation 7.2**

$$N + 1 = \frac{\log \left[ \left( \frac{x_A}{x_B} \right)_{distillate} \left( \frac{x_B}{x_A} \right)_{bottoms} \right]}{\log \alpha_{avg}}$$

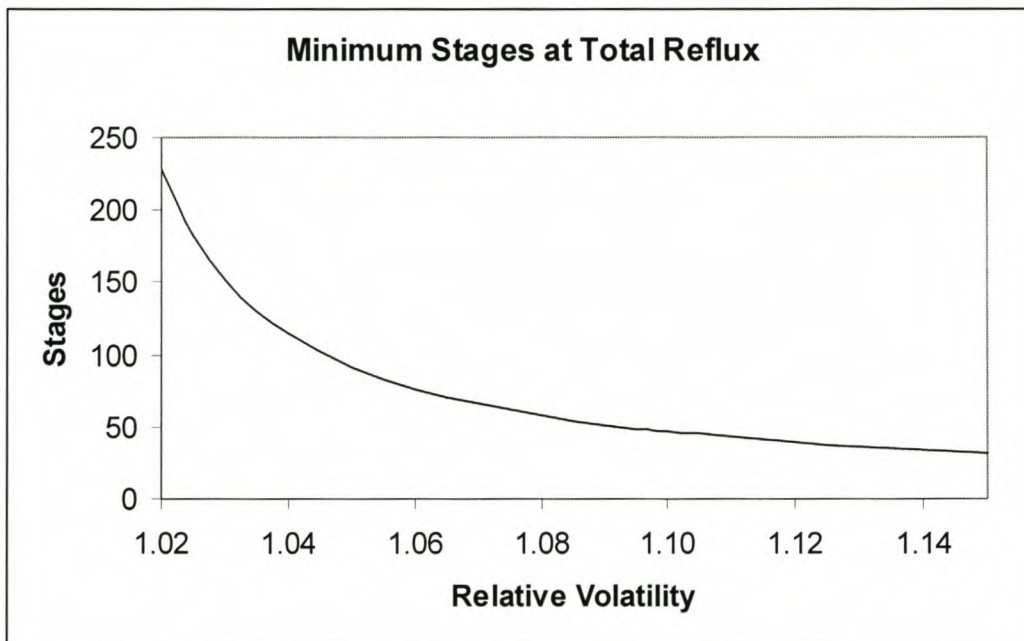
With

A: The more volatile component (1-Octene)

B: The less volatile component (The contaminants)

Using these assumptions a chart of the minimum number of stages required versus the relative volatility may be drawn, as shown in Figure 7.3.

Although this calculation is only an approximation, it gives a useful indication as to the effect of an apparently small increase in the relative volatility.



**Figure 7.3 Minimum Stages at Total Reflux with Fenske's Method**

From this graph we see that the estimated minimum number of stages required with NMP ( $\alpha_{12} = 1.02$ ) is approximately 230, whereas only 31 stages would be required with diphenyl sulfoxide ( $\alpha_{12} = 1.15$ )! There is a tremendous difference in the size of the columns required. Using the improved solvent may lead to significant saving on capital expenditure.

This example demonstrates that even for extremely difficult separations, it is possible to find improved solvents through computer-aided molecular design methods.

## 7.3 Liquid-Liquid Extraction Problems

### 7.3.1 Binary Systems

The ability of the SolvGen algorithm to design effective solvents will again be demonstrated on binary mixtures. In this case, the separation will be by means of liquid-liquid extraction.

The liquid-liquid extraction equivalent to relative volatility is the selectivity, which may be calculated with Equation 7.3

Equation 7.3

$$\beta_{ij} = \frac{x_i^I / x_i^{II}}{x_j^I / x_j^{II}}$$

As before, all the relative volatilities were estimated using Modified UNIFAC (Dortmund) unless noted otherwise. The boiling points were estimated using the MMPF-GC-NL method (Marrero-Morejón and Pardillo-Fontdevila, 1999).

#### ***Acetic Acid / Water***

Acetic acid may be produced through carbonylation of methanol, oxidation of acetaldehyde or as a by-product from the manufacturing of cellulose acetate (Seader and Henley, 1998). It is also formed as a by-product of the Fischer-Tropsch process as used by Sasol in the SAS reactor (Van Nierop et al, 2000).

In all of these cases, acetic acid will be found in a mixture with water. If water makes up 50% or more of the mixture, distillation is no longer an economically attractive option, due to the large amount of the more

volatile water that would have to be vaporized. Ethyl acetate has been used as a solvent to recover the acetic acid by means of liquid-liquid extraction (Seader and Henley, 1998). We will attempt to find an alternative solvent for this separation.

A water to acetic ratio of 9 : 1 (molar) was used as a representative feed composition (Seader and Henley, 1998). The solvent to feed ratio was 4 : 1 (molar). The temperature was set at 330K and the system was at its bubble point pressure. Table 7.13 shows the proposed solvents.

**Table 7.13 Solvents for the Acetic Acid / Water System**

Proposed Solvents	$\beta_{12}$	Acetic Recovery	Solvent Recovery	$T_b$ [K]
n-Hexane	120.0*	66.2%	100%	343.6
Adiponitrile	41.7	99.2%	100%	523.2
<b>Industrial Solvents</b>				
Ethyl Acetate	20.6	98.8%	100%	333.6

\*Forms homogeneous azeotrope with solute

The n-hexane has a very high selectivity and gives a reasonable recovery of acetic acid. Unfortunately, it forms a homogeneous azeotrope with acetic acid that will impede solvent recovery. The formation of this azeotrope was predicted by UNIFAC and has been verified in the literature (Gmehling et al, 1994).

Adiponitrile has a high selectivity and also has a very high recovery of acetic acid. It does not form an azeotrope with acetic acid and as such would be easily recoverable. The x-y diagrams estimated with UNIFAC at 1 atm for these solvents with acetic acid are shown in Figure 7.4 and Figure 7.5.



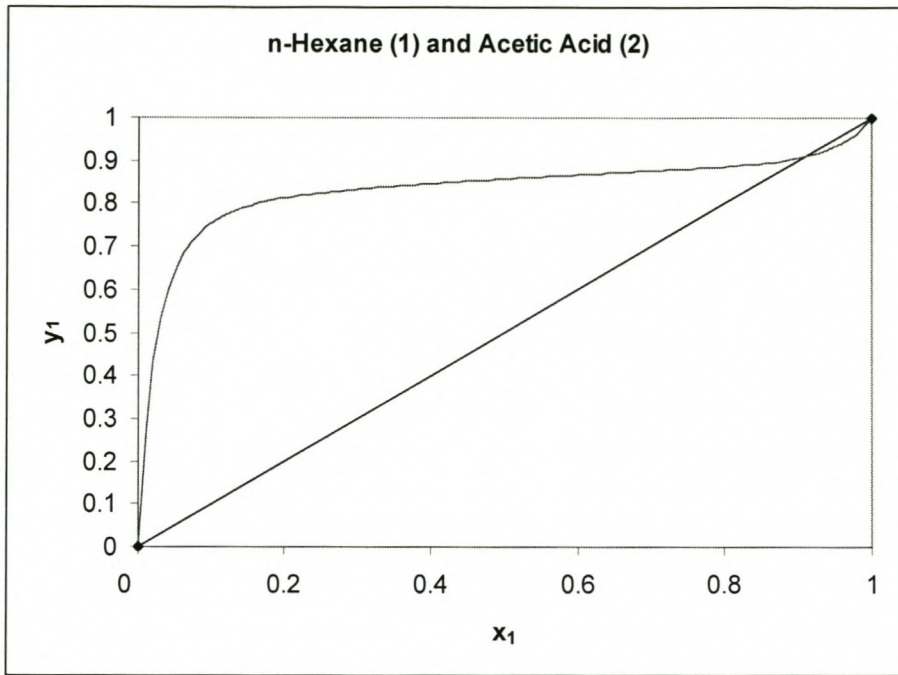


Figure 7.4 The x-y Diagram for n-Hexane and Acetic Acid

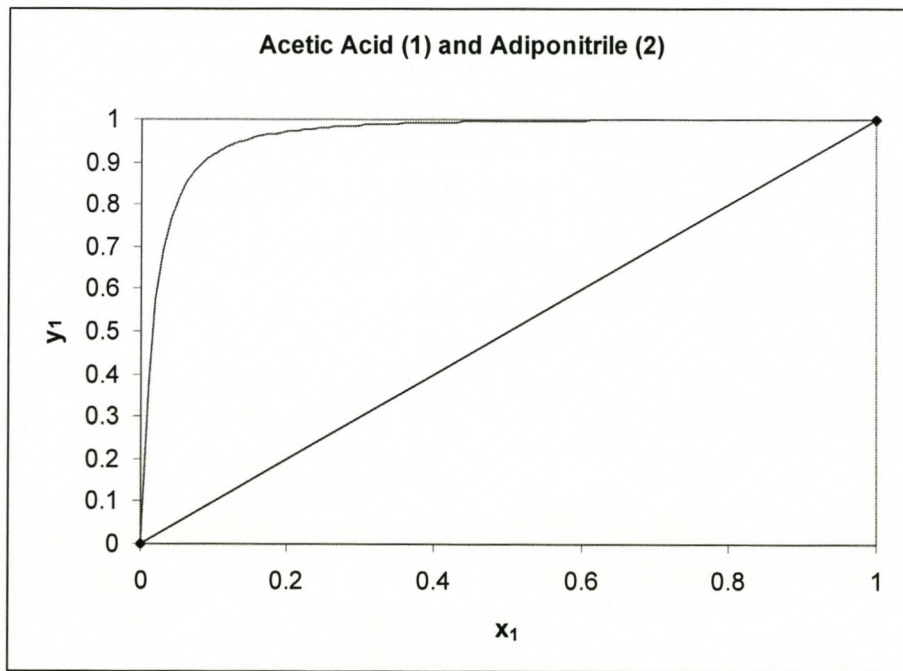


Figure 7.5 The x-y Diagram for Acetic Acid and Adiponitrile

### **7.3.2 Blended Solvents for Liquid-Liquid Extraction**

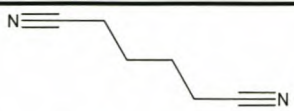
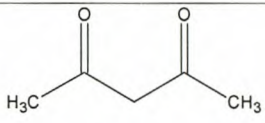
Liquid-liquid extractions processes may also benefit from the use of blended solvents. The binary system n-heptane / benzene was selected as an example. Liquid-liquid extraction may be used as an alternative to extractive distillation to separate this mixture.

#### ***n-Heptane / Benzene***

The separation of aliphatics and aromatics is often done by means of extractive distillation. If, due to process conditions, it is preferable to separate the mixture at lower temperatures liquid-liquid extraction is a viable choice for this separation.

The solvents designed for this system is listed in Table 7.14. The blend is an equimolar mixture of its components. A solvent to feed ratio of 4 : 1 was used at a temperature of 350K.

**Table 7.14 The n-Heptane (1) / Benzene System (2)**

Pure solvents			
Solvent	$T_b$ [K]	Benzene Recovery	$\beta_{12}$
 Adiponitrile	579.2 *	N/S*	N/S*
 Acetylacetone	413.7	82.4%	5.55
Blended Solvents			
Solvent		Benzene Recovery	$\beta_{12}$
Adiponitrile + Acetylacetone		96.5%	12.18

\* No liquid-liquid phase split.

Note that the adiponitrile cannot be used on its own as a solvent for liquid-liquid extraction, as it does not cause a phase split in the system

In this system, the addition of adiponitrile to the acetylacetone greatly enhanced both the selectivity and the capacity of the solvent. Not only can the purity of the benzene product be improved, but as the benzene recovery increased substantially, a lower solvent to feed ratio may be considered. The accuracy of these predicted values should however be tested by experiment.

### 7.3.3 The Recovery of Phenolics

A problem of some industrial importance is the separation of phenolics from so-called neutral oils via liquid-liquid extraction. In practise such mixtures would comprise of dozens of species. To simplify matters, we will consider only a mixture of phenol and aniline. The object of the case study is to find a solvent to recover phenol with a high selectivity and recovery.

The use of co-solvents and anti-solvents is a common practise for liquid-liquid extraction processes. In this case water and hexane will be used as the co-solvent and anti-solvent respectively. This will enforce the formation of two liquid phases of very different polarity. A water-to-feed mass ratio of 1:1 and a hexane-to-feed mass ratio of 4:1 will be used. The composition of the feed stream is listed in Table 7.15.

**Table 7.15 The Feed Composition (Combined with Water and Hexane)**

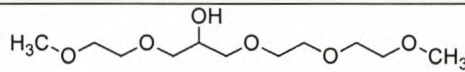
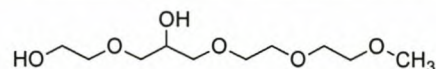
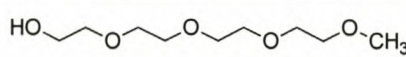
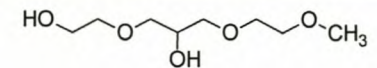
Component	Mass Fraction	Molar Fraction
Phenol	0.148	0.084
Aniline	0.019	0.011
Water	0.167	0.492
Hexane	0.666	0.413

The molar fraction of solvent was set at 0.15 with a temperature of 313K. Some of the chromosomes of the final generation are listed in Table 7.16, along with the predicted selectivities for each of these. These values were calculated using the Modified UNIFAC (Dortmund) model and Equation 7.3.

These proposed solvents are all very similar to polyethylene glycols. Polyethylene glycols are relatively easily obtainable solvents. As such they will be much cheaper than solvents that must be specially synthesised.

Using the interactive design mode of the SolvGen we find that the predicted selectivity for triethylene glycol, using the same solvent fraction, is 7.475, for tetraethylene glycol it is 7.840 and for pentaethylene glycol it is 8.141.

**Table 7.16. Candidate Solvents for Phenol Recovery**

Solvent Structure	Selectivity $\beta_{\text{Phenol / Aniline}}$
 <p>7-hydroxo-2,5,9,12,15-pentaoxahexadecane</p>	8.322
 <p>1,5-dihydroxo-3,6,9,12-tetraoxatetradecane</p>	8.447
 <p>1-hydroxo-3,6,9,12-tetraoxatridecane</p>	7.652
 <p>1,5-dihydroxo-3,7,10-trioxaundecane</p>	8.177

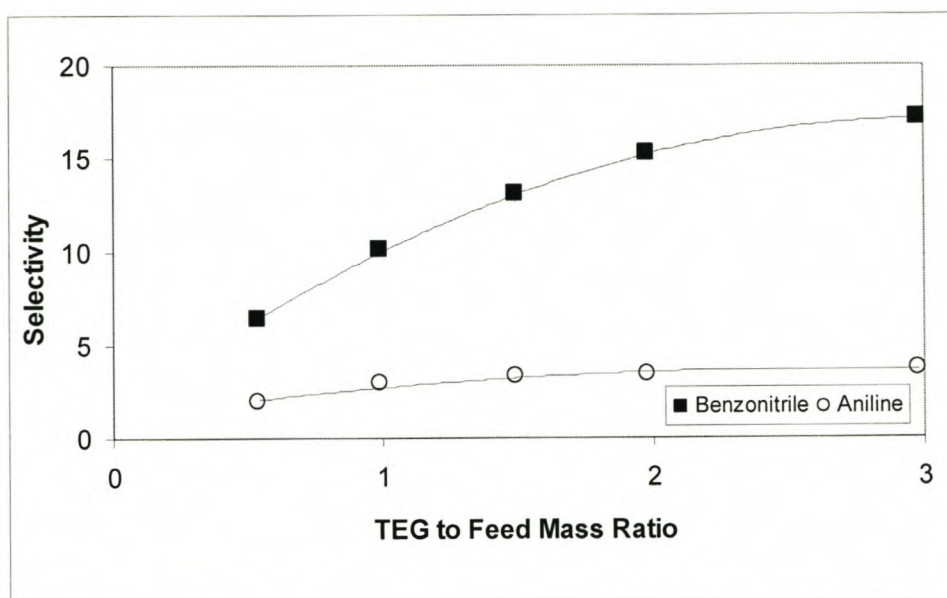
Venter and Nieuwoudt conducted a detailed study of the separation of phenolic compounds from neutral oils (Venter and Nieuwoudt, 1998; Venter and Nieuwoudt, 1999). In this study more complex feed streams were used so as to accurately represent the compositions of industrial feed streams.

The authors report that the polyethylene glycols, combined with water and hexane, are indeed very effective solvents for this separation. Triethylene glycol is recommended as the preferred solvent, based on their experimental results, some of which are given in Figure 7.6.

The feed composition for these equilibrium measurements is given in Table 7.17.

**Table 7.17. Feed for LLE Measurements (Venter and Nieuwoudt, 1999)**

<b>Mass Fractions</b>	
Phenol	0.710
Aniline	0.067
Benzonitrile	0.067
Mesitylene	0.090
Ethyl Methyl Pyridine	0.067
<b>Mass Ratios</b>	
Hexane : Feed (mass)	5:1
Water : Solvent (mass)	0.3:1

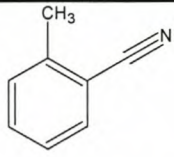
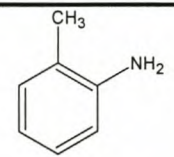
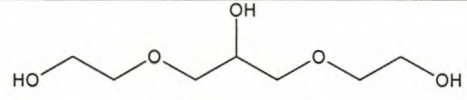
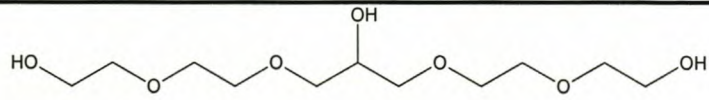


**Figure 7.6 Selectivity of Triethylene Glycol (TEG) for Phenol over Neutral Oils at 40°C (Venter and Nieuwoudt, 1999)**

From the results of the molecular design runs and the selectivities measured by Venter (Venter and Nieuwoudt, 1999; Venter and Nieuwoudt, 2000) for various phenolic-neutral oil systems, it was concluded that long-chain polyethers are the optimal solvents for this separation. It was also found that hydroxyl groups promote the recovery of phenolics from neutral oils (Venter and Nieuwoudt, 2000).

Two solvents derived from ethylene glycol and diethylene glycol respectively, were synthesised and tested by Venter and Nieuwoudt. The results of these experiments are summarised in Table 7.18, along with similar results for other solvents that have been used for the recovery of phenolics from neutral oils. (Venter and Nieuwoudt, 2000)

**Table 7.18 Solvents for the Separation of Phenolics and Neutral Oils**  
(Venter and Nieuwoudt, 2000)

Solvent	$\beta_{ij}$ (Selectivity)			% Recovery		$n_{m\text{-Cresol}}$	$n_{\text{Xylenol}}$
	m-Cresol	2,4-Xylenol		m-Cresol	2,4-Xylenol	-----	-----
	Nitrile	Nitrile	Amine			$n_{\text{Solvent}}$	$n_{\text{Solvent}}$
EG derived	8.9	-	-	88.2	-	1.2	-
DEG-derived	19.1	12.5	3.5	95.1	90.8	1.6	0.6
TEG	13.1	9.6	3.5	93.9	86.7	1.2	0.4
Tetra EG	16.5	11.1	3.6	95.3	90.7	1.3	0.5
Glycerol	3.8	10.1	1.1	60.1	2.1	0.7	0.0
Tetraglyme	3.3	-	0.7	83.2	-	1.3	-
Methanol	2.2	4.7	0.7	67.0	1.6	0.5	0.1
Key							
Nitrile	 <p>o-Tolunitrile</p>						
Amine	 <p>o-Toluidine</p>						
EG-derived	 <p>1,3-(ethoxy-2-hydroxy)-propane-2-ol</p>						
DEG-derived	 <p>1,3-(diethoxy-4-hydroxy)-propane-2-ol</p>						
$n_{m\text{-Cresol}}$ , $n_{\text{Xylenol}}$ , $n_{\text{Solvent}}$ *	Molar amount of each species to indicate feed ratios						



From these results it can be seen that the solvent synthesised from diethylene glycol has among the highest selectivities and recoveries for both the two phenolics, m-cresol and 2,4,-xylenol, over the neutral oils, o-tolunitrile and o-toluidine.

The insights required to develop the molecular structure for this solvent came about partly due to the solvents proposed by the SolvGen algorithm (Venter and Nieuwoudt, 2000).

### **7.4 Heterogeneous Azeotropic Distillation**

In this section, the ability of the SolvGen algorithm to find suitable entrainers to separate binary systems with heterogeneous azeotropic distillation will be demonstrated. The systems listed in Table 7.19 will be used. The entrainers used industrially to form heterogeneous azeotropes are also given.

**Table 7.19 Test Systems for Heterogeneous Azeotropic Distillation**

<b>System</b>	<b>Industrial Entrainer</b>
Ethanol / Water	Benzene
Water / Acetic Acid	Ethyl Acetate

In the calculations used to locate azeotropes, the accuracy of the vapour pressures of the pure components is much more important than with the other separation process discussed here. Unfortunately, there is not yet a generally applicable group contribution method for estimating vapour pressures, although the work done by Fredenslund et al (Jensen et al, 1981; Ben Yair and Fredenslund, 1983) does show much promise.

Fredenslund et al relate the Gibbs energy of a pure component to its vapour pressure by the following equation (Fredenslund and Rasmussen, 1979):

#### Equation 7.4

$$RT \ln(\phi_i^{sat} P_i^{sat}) = \sum_k v_k^{(i)} \Delta g_k + RT \sum_k v_k^{(i)} \ln \Gamma_k^{(i)}$$

With

- $\phi_i^{sat}$  : Saturation fugacity coefficient of component i
- $P_i^{sat}$  : The vapour pressure of component i
- $v_k^{(i)}$  : The number of UNIFAC groups of type k in component i
- $\Delta g_k$  : The difference between the Gibbs energy and the reference energy of UNIFAC group k
- $\Gamma_k^{(i)}$  : The activity coefficient of UNIFAC group k in component i

The Gibbs energy difference of a UNIFAC group,  $\Delta g_k$ , is given by a function of temperature with up to twelve parameters. The activity coefficient of a UNIFAC group is calculated from the residual part of the UNIFAC model (Fredenslund et al, 1975). Unfortunately the method is not yet widely applicable, as only a limited number of parameters are available for the Gibbs energy difference function.

The method currently used in SolvGen (Van Dyk, 1998), fits a simplified version of the Antoine equation through the estimated boiling and freezing point data. This is sufficiently accurate near the boiling point of the component, but further away from the normal boiling point the accuracy is variable.

The magnitude of this problem is illustrated by the ethanol / benzene / water azeotrope. The composition of this azeotrope from the literature (Gmehling et al, 1994) is compared with that predicted by SolvGen (using UNIFAC) in Table 7.20

**Table 7.20 Comparison of Azeotropic Compositions, 338K**

Literature Composition		Predicted Composition	
Ethanol	0.2281	Ethanol	0.2806
Benzene	0.5387	Benzene	0.5200
Water	0.2332	Water	0.1994


This lack of accurate group-contribution methods is the Achilles Heel of all CAMD methods. Even the most advanced design algorithm can only function in the search space provided by the group-contribution methods it employs.

The effect of the problem may be controlled by setting the boiling point requirements for the entrainer to a narrow band around the working temperature. The algorithm should then be run with different temperatures, to find all possible entrainers. By confining the entrainer to a narrow boiling point range, it is also confined to the range of highest accuracy in the vapour pressure estimation.

### ***Ethanol / Water***

The dehydration of ethanol with benzene as the entrainer in a heterogeneous azeotropic distillation process is a classic textbook example. As benzene is a suspected carcinogenic, the possibility of using alternative entrainers should be investigated. The azeotropic composition of the ethanol / water / benzene system (predicted with UNIFAC) is given in Table 7.21 and for the proposed entrainers, in Table 7.22.

**Table 7.21 Industrial Entrainers for the Ethanol / Water System (350K)**

 <span style="float: right;"><b>Benzene</b></span>				
Component	Vapour	Liquid 1	Liquid 2	$\beta_{12}$
Ethanol	0.3226	0.4658	0.1854	7.75
Water	0.2308	0.4479	0.0230	$\theta$
Entrainer	0.4465	0.0863	0.7916	0.511

The  $\beta_{21}$  value is the selectivity, calculated between the two liquid phases using Equation 7.3.  $\theta$  is the liquid phase ratio and may be calculated with

**Equation 7.5**

$$\theta = \frac{L_2}{L_1 + L_2}$$

With

$\theta$ : The phase ratio

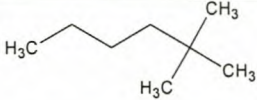
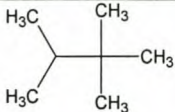
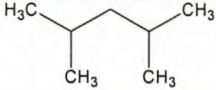
$L_j$ : The total molar amount of liquid phase j

As was discussed in chapter 5, the selectivity is only one of the indicators of the suitability of an entrainer. A good entrainer must not only have a high selectivity, but also a high capacity. This implies that the molar fraction of the entrainer in the azeotrope must be as small as possible. Furthermore, the separation between the two liquid phase compositions should be as wide as possible.

If the entrainer constitutes a large percentage of the azeotrope, a lot of energy will be spent evaporating the entrainer. A larger diameter column will also be required due to the high flow rates caused by the large amount of entrainer in the column. Thus, both the capital and running cost of the process will be increased.

All the azeotropic compositions were calculated with UNIFAC at 350K and the bubble point pressure of the mixture.

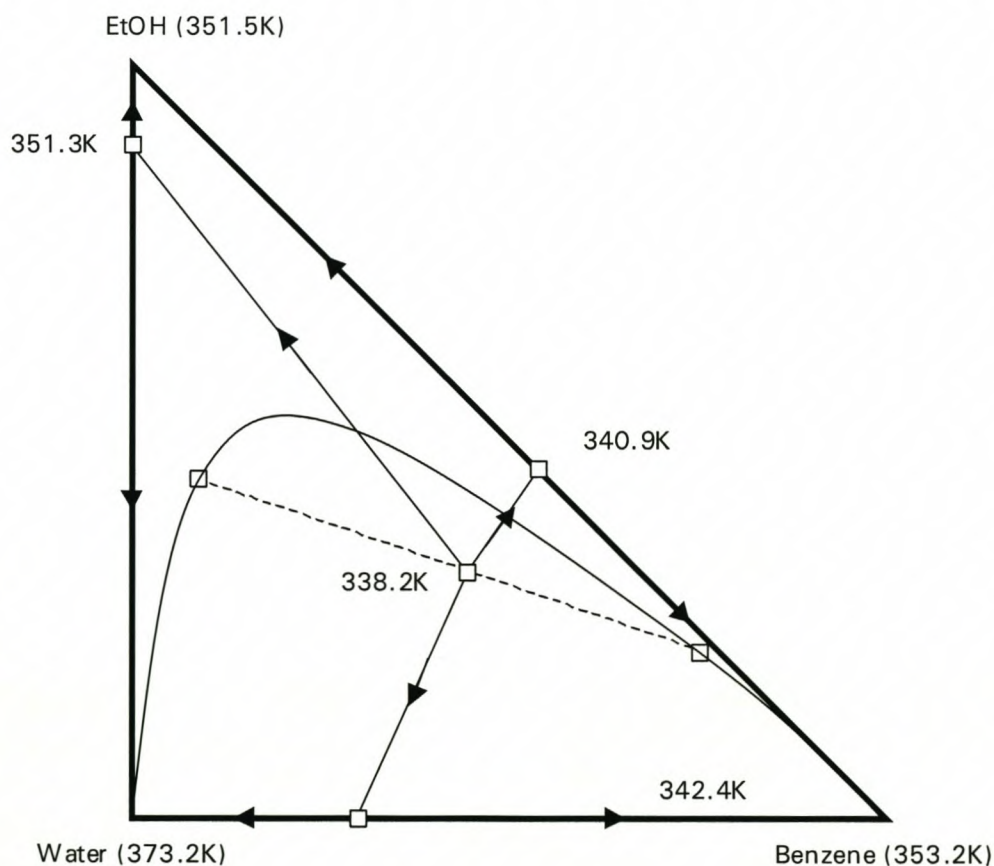
**Table 7.22 Entrainers for the Ethanol / Water System (350K)**

 <p style="text-align: right;"><b>2,2-Dimethylhexane</b></p>				
<b>Component</b>	<b>Vapour</b>	<b>Liquid 1</b>	<b>Liquid 2</b>	$\beta_{12}$
<b>Ethanol</b>	0.4466	0.6468	0.1164	7.78
<b>Water</b>	0.1821	0.2886	0.0067	$\theta$
<b>Entrainer</b>	0.3713	0.0645	0.8769	0.377
 <p style="text-align: right;"><b>2,2,3-Trimethylbutane</b></p>				
<b>Component</b>	<b>Vapour</b>	<b>Liquid 1</b>	<b>Liquid 2</b>	$\beta_{12}$
<b>Ethanol</b>	0.3235	0.5903	0.1017	8.62
<b>Water</b>	0.1587	0.3410	0.0068	$\theta$
<b>Entrainer</b>	0.5187	0.0687	0.8915	0.546
 <p style="text-align: right;"><b>2,4-Dimethylpentane</b></p>				
<b>Component</b>	<b>Vapour</b>	<b>Liquid 1</b>	<b>Liquid 2</b>	$\beta_{12}$
<b>Ethanol</b>	0.3412	0.6019	0.0992	8.70
<b>Water</b>	0.1615	0.3287	0.0062	$\theta$
<b>Entrainer</b>	0.4973	0.0694	0.8946	0.519

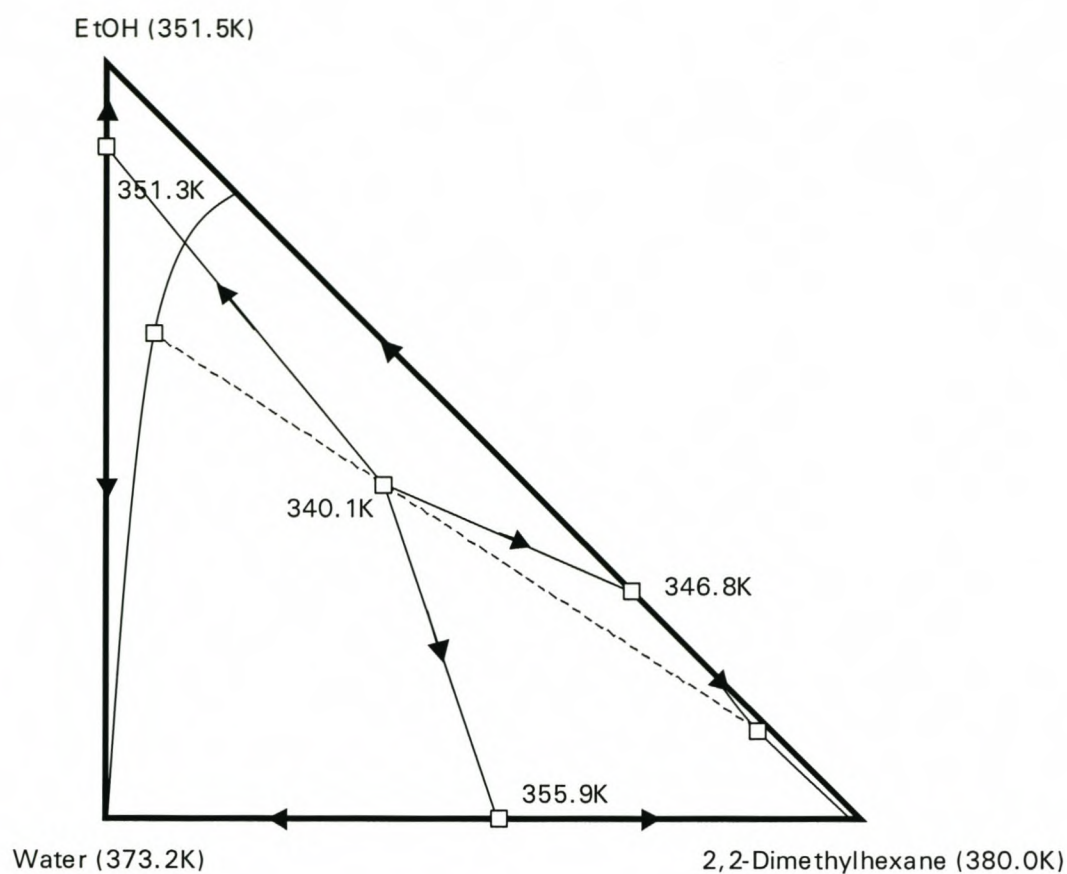
The 2,2-dimethylhexane has a selectivity only marginally higher than benzene, but comprises a significantly smaller portion of the azeotrope. The 2,2,3-trimethylbutane and 2,4-dimethylpentane each make up a larger fraction of their respective azeotropic compositions, but have much better selectivities than benzene. Which of these two factors carries the most weight will have to be determined by a more detailed study of the process economics.

Very importantly, all three of the proposed entrainers are completely non-toxic, while benzene is both toxic and a suspected carcinogenic. This weighs heavily in favour of the proposed entrainers.

The residue curve maps for the systems ethanol / water / benzene and ethanol / water / 2,2-dimethylhexane are shown in Figure 7.7 and Figure 7.8. These figures show that the same separation train design may be used with both entrainers. However, the separation between the compositions of the aqueous and organic phases formed in the decanter are significantly wider for 2,2-dimethylhexane, as indicated by the length of the tie-line in Figure 7.8.



**Figure 7.7 Residue Curve Map for Ethanol / Water / Benzene**



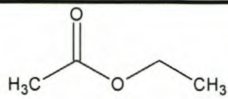
**Figure 7.8 Residue Curve Map for Ethanol / Water / 2,2-Dimethylhexane**

### ***Water / Acetic Acid***


As discussed above, the water acetic acid system may be separated by means of liquid-liquid extraction when the water concentration is above 50%. For low water concentrations, distillation may also be considered for this separation.

Ethyl acetate may be used as the entrainer in this separation process. It forms a binary heterogeneous azeotrope with water, as is shown in Table 7.23. The SolvGen algorithm was applied to this problem in order to find an alternative entrainer. The results are shown in Table 7.24

**Table 7.23 Industrial Entrainer for the Water / Acetic Acid System (350K)**

 <b>Ethyl Acetate</b>				
Component	Vapour	Liquid 1	Liquid 2	$\beta_{12}$
Water	0.3194	0.9913	0.1722	n/a
Acetic Acid	-	-	-	$\theta$
Entrainer	0.6806	0.0087	0.8278	0.8208

**Table 7.24 Entrainers for the Water / Acetic Acid System (350K)**

 <b>Tetrachloromethane (Carbon Tetrachloride)</b>				
Component	Vapour	Liquid 1	Liquid 2	$\beta_{12}$
Water	0.3005	0.9998	0.0019	n/a
Acetic Acid	-	-	-	$\theta$
Entrainer	0.6995	0.0002	0.9981	0.7008

Tetrachloromethane forms a binary heterogeneous azeotrope with water that is recovered in the distillate. As water and tetrachloromethane are almost completely immiscible, the two phases that form are almost pure. As acetic acid is not part of the azeotrope, the selectivity for acetic acid between the two liquid phases is not applicable in these systems.

The molar fractions of ethyl acetate and tetrachloromethane in their respective azeotropes do not differ significantly. The tetrachloromethane does however give a much wider separation between the liquid phase compositions than ethyl acetate.

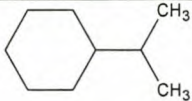
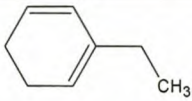
For both entrainers the aqueous phase is almost pure water. With tetrachloromethane the organic phase is also almost pure, while a



significant amount of water is present in the ethyl acetate organic phase. This water will be recycled to the column and will be continuously re-evaporated, increasing the energy use of the process.

As tetrachloromethane is toxic a further design was done to find an alternative. In this design run, all genes containing chlorine were disallowed. This was achieved by setting the selection probabilities of these genes to zero. In this case it was decided to search for a ternary azeotrope. The results of this are given in Table 7.25.

**Table 7.25 More Entrainers for the Water / Acetic Acid System (350K)**

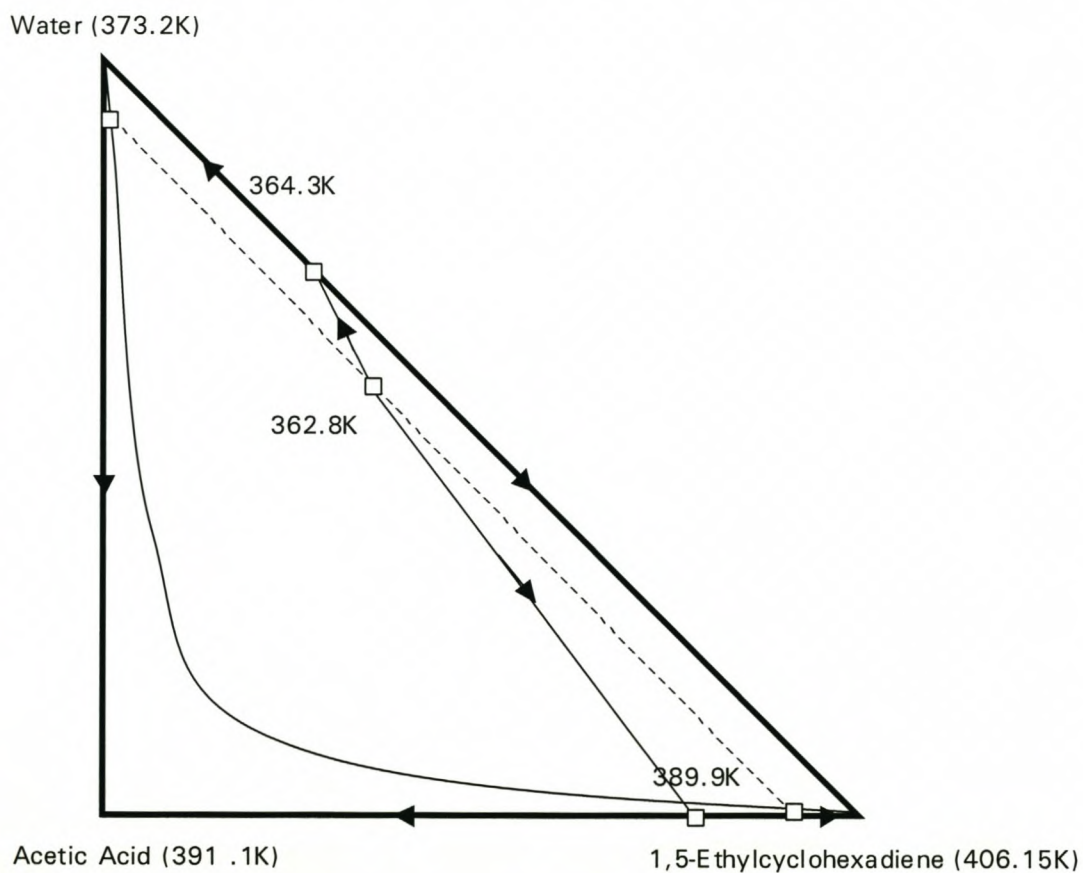
 <b>Isopropylcyclohexane</b>				
Component	Vapour	Liquid 1	Liquid 2	$\beta_{12}$
Water	0.5624	0.8870	0.0041	84.45
Acetic Acid	0.0877	0.1129	0.0444	$\theta$
Entrainer	0.3499	0.0001	0.951	0.3676
 <b>1,5-Ethylcyclohexadiene</b>				
Component	Vapour	Liquid 1	Liquid 2	$\beta_{12}$
Water	0.5425	0.9278	0.0407	14.59
Acetic Acid	0.0608	0.0720	0.0461	$\theta$
Entrainer	0.3968	0.0002	0.9132	0.4344

These entrainers are clearly much less dangerous than tetrachloromethane. Both these entrainers also have significantly smaller molar fractions in the azeotropic compositions. As much less entrainer need be evaporated, this will allow a significant saving in energy.

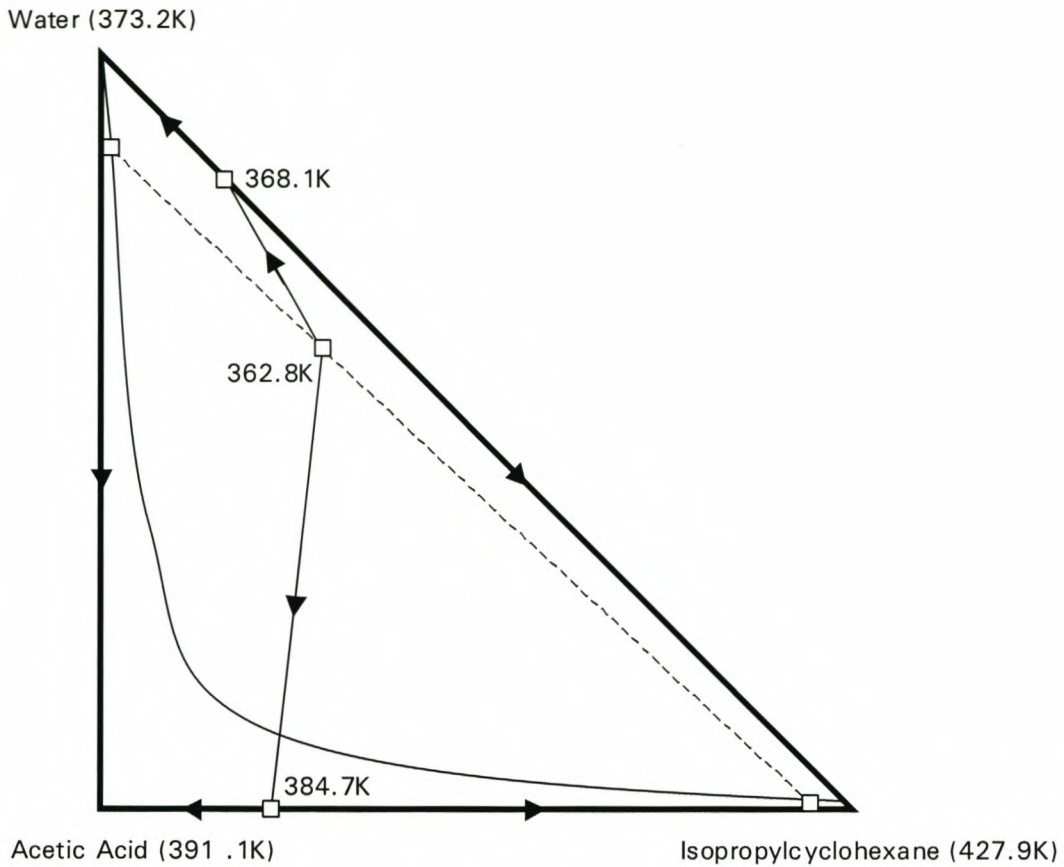
The final test of the suitability of an entrainer is to construct a residue curve map. The residue curve map for the system water / acetic acid /

1,5-ethylcyclohexadiene is shown in Figure 7.9 and that for water / acetic acid / isopropylcyclohexane in Figure 7.10

From these residue curve maps, we see that water and acetic acid fall into the same distillation region. This will always be the case, as there is no azeotrope that forms between water and acetic acid that may form the endpoint of a separatrix. Acetic acid is the stable node of this region and will be recovered in the bottoms-product of the column.



**Figure 7.9 Residue Curve Map for Water / Acetic Acid /  
1,5-Ethylcyclohexadiene**



**Figure 7.10 Residue Curve Map for Water / Acetic Acid / Isopropylcyclohexane**

The distillate separates into two layers. The first of these layers is mostly entrainer and may be recycled to the column. The second layer is approx. 93% water with 1,5-ethylcyclohexadiene and approx. 89% water with isopropylcyclohexadiene. If desired, the acetic acid can be recovered from this stream by a further process. Due to the high percentage water, distillation would not be economically attractive and a liquid-liquid extraction process should be considered. This separation was discussed as a case study in liquid-liquid extraction in section 7.3.1.

## **7.5 Chromatographic Separations**

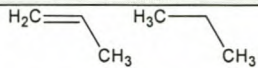
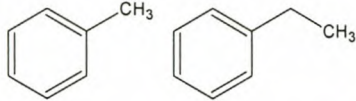
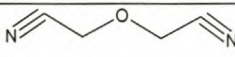
Chromatographic methods are used in industry for the separation and purification of macromolecules and some smaller naturaceuticals (Cramer and Jayaraman, 1993). As UNIFAC is not currently accurate enough to handle this type of system, we will instead consider problems from analytical chemistry. As the UNIFAC method is continuously improved and expanded, it should in the foreseeable future be possible to accurately model macromolecules. The algorithm that was developed in this work may then be directly applied to these systems.

Both liquid-liquid and gas-liquid chromatography will be considered.

### **7.5.1 Liquid-Liquid Chromatography**

We will consider two systems for liquid-liquid chromatography. These are listed in Table 7.26 together with the mobile and stationary phases commonly used for their separation (Park et al, 1991). The partition coefficient ratios (estimated with UNIFAC) give a good indication as to the separation attained with these solvents. The specific ratio of retention times will depend on the column volume and flow rates. All the partition coefficients were calculated with Modified UNIFAC (Dortmund) at 300K.

**Table 7.26 Test Systems for Liquid-Liquid Chromatography**

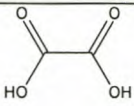

System	Stationary Phase / Mobile Phase	Partition Coefficient Ratio
 <p>Propene / Propane</p>	$\text{H}_2\text{O}$ $\text{CH}_3(\text{CH}_2)_{14}\text{CH}_3$ Water /Hexadecane	1.299
 <p>Toluene / Ethylbenzene</p>	 $\text{CH}_3(\text{CH}_2)_{14}\text{CH}_3$ $\beta,\beta'$ -oxydipropionitrile / Hexadecane	1.562

For both of the test systems, the component listed first will exit the column last. We will attempt to find solvents that will increase the separation between these components by increasing the ratio of their partition coefficients. A larger ratio will lead to a larger difference in retention times or allow a good separation at higher flow rates.

### ***Propene / Propane***

Two stationary phase solvents were designed for this system. As with the examples given by Park et al (Park et al, 1991), hexadecane was used as the mobile phase. This allows a direct comparison of the stationary phases with those used by Park et al.

**Table 7.27 Stationary Phases for the Propene / Propane System**

Stationary Phase Solvent	Partition Coefficient Ratio
 Oxalic Acid	3.351
 Formic Acid	2.909

Both of these solvents are completely immiscible in hexadecane. As can be seen from the ratios of partition coefficients, these solvents should give a much better separation for propane and propene than will water.

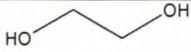

Both of these stationary phases are acids. Formic acid in particular is very corrosive. To counter the problem of corrosion, formic acid may be used in an aqueous solution. The acid/water mixture could also be used as the mobile phase with hexadecane or octadecane as the stationary phase in a stainless steel column. When the mobile phase is the polar solvent, the term reverse phase chromatography is used and the order in which the components exit the column will be reversed.

### ***Toluene / Ethylbenzene***

Alternative solvents were also designed for the toluene / ethylbenzene system. These are listed in Table 7.28. Again, these solvents perform very well in separating the mixture, especially formic acid.

As discussed in the previous example, formic acid is highly corrosive, it may be used in an aqueous solution as the mobile phase with the hexadecane or octadecane as the stationary phase in a stainless steel column. This is called reverse phase chromatography, as the mobile phase is now polar and the stationary phase non-polar. The order in which the components leave the column will be reversed.

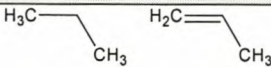
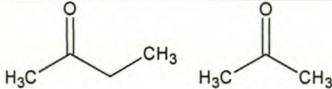
**Table 7.28 Stationary Phases for the Toluene / Ethylbenzene System**

Stationary Phase Solvent	Partition Coefficient Ratio
$\text{H}_2\text{O}$ Water	3.898
 Ethylene glycol	1.974
 Formic Acid	16.019

### 7.5.2 Gas-Liquid Chromatography

The propane / propene system may also be separated with gas-liquid chromatography. Park et al (Park et al, 1991) used hexadecane as the stationary phase for this separation, as is shown in Table 7.29.

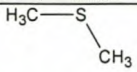
**Table 7.29 Test Systems for Gas-Liquid Chromatography**

System	Stationary Phase	Partition Coefficient Ratio
 Propene / Propane	$\text{CH}_3(\text{CH}_2)_{14}\text{CH}_3$ Hexadecane	1.284
 2-Butanone / Acetone	$\text{CH}_3(\text{CH}_2)_{14}\text{CH}_3$ Hexadecane	3.374

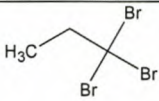
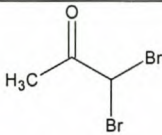

As before, the component listed first will exit the column last.

As an alternative to the highly non-polar solvent used for both the systems in Table 7.29, we attempted to design polar solvents. The results are shown in Table 7.30 and Table 7.31.

**Table 7.30 Stationary Phases for the 2-Butanone / Acetone System**

Stationary Phase Solvent	Partition Coefficient Ratio
 Methylsulfanylmethane	203.37

**Table 7.31 Stationary Phases for the Propane / Propene System**

Stationary Phase Solvent	Partition Coefficient Ratio
 1,1,1-Tribromopropane	2.295
 1,1-Dibromoacetone	1.9285
 3-Bromo-propionitrile	2.345

As can be seen from these results, the polar stationary phase worked extremely well for the propane / propene separation. For the more polar ketones, a non-polar stationary phase like hexadecane is more effective.

Experience with gas chromatography, shows that silicon compounds make very effective non-polar stationary phases. Although UNIFAC does have some silicon groups available (SiO and SiH<sub>2</sub> are available in UNIFAC (Hansen et al, 1991), but not in Modified UNIFAC (Gmehling et al, 1998)), very few of the necessary interaction parameters have been published. For this reason, no silicon compounds are currently included in the SolvGen gene set.



## **7.6 Conclusions**

In this chapter, separation problems of industrial significance in extractive distillation, liquid-liquid extraction and heterogeneous azeotropic distillation were investigated. Analytical problems in liquid-liquid and gas-liquid chromatography were also considered.

In each case it was possible to find alternative solvents to those that are currently in use in industry. These solvents performed better than the industrially used solvents in many aspects.

Even in extremely difficult separations, like the final purification step for alpha olefins, it was possible to find co-solvents that significantly increased the ability of NMP to remove impurities from the product.

The possible applications of CAMD are by no means limited to those areas that were investigated here. In any problem where molecules with specific properties are required, and group-contribution methods exist to estimate those properties, CAMD may be applied. As the accuracy and generality of group-contribution methods are improved, so too will the quality of the results produced by the CAMD algorithms.

# 8

## 8 Conclusions and Recommendations

### 8.1 Conclusions

The goal of this work was to turn the basic SolvGen algorithm (Van Dyk, 1998) into a tool with practical uses in solving real world separation problems. This was achieved in a number of steps. First the speed and efficiency of the algorithm was dramatically improved – up to 500% in certain cases. The quality of the results produced by the algorithm was also improved by new checks for physical viability. The algorithm was then extended in order to apply it to a wide range of industrially important separation problems.

SolvGen may now be used not only to design solvents for extractive distillation, but also for liquid-liquid extraction, heterogeneous azeotropic distillation and chromatographic separations.

In order to enable the design of entrainers for heterogeneous azeotropic distillation, two new, efficient methods for the location of heterogeneous azeotropes were developed. This was necessary due to the computational inefficiency of previously published methods. These methods are also

readily extendable to quaternary and higher mixtures and a methodology for their application to these mixtures was proposed.

The design of solvents is no longer limited to single components – solvent blends may now also be designed. The extension to blended solvents required the development of new data structures and new genetic operators. Two algorithms were developed for blended solvent design. The first of these algorithms was a two-step group assembly method. This algorithm was critically evaluated and an alternative method was developed to overcome the shortcomings of the first. This second method was based on the concept of symbiosis and allows the simultaneous evolution of the blend components. This algorithm was successfully applied to problems in both extractive distillation and liquid-liquid extraction.

The original motivation for blended solvents was to enable the use of simpler molecular structures by spreading active functional groups over several molecular backbones. In the course of this work systems were found where the blend outperformed its individual components. It is proposed that this is due to synergistic interactions between the blend components.

To illustrate the ability of the algorithm to find improved solvents, several problems of industrial importance were investigated, including the recovery of phenolics from neutral oils and the extremely difficult final purification of alpha olefins. Both of these problems are of immediate industrial significance. Other case studies included the design of pure and blended solvents for extractive distillation and liquid-liquid extraction, the design of entrainers for heterogeneous azeotropic distillation and the design of mobile and stationary phases for chromatographic separations.

In almost all of these test cases, the designed solvents are predicted by UNIFAC to outperform the solvents currently used in industry. In a number of extractive distillation problems, solvents were designed that reverse the natural relative volatility of the key mixture components. The ability to manipulate which component is recovered in the distillate gives great flexibility in the design of separation processes.

In many cases these predictions were tested by experiment and found to hold true. In the alpha olefins case study, experimental evidence was found for the synergistic interactions that were predicted to exist in case studies with blended solvents.

In summary, a flexible tool has been developed that has been used to successfully solve a wide range of industrially important separation problems.

## ***8.2 Recommendations***

### **8.2.1 Solvent Evaluation**

#### ***Toxicity***

In some of the design case studies discussed in the previous chapter, it was deemed necessary to find alternative solvents because those currently in use were toxic. This is for example the case when benzene is used as an entrainer to dehydrate ethanol through heterogeneous azeotropic distillation. The alternative entrainers designed for this separation were manually evaluated based on their toxicity. If a quantitative measure of toxicity could be estimated from the molecular structure, this process can be automated. This would allow toxicity to become a design specification in SolvGen.

### ***Other Physical Properties***

Other solvent properties, like surface tension and viscosity, may be of importance in certain cases. These properties could easily be included by small modifications to the fitness functions used by SolvGen.

### ***Improved Property Estimations***

The shortcomings of the various group contribution methods used in SolvGen were discussed. Any improvements in the accuracy or generality of these methods would benefit all CAMD algorithms.

There is especially a need for an accurate and generally applicable group contribution method for estimating vapour pressures. Methods exist that are fairly accurate, but are either applicable only to certain types of molecules, or require accurate values for other properties, e.g. the critical temperature. Inaccuracies in the estimation of these properties will then propagate to the estimation of the vapour pressure. Work in this field is continuing and suitable methods may well be available in the near future.

## **8.2.2 New Applications**

If suitable fitness functions are developed, the SolvGen algorithm may be applied to any molecular design problem. Possibilities for future developments include extending the method to homogeneous azeotropic distillation and liquid-liquid extraction of ionic systems by using versions of UNIFAC extended to electrolytes (Achard et al, 1994; Li et al, 1994).

In the case of homogeneous azeotropic distillation, an algorithm for the automatic evaluation of distillation region diagram or residue curve maps must be developed.

The algorithm may also be applied to the design of polymers and polymers blends by using the free volume modification of UNIFAC and the various

group contribution methods developed by Van Krevelen (Van Krevelen, 1990).

# 9

## 9 References

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