Friedrich-Alexander-Universität Erlangen-Nürnberg
Technische Fakultät

and

Indian Institute of Chemical Technology

Optimization of Chemical Processes Towards Pollution Prevention

Diploma Thesis by

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June 2001

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Erlangen, 12. Juni 2001

Ulrike Krewer

Die vorliegende Arbeit wurde am Indian Institute of Chemical Technology (IICT, Hyderabad, Indien) unter Leitung durch den Lehrstuhl für Prozessmaschinen und Anlagentechnik der Friedrich-Alexander-Universität Erlangen-Nürnberg erstellt.

Beginn: 15. Dezember 2000
Abgabe: 12. Juni 2001

Betreuung: Dr. K.V. Raghavan, Dr. M. Ramakrishna, Dr. M.A. Liauw
Leitung: Prof. Dr.-Ing. E. Schlücker

Acknowledgements

I would like to thank the Indian Institute of Chemical Technology for providing the facilities to enable this work and the Director Dr. K.V. Raghavan and Dr. M. Ramakrishna for their supervision and technical help during the thesis.

Furthermore I would like to thank Prof. Dr. E. Schlücker for supervising this thesis and Dr. M. A. Liauw for the productive discussions and supervision during the last part of my thesis.

I am grateful to Ashutosh Ugle, who organized my stay, lodge and many more things in IICT/Hyderabad and to the Ernest-Solvay-Stiftung for the financial support to conduct the diploma thesis.

Finally I want to thank all the staff of the Design and Engineering Division who admitted me to their tea club and whom I had many interesting discussions with.

Contents

Chapter 1

Introduction

As late as the 60s and 70s of the last century ideas about protection of the environment in the chemical process industries were rare. Consciousness for pollution of environment and the resulting effects on the quality of life were just starting to spread. Rising awareness of the problem lead to public discussions followed by governmental regulations for the industries. Most branches of the chemical process industries reacted to this with the application of 'end-of-pipe' technologies to their processes in order to fall below the thresholds. Today these technologies are very widespread, common and elaborated.
Applying 'end-of-pipe' technologies to lower environmental pollution has some disadvantages, which the industry realizes more and more: Instead of preventing waste or pollution, this method usually leads the pollution, which previously was spread over the industries surrounding, to single localities, where the harmful material is then concentrated. Energy, additional material and effort have to be invested in these procedures, leading to a rise in capital expenditure, whereas at the same time other waste is produced, e.g. highly toxic filters, chemicals for water treatment and the global warming gas CO_2 through energy consumption. It is obvious that a better approach towards improving the environmental condition and the reduction of capital expenditure is to reduce waste and energy consumption through prevention, i.e. to avoid producing substances that have to be removed in following processes.

In this thesis we present two important aspects of pollution prevention. We developed concepts for waste minimization and solvent substitution, in which chemical process industries and related research institutes can examine processes in development or production for their degree of optimization towards pollution prevention. For a convenient application of these concepts we translated them into software, that requires only little and basic input data.

Waste minimization for pollution prevention:
Many reactions commonly used today in the chemical processing industry have undesired or hazardous by-products. Furthermore a lot of solvents and other additional agents which are used in large amounts are neither recycled nor used somewhere else. In the past and often still today, these by-products were tackled using waste treatment or disposal practices, which are so called 'end-of-pipe'-processes. As a result of the significant rise in capital expenditure for 'end-of-pipe'-processes due to stricter governmental regulations, there has been a growing industrial trend to minimize the generation of waste. The most efficient approach towards waste minimization is the modification of the process itself:
A. Steinbach developed a systematic approach to find weak points of a process [1]. We expand his concept in several aspects and modify it in a way which makes it easier to apply and implement it as software. The parameter 'productivity' plus several sub-parameters are introduced and the composition of input and output flows are analyzed. The software itself will ask the user for basic information about the process and guides her through some steps required for the calculation. Ultimately the parameters are discussed and the user will be given hints about optimization possibilities.

Solvent substitution for pollution prevention:
In many processes the amount of solvents represents a large portion of the total material input. Many solvents are relatively cheap and easily available in large quantities and there is little financial incentive to recycle such solvents. But solvents do not only represent an environmental hazard or pollution if they leave the process, they also may be hazardous during their usage in a process. Therefore solvents constitute a major source of pollution in the chemical process industries and it is an important step towards pollution prevention to select solvents which are environmentally compatible and have a high performance and thus reduce the amount used.
K.G. Joback has already developed a basic concept to find the best performing and environmentally benign solvents for extraction purposes [2]. By altering, expanding and refining his concept, we developed a software which selects best performing and environmental acceptable solvents for various applications. Since only little and basic input data have to be given, the software is easy to handle and can be applied with negligible expenditure of time.

Chapter 2

General Concepts for Pollution Prevention

Virtually every chemical process leads to an increase in global pollution. Throughout the whole life cycle of a product, starting from its manufacturing date until recycling or the treatment of waste, each step increases the consumption of material or energy or the amount of produced waste, i.e. to prevent or reduce pollution means drawing attention to the optimization of each step. Because of economic factors and governmental regulations as well as a higher awareness of the sensitivity of the environment the manufacturing industry in recent years started to give more importance on environmental aspects.
In particular the following aspects need special attention:

- maintenance of quality of air, soil and water
- reduction of pollution by noise and vibration
- safe transport, handling and storage to prevent accidents
- minimization of waste

Below some questions are listed which can serve industrial decision takers to achieve mentioned objectives. Each one applies to each step in a products' life. How is it possible

- to cut resource consumption?
- to cut down waste and emissions?
- to reduce potential harm?

- to prolong service life?
- to increase recyclability?

It is not necessary to optimize each segment of the product life cycle, because some only cause little pollution. Improving several segments according to these guidelines usually leads to a significant decrease in pollution. Which ones are most effective has to be discovered for a given process. Table 2.1 gives an overview over the various possibilities of how to improve a process towards pollution prevention. For each step of the life cycle some suggestions are given to answer the questions mentioned above.

As an EXAMPLE we want to inspect how to decrease the use of resources during the manufacturing stage.

1. Good quality of raw materials
   Reactants and additional agents with low quality and high amount of soiling not only cause problems during the manufacuring step (unwanted reactions that may occur) but also increase the amount of residue.
2. Good reaction conditions and process control
   They help to improve the yield of product and therefore lower the consumption of raw material.
3. A short process chain
   This generally leads to less byproducts, less consumption of energy and less plant equipment.

As a general rule we can say that the higher the efficiency of the process the less raw material is needed.

In subsequent chapters we want to focus on two aspects:

1. waste minimization
2. solvent substitution which gives better performance and has better environmental properties

Both approaches take place during the manufacturing stage and cover the cutting of resource consumption and waste production and the reduction of potential harm and therefore cover a large part of the possible pollution prevention methods in this segment of the product life cycle.

Segment of product life cycle	Cutting resource consumption, waste and emissions	Reducing potential harm	Increasing service life	Increasing recyclability
Manufacturing/ production -Product design -Extraction of raw materials -Production of finished product -Distribution	*High direct yield* *-High efficieny* *-Process control* *-Continuous processing* *-Short process chains* *-Material selection* *-Optimal processes* *-Miniaturization* *-Logistics* *-Lightweight design* *High concentration* *Low dissipation*	Low-polluting processes and feedstocks -Renewable resources -Process control -Additive environmental protection	Performance of function -Process safety -Appropriate materials -Durable joints and fastenings Durable design (stable, wear and corrosion resistant -Composite materials -Material compatibility -Suitable processes	Design for disassembly and recycling -Few materials Compatibility of reclaimed waste Few composites Detachable joints and fastenings Identifiability Modular systems
Product use -Use -Consumption	Low energy consumption Low consumption of water, other utilities Selection -Minimum consumption -Proper disposal	Selection -Minimum consumption	Appropriate use and consumption -Maintenance and care	
Recycling -Collection -Re-use -Rehabilitation -Reclamation of components -Reclamation of materials -Distribution	High direct yield -High efficiency -Process control -Continuous processing -Short process chains -Logistics -Suitable recycling processes	Low-polluting processes and feedstocks -Process control -Additive environmental protection	Gentle handling -Gentle cleaning and disassembly Suitable processes	Suitable recycling processes
Waste processing -Collection -Physical, chemical thermal processes	High direct yield -High efficiency -Process control	Feedstocks -Process control -Additive environmental protection		
Landfill disposal	Volume reduction	Immobilization -Encapsulation/ sealing		

Table 2.1: Possibilities of Pollution Prevention taken from Ullmann [3]

Chapter 3

Waste Minimization

3.1 Introduction

Many reactions commonly used today in the chemical processing industry have undesired or hazardous by-products. Furthermore a lot of solvents and other additional agents which are used in large amounts are neither recycled nor used somewhere else. In the past and still today, these by-products were tackled using waste treatment or disposal practices, which are so called 'end-of-pipe'-processes. This approach was acceptable and economical. Environmental concerns and regulations were less stringent than they are today and could be met without extensive and costly waste treatment practices. These circumstances allowed industries to maximize profit with little concern for waste materials. Today, however, the chemical processing industry has to comply with many environmental regulations. If undesired chemicals are formed, they must be separated from the product and treated or disposed of safely. As a result of the significant rise in capital expenditure for waste treatment, there has been a growing industrial trend to minimize the generation of waste. The most efficient approach to waste minimization is the modification of the process itself.

Steinbach developed a systematic approach in finding weak points of a process [1]. Most processes in chemical process industries are designed towards high stoichiometric yield (RA, 'relative Ausbeute') neglecting byproducts and other residues. This method is not only a disadvantage from the environmental point of view but also from the economic point of view (75% of raw materials often end up as residues). Therefore Steinbach exchanged RA for the balance yield BA ('Bilanz Ausbeute'), which has more relevance towards the minimal use of chemicals. The balance yield is a measure of productivity and is defined as the ratio of the output of desired product to the input of

material. Along with this the method introduces four factors accounting for different influencing parameters of the balance yield.
In this work Steinbachs concept is systematically translated into software, which can help finding weak points of a chemical process according to [1], when basic process data, i.e. the chemical brutto reaction and mass flow is given as input.

3.2 Theory

3.2.1 Productivity Function BA

Processes in the chemical industry are never 100% optimized relating to waste prevention since they always produce some amount of residue, consisting of byproducts, reactants which were used in excess, disposed solvents or other disposed material. For a process producing nothing but valuable output it is right to say: the process is optimal towards waste prevention and in this sense as productive as possible. Exactly the opposite holds for a process which produces nothing but waste, i.e. the process is 0% optimal and in this sense also 0% productive. Using this idea and following [1] Steinbach defines:

$$\text{Productivity } BA := \frac{m_{P,act}}{m_{In}} \tag{3.1}$$

where $m_{P,act}$ is the actual output of desired product(s)[kg]
m_{In} is the input of raw material [kg]

This is a simple mass balance, as we can see in figure 3.1. Any material which enters the process is raw material, whether it is a reactant or additional material, e.g. solvents. As output of the process we get two streams: one stream containing the desired product, and the other one consisting of byproducts, not recycled additional agents and other material, is of little value and is therefore disposed. The input-stream itself can be divided into two sub-streams,

- primary raw material, i.e. reactant
- secondary raw material, i.e. additional agents like catalysts, solvents, etc.

which will be discussed later.

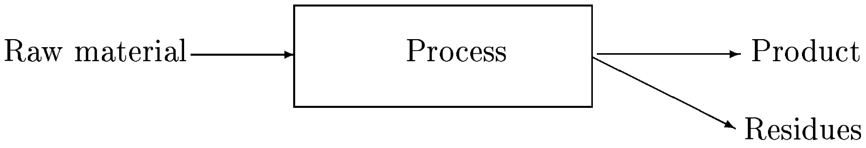

Figure 3.1: In- and Output flow of a chemical process

Inspecting (3.1) we can conclude that the productivity BA is a measure of efficiency of raw material. The more product per input the more efficient the process.

To illustrate the relevance of the productivity BA for chemical processes we now want to discuss an example with common in- and output values for the pharmaceutical or fine chemicals industries:

We imagine the hypothetical reaction

$$1 \text{ mol A} + 2 \text{ mol B} \rightarrow 1 \text{ mol product} + 1 \text{ mol byproduct}$$

to take place in a small pilot plant. The input of reactants and additional agents and the output of product and residues is listed in table 3.1.

material	kg input	kg output
product	0	1
A	2	0
B	4	2
catalyst	3	3
solvent	11	11
byproducts	0	3
total	20	20

Table 3.1: example of in- and output of a chemical process

According to (3.1) the following productivity BA is obtained for this process:

$$BA = \frac{1 \text{ kg product}}{2 \text{ kg A} + 4 \text{ kg B} + 3 \text{ kg catalyst} + 11 \text{ kg solvent}} = \frac{1}{20} = 5\%$$

Obviously this value is very small. But in fact it is a common value in pharmaceutical or fine chemicals industries. These branches usually have a very high material input and receive a small amount of product. They often use more than two or three complicated subsequent reaction steps to obtain the product.

With calculating the productivity BA we know the basic degree of optimization of the process. But this value has a disadvantage: It is still too coarse to help us improving the process and finding the weak points. The BA still does not tell us how and where we have to improve the actual process if the productivity is low. Therefore Steinbach splits the productivity BA into different factors, so called *productivity factors*, where each factor accounts for a separate aspect of possible improvement.

3.2.2 Productivity Factors

An increase in productivity requires knowledge of the main influencing parameters. These parameters and their influences can be expressed in terms of a *productivity function*, which consists of two parts: The first part is based on the chemical reaction equation itself, while the second part is the degree of optimization of the existing process.

We define:

$$\text{Productivity } BA = BA_{TH} \cdot BA_{SP} \tag{3.2}$$

where BA_{TH} is the *theoretical* balance yield and is subject to the atomic balance of the chemical reaction

BA_{SP} is the *specific* balance yield and is a measure for the degree of the optimization of the process

If the process is 100% optimized the specific yield is 1.0, whereas a process in which no product is produced has a BA_{SP} of 0.0, i.e. the process is 0% optimized. The BA_{SP} itself consists of three factors.

- the relative yield RA,
- the excess factor MA_{TR} and
- the additional agents factor EA_P.

The first accounts for the achieved stochiometric yield, the second for any excess of reactants and the third for any disposed additional agents.

To obtain the productivity BA from these productivity factors, they are multiplied:

$$BA = BA_{TH} \cdot \underbrace{RA \cdot MA_{TR} \cdot EA_P}_{BA_{sp}} \tag{3.3}$$

On the following pages each factor is discussed and a small example is given to illustrate its meaning.

Factor 1: Theoretical Balance Yield BA_{TH}

The *theoretical balance yield* BA_{TH} is the theoretical amount of product divided by the theoretical amount of reactants:

$$BA_{TH} := \frac{m_{P,th}}{m_{R,th}} = \frac{\sum_{j=1}^{z} n_{P_j} \cdot mw_{P_j}}{\sum_{i=1}^{z} n_{R_i} \cdot mw_{R_i}} \tag{3.4}$$

where	z	is the number of reactants or products
	$m_{P,th}$	is the theoretical output of desired product(s)[kg],
	$m_{R,th}$	is the theoretical input of reactants [kg]
	$mw_{P,j}$	is the molecular weight [kg/mol] of product j,
	$mw_{R,i}$	is the molecular weight [kg/mol] of reactant i and
	$n_{P,j}$	is the number of mols of product j [mol],
	$n_{R,i}$	is the number of mols of reactant i[mol]

Every atom of the reactants which is not used as part of the product has to be dumped. All these atoms together form the byproducts. If every atom of each reactant reacts to a part of the product, the theoretical balance yield is optimal, i.e. $BA_{TH} = 1.0$. On the other hand if no product is formed from the reactants, the theoretic balance yield is $BA_{TH} = 0.0$. Values of BA_{TH} usually lie between 30% and 100% depending on the chemical reaction.

We look again at the EXAMPLE from section 3.2.1:

$$\begin{array}{llll} 1\text{ mol A} + 2\text{ mol B} & \rightarrow & 1\text{ mol product} + 1\text{ mol byproduct} \\ 10\text{ g/mol} \quad 5\text{ g/mol} & & 7\text{ g/mol} \qquad\qquad 13\text{ g/mol} \end{array}$$

According to (3.4) we obtain:

$$BA_{TH} = \frac{1mol \cdot 7g/mol}{1mol \cdot 10g/mol + 2mol \cdot 5g/mol} = \frac{7}{20} = 0.35$$

The theoretical balance yield is 35% optimized. Since BA_{SP} can not be greater than 1.0, 35% is therefore the maximum balance yield BA which can be obtained.

Factor 2: Relative Yield RA

RA is the *relative or stoichiometric yield* calculated using parameters of the principal raw material:

$$RA := \frac{m_{R,th}}{m_{R,act,stoich}} \tag{3.5}$$

where $m_{R,th}$ = theoretically necessary amount of reactants [kg]
$m_{R,act,stoich}$ = actual amount of stoichiometrically added reactants [kg]

We want to derivate this postulate from the classical definition [4]:

Using the original definition:

$$RA = \frac{n_P - n_{Po}}{(n_P - n_{Po})_{max}}$$

we obtain

$$RA = \frac{n_P - n_{Po}}{(n_P - n_{Po})_{max}} = \frac{\nu_P \cdot \xi_P}{\nu_P \cdot \xi_{P,max}} = \frac{\xi_P}{\xi_{P,max}} = \frac{\xi_{R_{lim},act}}{\xi_{R_{lim},max}}$$

where n_P = amount of product [mol]
n_{Po} = amount of product before reaction [mol]
ν_P = stoichiometric coefficient of product
ξ_P = turnover rate of product [-]
$\xi_{R_{lim},act}$ = actual turnover rate of limiting reactant [-]
$\xi_{R_{lim},max}$ = maximum turnover rate of limiting reactant [-]

The ratio actual turnover rate of limiting reactant per maximum turnover rate is equivalent to the theoretically necessary amount of this reactant for $\xi_{R_{lim},act}$ divided by the actually added amount, i.e.:

$$\frac{\xi_{R,act,stoich}}{\xi_{R_{lim},max}} = \frac{n_{R,th}}{n_{R,act,stoich}} = \frac{m_{R,th}}{m_{R,act,stoich}}$$

where $n_{R,th}$ is the theoretically necessary amount of reactants
$n_{R,act,stoich}$ is the actual amount of stoichimetrically added reactants

During the last years the average RA for processes has been approximately 90% (see [1]), which is very high. As a result we can point out that widespread thinking in industry until now was that the higher RA the better the process. But the relative yield represents only one factor of the BA. And if, for instance, the company seeks to raise RA by adding a significant excess of a raw material, this excess leads to a decrease in other factors and as a result maybe to a decrease in BA, i.e. we contraproductively obtain a productivity of the process lower than before the improvement of RA.

We come back again to the EXAMPLE from section 3.2.1:
As already calculated in the previous section

$$m_{P,th} = 7 \text{ g}, \; m_{A,th} = 10 \text{ g and } m_{B,th} = 10 \text{ g}.$$

For the production of 1 kg we theoretically need

$$\tfrac{10}{7} = 1.42 \text{ kg of A and } 1.42 \text{ kg of B, i.e. } m_{R,th} = 2.84 \text{ kg reactants.}$$

Actually 2 kg A and 4 kg B are used to produce 1 kg product (see table 3.1), i.e.

$$m_{R,act} = 6 \text{ kg}.$$

Stoichiometrically only 2 kg B are needed, therefore

$$m_{R,act,stoich} = 2 \text{ kg A} + 2 \text{ kg B} = 4 \text{ kg reactants.}$$

As defined, RA is obtained through:

$$RA = \frac{m_{R,th}}{m_{R,act,stoich}} = \frac{2.84}{4} = 0.71,$$

i.e. the relative yield is only 71 % optimal.

Factor 3: Excess Factor MA_{TR}

The *Excess Factor* MA_{TR} ('Mengenanteil Theorie Real') is the factor accounting for the excess of reactants:

$$MA_{TR} := \frac{m_{R,act,stoich}}{m_{R,act}} \tag{3.6}$$

i.e. the factor is the actual stoichiometrical amount of reactants divided by the actually used amount of reactants.
If no reactant is added in excess, the factor is 1. If the kg excess of one reactant is equal to the amount of reactants without excess, MA_{TR} is only

0.5.

We look again at the EXAMPLE from section 3.2.1:
$m_{R,act,stoich}$ and $m_{R,act}$ have already been calculated in the RA section. Therefore the calculation of MA_{TR} gives:

$$MA_{TR} = \frac{\text{4 kg stoich. reactants}}{\text{6 kg actual reactants}} = 0.667$$

The excess factor is only 67% optimized.

Factor 4: Additional Agents Factor EA_P

The *additional agents factor* EA_P ('Einsatzstoffanteil primär') accounts for the amount of additional material used in the process.

$$EA_P := \frac{m_{R,act}}{m_{In}} \tag{3.7}$$

i.e. the additional agents factor is the amount of reactants divided by the amount of reactants plus additional agents. If 50% of the material input is additional material, the EA_P is only 50%. As a result the productivity of the process is halved. On the other hand if all solvent is recycled and no other additional material is fed into the process, the factor is optimal and $EA_P = 1.0$. Additional agents are for example catalysts, solvents, viscosity enhancer, impurities and diluting substances in raw materials.
The additional agents factor is very important since often 50% or more of the material input consists of additional agents, which constitutes a non-negligible amount of mass that has to be dealt with. Solvents for example are often basic chemicals which are easy to obtain and relatively cheap and are therefore used in high amounts. As a result this factor lowers the productivity BA often drastically.

We look again at the EXAMPLE from section 3.2.1:
$m_{R,act}$ has already been calculated in the RA section and m_{In} in the example in section 3.2.1:

$$EA_P = \frac{m_{R,act}}{m_{In}} = \frac{6\ kg}{20\ kg} = 0.3,$$

i.e. the additional agents factor is only 30% efficient.

3.2.3 Influencing the Process

After discussing each productivity parameter of the productivity BA we can discuss how to improve the values, if they are low.

As we know from (3.3), BA consists of four influencing factors:

- BA_{TH}, RA, MA_{TR} and EA_P

Since the productivity is lowered by lowering any factor, we look at each of them individually.

$\mathbf{BA_{TH}}$

The theoretical balance yield BA_{TH} represents the percentage of usage of the reactant atoms in the product. Therefore the only possibility to improve this factor is to exchange the chemical reaction through one with better usage of reactant atoms, i.e. a different chemical reaction with different reactants and less byproducts has to be selected.
In most already existing processes it is difficult to translate this step into action, since a new chemical reaction usually needs new process compounds and equipment.

As a successful and early realization of improvement of BA_{TH} we can present the production of maleic anhydride (see [19]). Until the beginning of the 60s, maleic anhydride was exclusively produced with benzene as the main reactant. With growing demand for maleic anhydride this route became economically inacceptable since only four of the six C-atoms are included in the product. Therefore the chemical process industries exchanged the inefficient reaction path for a new one with butene:

- Production via benzene:

$$\underset{\text{benzene}}{C_6H_6} + 4.5O_2 \rightarrow \underset{\text{maleic anhydride}}{C_4O_3H_2} + 2CO_2 + 2H_2O$$

- Production via n-butene:

$$\underset{\text{n-butene}}{C_4H_8} + 3O_2 \rightarrow \underset{\text{maleic anhydride}}{C_4O_3H_2} + 3H_2O$$

For the reaction with benzene we get a $BA_{TH} = 0.442$, while the second reaction results in a BA_{TH} of 0.644. This shows a 20% absolute higher usage of reactant atoms in the second reaction.

RA

The relative yield RA represents the ratio of theoretically needed reactants per actually needed reactants without excess, i.e. the closer the turnover rate to the maximum turnover rate the better is the RA. Usually we can influence this factor by optimizing the condition of the reaction. For example, a reaction which takes place at a certain temperature may have a low RA if the inserted energy is not sufficient. Increasing the reactor temperature therefore leads to better results of the turnover rate and in consequence to a higher relative yield. Other influencing parameters to the reaction condition and therefore to RA are e.g.:

parameters:	*influence on:*
pressure/temperature	chemical equilibrium
amount and type of solvents	solubility of reactants, grade of absorption, etc.
amount and type of catalysts	chemical equilibrium by lowering the activation energy

More ways of influencing the relative yield can be found by looking at the specific process equipment and material (purity of reactants, additional agents like viscosity enhancer). The probability that a low RA of an existing process can be increased is high since there are many influencing parameters.

As an example for the suggestibility of RA we discuss the production of cyclododecatriene, a reactant for dodecanedioic acid. Dodecanedioic acid is used for polyamide and polyester (see [19]).
Cyclododecatriene is produced by trimerisation of three butadiene molecules:

$$3\ CH_2CHCHCH_2 \xrightarrow{[Kat]} \underset{\text{Cyclododecatriene}}{C_{12}H_{18}}$$

The catalyst used is a mixture of $\mathrm{TiCl_4}$ and $\mathrm{(C_2H_5)_2AlCl}$. If the single catalysts are added in a ratio 1:1, the selectivity is low and butadiene preferably reacts to 1.4-trans-polybutadiene. The highest selectivity (ca. 90%) for 1.10-decandicarbon acid and hence the highest RA is obtained when adding Ti- and Al-atoms in the ratio 1:4 to 1:5.

$\mathbf{MA_{TR}}$

The excess factor MA_{TR} represents the ratio of stoichimetrically to actually added reactants. A 100% excess of a reactant (when there are only two reactants) leads to a MA_{TR} of only 66%, as can be seen in the example of the previous subsection "Factor 3: Excess Factor MA_{TR}". The excess factor is directly and exlusively connected to the amount of added reactants. Lowering the excess of one reactant directly increases MA_{TR}. But lowering the input of one reactant usually also leads to a decrease in turnover rate and therefore to a lower relative yield RA. In changing the excess of reactants therefore the reaction conditions may need optimization.

To demonstrate a possible way of MA_{TR} improvement we look at the production of Etinol via vinyl ketone and acetylene described in [3]:

$$R^1COCH = CH_2 + HC \equiv CH \underset{2)H_2SO_4}{\overset{1)LiNH_3}{\longrightarrow}} R^1C(OH)(C \equiv CH)CH = CH_2 + Li_2SO_4$$

In the original process, considerable quantities of acetylene and ammonia had to be disposed of as waste products. The acetylene balance (percentage of total consumption) was approximately as follows:
30% consumption in the reaction, 20% waste gas as ethylene and 50% waste gas as acetylene.
To lower the important loss of 50% acetylene, the waste gases are fed to a central waste-gas recovery system where most of the acetylene is removed from the waste-gas stream by absorption in supercooled ammonia. Both substances are separated afterwards and are again inserted in the process. Subsequent to the acetylene absorption the waste-gas saturated with ammonia is fed into a scrubbing process and the ammonia is recovered. Thus the excess use of acetylene and ammonia is reduced and the MA_{TR} is improved.

$\mathbf{EA_P}$

The additional agents factor EA_P represents the usage of additional agents in a process. The more agents like solvents or catalysts are used the smaller is the value.
If a major part of the additional agents consists of solvents, the following possibilities help increasing the EA_P:

- minimization of the amount of used solvents
- instead of disposing the solvent, it should be recovered and reused
- searching for a solvent which is more efficient in the process so that less solvent is needed (see chapter 4)

The user herself has to decide which one of the points above will fit best in her process and is most efficient. Economic points of view may play an important role since each possibility requires changes in the process.

If the raw material contains a high portion of non-reactants, i.e. impurities or diluting chemicals for reactants, a possible way to lift EA_P is exchanging this raw material by one with a higher concentration or purity. Changing the amount or type of any added additional agents may influence the turnover rate and through this the relative yield. As a result the reaction condition may need optimization to keep an acceptable RA-value.

As an example for the suggestibility of EA_P we look at the production of 2-acetaminonaphtalene-8-sulfonic acid described in [3]:
The acetylation of 2-naphtylamine-8-sulfonic acid was formerly carried out in an aqueous medium with acetic anhydride. The product was salted out from the aqueous medium by addition of ammonium sulfate, filtered off and as a result 2200 kg residue per 1000 kg product had to be treated in a wastewater treatment plant.
To avoid the high amount of contaminated material the company changed the process to dry acetylation: The two reactants 2-aminonaphtalene-8-sulfonic acid and acetic anhydride are reacting in the process without addition of water or ammonium sulfate and in the end instead of producing 2200 kg residues the process produces only 200 kg residues per 1000 kg product, thus improving the EA_P.
In addition to this the new process has a further advantage: The byproduct Acetic acid obtained now can be utilized as a further product and the theoretical balance yield BA_{TH} is increased.

3.3 Software

In chemical process industries or research facilities we usually find many different chemical processes from various periods of time. Especially in situations where a more or less frequent change in the design of a process is desired, environmental ideas are often not applied due to lack of time or because of financial reasons. It is desirable to apply the ideas presented in this thesis even in such situations. It is also desirable that the company or research institute is able to apply this concept without being trained in Steinbachs concept. Chances for the application of the concept presented in this thesis will rise significantly if optimized results can be obtained

- even by relatively untrained staff
- quickly at nearly no extra cost
- reliable and repeatable.

All this suggests the design of software which aides the process designer in applying Steinbachs concept.
The software presented in this thesis will ask the user for basic input about the chemical reaction and material flow of the process and guides her through some steps required for the calculation. As a result the user will be told some possibly weak points of the process and be given hints about optimization possibilities. Ultimately each factor discussed previously is given with its grade of optimization. Some values of the grades of optimization might be smaller than the chosen upper bound and hence declared as necessary to be improved: A warning and some hints are given for a value < 0.95. Values smaller than 70% are emphasized. In any case the user will be informed that a given process is not optimal. To illustrate this the procedure we show the output of the example given in section 3.2.1:

```
**********************************************************
   OPTIMIZATION OF A PROCESS TOWARDS WASTE MINIMIZATION
                         RESULTS
**********************************************************
OPTIMIZATION OF THE PROCESS
 1 A + 2 B -> 1 prod

*REACTANTS
2 kg A, 4 kg B

*PRODUCTS
1 kg prod
*ADDITIONAL AGENTS FOR REACTION STEP
14 kg
*ADDITIONAL AGENTS FOR DOWNSTREAM STEP
(this value has not gone into the calculation)
0 kg
----
**CALCULATION SHOWS THE FOLLOWING RESULTS:

*THE CHEMISTRY/CHEMICAL REACTION IS ONLY 35 % OPTIMAL.
IMPROVEMENT CAN BE DONE IN SELECTING A CHEMICAL REACTION WITH
LESS BYPRODUCTS
*THE RELATIVE YIELD IS 71.4286 % OPTIMAL.
IMPROVEMENT CAN BE DONE THROUGH BETTER REACTION
CONDITIONS (E.G. TEMPERATURE, CATALYSTS)
*THE USE OF REACTANTS (REGARDING EXCESS) IS ONLY 66.6667 % OPTIMAL.
 Excess B: 100.000000 %
IMPROVEMENT CAN BE DONE BY MINIMIZING THE EXCESS USE
OF REACTANTS
```

```
*AVOIDING OF ADDITIONAL AGENTS IS ONLY 30 % OPTIMAL.
IMPROVEMENT CAN BE DONE BY RECOVERING ADDITIONAL AGENTS
(E.G. SOLVENTS & NEUTRALIZERS) OR REDUCING THEIR ACTUAL
USED AMOUNT
-
**INCLUDUNG ALL THESE ASPECTS THE ACTUAL PROCESS IS
 5 % OPTIMIZED TOWARDS WASTE-MINIMIZATION
**********************************************************
```

The program saves all necessary data into files and keeps track about already entered data. In this way, the user can easily check the process again without remembering already given process data. This feature of the program gives the user the ability to easily have a database of all processes used in her facility which can be quickly looked up and saved for future reference. Its exact procedure can be seen in figure 3.2.

Various hardware platforms and even more operating systems are used in chemical process industries and related institutes, from desktop systems to industrial-strength mainframe computers. Often the same location uses many different platforms and each platform can be run by different combinations of operating system and software. A software project which is not focused to run on few machines with the correct combination of software should try to assume as little as possibly about the machine it will run on eventually. As with any scientific software, future requirements on the software will change (scientific progress) or the specific needs of an institution will differ, i.e. software should be easily changeable. The approach to these problems is the well-proven combination of a text-based user interface, ASCII and ANSI-C. ASCII is a well-known standard that can be processed by nearly every operating system and for nearly every computing environment there is an ANSI-C compliant development system. Furthermore, most programmers are skilled in programming in ANSI-C and can easily read and change the program source code.

3.4 Summary and Outlook

In this chapter we discussed a method of how to minimize waste production that is connected with chemical processes. We introduced the balance yield BA, which is a measure of the productivity of a process and which compares the amount of output of product to the amount of input of reactants and additional agents. To further specify the weak points of a given process and, as a result, how to improve the process towards a higher productivity, four productivity factors have been introduced, respectively for the reaction

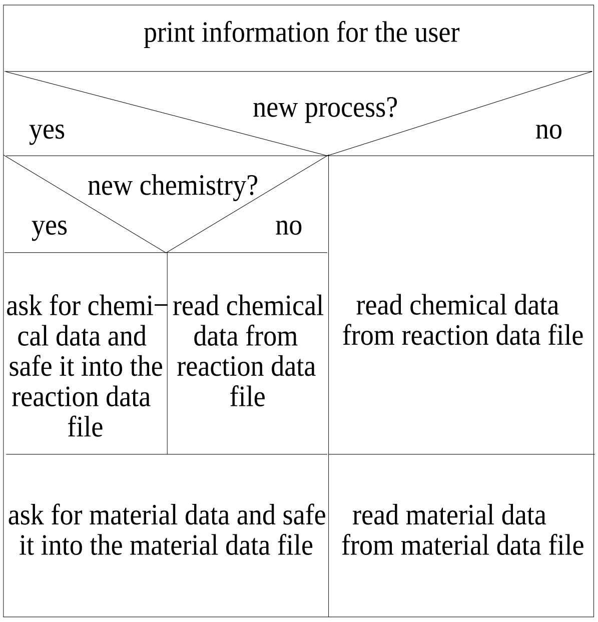

Figure 3.2: program flow in input data

equation related production of byproducts, the grade of optimization of reaction conditions, excess of reactants and use of additional agents. Changing parameters like material flow and temperature directly leads to a change in these productivity factors.

The developed software calculates each productivity factor and by this obtains the grade of optimization of each of the four aspects. It recommends which factor should be improved to obtain a higher productivity and through which type of changes in the process this can be realized. Because only little and basic input has to be given (chemical reaction, molecular weights and mass flows) the software is easy to handle and can be applied with negligible expenditure of time. It finds the weak points of a process efficiently and recommends some changes in the process according to this. It can be applied in various stages of process development (laboratory scale, pilot plant,...) or at already working chemical plants. The software can be used as a standard software for every existing and newly developed reaction or process in order to minimize waste production and therefore prevent pollution.

However, the focus has been laid mainly on chemistry and efficient process operation, without taking capital and operating costs and raw-material and product prices into account. A company will not improve a process factor and as result a process, if a change is connected to a heavy increase in capital expenditure. It will be a strong advantage for the industries to supplement the analysis by incorporating economic factors. Therefore Steinbach [1] has realized a cost flow analysis which is linked interactively with technical process models, so that switching readily back and forth between the technical view of the process (productivity and related factors) to the business view (process costs, environmental protection costs and other factors) leads to the optimum between ecological and economical aspects.

Chapter 4

Solvent Selection

4.1 Introduction

In many processes the amount of solvents represents a large portion of the total material input. Many solvents are relatively cheap and easily available in large quantities. There is little financial incentive to recycle such solvents and as a result they are directly dumped, often even without further treatment if governmental regulation does not require it. Another hazard of pollution is the process itself. Solvents do not only represent an environmental hazard or pollution if they leave the process but are also hazardous during their usage in a process. If an accident occurs within the manufacturing section, e.g. through explosion or leakage, they represent a potential harm when released directly into the environment and may cause some damage. Therefore spent solvents constitute a major source of pollution in the chemical and pharmaceutical industries and it is an important step towards pollution prevention to select solvents which are:

- environmentally compatible or
- possess high performance thus reducing the amount used.

K.G.Joback has already developed a basic concept for finding the most appropriate and environmentally benign solvents for extraction purposes [2], in which he uses a four step methodology to select solvents. In the first step he identifies constraints on important solvent properties. Afterwards he compiles data for all properties and then ranks the solvents which satisfy the target constraints. In the last step he evaluates top solvent candidates using simulation technics. Each step is not suitable for software-implementation, in which only basic input should be required by the user. In step one Joback lists solvent constraints and the user of this method has to select according to her needs which are the most important ones for a given process. This may lead to neglecting some important solvent constraints and not necessarily lead to the implementation of environmental constraints. Since he gives a large variety of possible constraints, in the second step a lot of different data for all these constraints is needed. This is difficult since usually not all physical and chemical properties are readily available for the concerning engineer. In the third step one has to select weights for each chosen constraint. For this we require insight knowledge about the method and calculation to make reasonable choices. The last step has to be neglected totally for automatization of solvent selection since the behaviour of solvents in a given process should be simulated in this step. As result the amount of required information about the process would increase significantly. All in all a lot of input of time and action is required to obtain good results. A much better approach is to leave only very basic decisions to the user and automatize the solvent selection method based on Jobacks ideas.

The concept explained on subsequent pages will discuss this automatization in further detail. Although including just one solvent function, it is already applicable to chemical process industries in which solvents used as reaction media are common.

4.2 Theory

4.2.1 Methodology

We already mentioned that a good performance of a solvent leads to less production of waste and less potential harm for safety and health when released into the environment. Furthermore environmentally benign solvents influence storage and treatment of waste and the potential harm in a positive way since they are less harmful and therefore need less or no safety measures. Both aspects therefore have to be included as important points in the concept. But there are more than these two types of desirable properties of solvents. Joback discusses and lists the main group of constraints in [2] :

constraint	example
Performance:	solubility, capacity
Environmental:	toxicity, global warming potential
Recovery:	enthalpy of vaporization
Reactivity:	non-reactive
Cost:	recycling costs
Other:	freezing point, purity

To simplify the handling and calculation of all these constraints in the concept, we expand the two constraint types 'performance' and 'environment' by including all other constraints either in the first or second group. This is possible since the additional constraints indirectly contribute to either of the chosen constraint types:

- Recovery constraints like enthalpy of vaporisation are as important for environmental as for performance behaviour:
  On the one hand a higher enthalpy of vaporisation leads to more energy usage and as a result to more pollution while on the other hand in several processes, e.g. extraction, recovering of the solvents is necessary to obtain the product.
- Reactivity constraints are also part of both constraint types:
  A highly reactive and as a result maybe explosive material poses a non-negligible potential harm for the safety of the process and therefore for the environment as a whole. Furthermore may reactive material influence the performance of the process by inhibiting or irritating the reaction through unwanted side-reactions of the solvent with another chemical.
- Other constraints, e.g. a good density and viscosity are likely to increase the performance by making the handling of material more simple.

Since the two constraints 'environment' and 'performance' are totally independent qualities of the solvent, we look at them separately in this thesis. Industry did not care for the environmental aspect for centuries and also today the consideration of importance of the environmental constraints may vary. As a result the ratio 'importance of environmental constraints' to 'performance constraints' cannot be fixed. Environmental constraints in common can become more stringent in the future and several factors may prove more or less relevant. Also governmental regulations usually play a large, often local role. Therefore we rank the solvents respectively according to their performance and to their environmental constraints. The performance constraints, which are not very likely to vary in importance, constitute the base for the final ranking. Within the best performing solvents the solvents with the best environmental constraints are highlighted. In the following chapters we develop a performance and environmental test respectively for the ranking of solvents.

4.2.2 Performance Test

Two main points have to be considered to obtain good solvent performance in a process: the first is the process temperature and the second is the choice of necessary solvent properties according to the solvent function. While the first point is a necessary condition for any chemical reaction the second can vary strongly in the concerned constraints and their grade of importance respectively.

Temperature

Solvents are usually used in liquid condition. In various cases they are used in boiling condition in order to control temperature. Furthermore they are never used in frozen state of condition. As a result we have to sort out solvents whose solidification point is above the process temperature.
The boiling temperature is strongly related to the pressure of the process, butsince a high percentage of processes works under atmospheric pressure we only consider the case of atmospheric pressure for the first version of this concept.
We therefore define a necessary condition for a solvent:

$$T_{Solidification} < T_{Process} \tag{4.1}$$

If the solvent is supposed to work below its boiling point, i.e. in liquid condition, the second obligatory constraint for the solvent is:

$$T_{Boiling} > T_{Process}. \tag{4.2}$$

Whereas a solvent which should be used above its boiling point requires the condition:

$$T_{Boiling} \leq T_{Process} \tag{4.3}$$

In further improvements of this concept it should be considered to include a variation of pressure and as a result a variation of the solidification and boiling points.

Solvent Functions and Their Constraints

Solvents have to fulfill various tasks: there are solvents for extraction, solvents for refrigeration, solvents for heat transfer, solvents as reaction medium and many more. For each task the solvent needs special properties, e.g. a high solubility to a solute or a low boiling point to enhance regeneration after extraction. The three most important functions in chemical manufacturing industry are:

- reaction medium
- extraction (liquid-liquid or solid-liquid)
- heat transfer

→ Reaction medium:
A lot of reactions need the help of a solvent, either to dissolve solid reactants or to dilute already dissolved reactants. Important constraints are therefore a high solubility to reactants and a low reactivity, so that the solvent does not react with other substances like reactants and catalysts. More information is given below since this solvent function is implemented in the software.

→ Extraction:
A lot of natural solid products need the help of solvents to obtain a valuable extract. These solvents should dissolve the desired substance and leave as residue worthless material. As a consequence high solubility is needed for the extract and low solubility for the residue. Furthermore recovery constraints like enthalpy of vaporization should be considered. Equivalent thoughts can be made for liquid-liquid extractions.

→ Heat Transfer:
Some processes use solvents as temperature regulators. When the solvent boils the system stabilizes at a special temperature under which the reaction takes place. Like this e.g. exothermic processes can be controlled. Other applications are direct and indirect heat exchangers respectively with direct or no contact solvent-fluid. They are used to remove or add heat. For all these applications a high capacity of heat is useful.

The solvent function 'Reaction Medium'

Out of the three mentioned solvent functions 'reaction medium', 'extraction' and 'heat transfer' we select the first function to be implemented in the software since a solvent as reaction medium is the most important and common case for chemical process industries and the other functions can be easily included if required. As a result we have to estimate the solubility of each solute to a solvent and the reactivity of the solvent.

1. Solubility Calculation concepts
The usual way to select a solvent for a special chemical reaction or process is to look at the chemical structure of the solvent and solute, estimate on

a basis of experience whether a solvent may dissolve the substance and afterwards test some results in experiments. This leads to a concentration on a small number of solvents. With the existence of various solubility estimation methods it is possible to estimate the solubility of one substance in another without conducting laboratory experiments and to consider much more solvents than the usually used ones. This is a large advantage since only basic information is required about the substances dissolved for solubility calculation. Furthermore these methods are much less time-consuming than experiments. On the other hand we have to state that all methods existing at the moment give more or less wrong results for some solvent-solute combinations (see [5]). As a side-effect these methods are to some degree not reliable, but usually give a good clue of solubility.

To automatize solubility estimation we cannot dispense with solubility estimation methods since it is not possible to automatize solubility estimation through laboratory data. On the following page we are shortly reviewing the main estimation methods:

- Robbins chart, which is a qualitative guide to identifying general classes of solvents.
- UNIFAC, which is a group contribution method for estimating an activity coefficient and by this for assessing solubility.
- Hansens "Radius of interaction" analysis, which is utilizing solubility parameters.
- The extended Hansen model, which is a quantitative use of Hansen solubility parameters.

Robbins chart
Robbins chart consists of twelve general classes of functional groups, e.g. tertiary amines, ketones, phenol. The solubility of one to another group is categorized in three cases: attractive interaction, no interaction and repulsive interaction of molecules. Attractive interaction is equivalent to a high solubility in each other, no interaction to a medium solubility and repulsive interaction leads to insolubility of the substance in the solvent. Robbins chart is a simple but not very exact method for solubility estimation since only three grades of solubility are used and every substance of one class is assumed to be equivalently soluble in each substance of another class.

UNIFAC

The UNIFAC method calculates activity coefficients which consist of two parts, the first includes pure component properties while the second includes interaction between solvent/solute group pairs. The resulting activity coefficient can be used to calculate the fraction of solute dissolved in the liquid. Tables for the required parameters can be found in [6].

Hansens Radius of Interaction

The "Radius of Interaction" method is used in this thesis, since parameters are easily accessable and furthermore can be easily calculated. It is based on regular solution theory (see [5]). Three different physical effects are included in the solubility calculation:

- nonpolar effects (dispersion)
- polar effects
- hydrogen-bonding effects

Each chemical substance has three *solubility parameters* respectively for each effect. According to regular solution theory, the better solvents are the ones whose parameters match the solutes values most closely. This is a formal expression of the well known general chemical rule "like dissolves like". Further details about Hansens concept and some examples will be given below.

Extended Hansen model

The extended Hansen solubility method is a more precise but also more complicated method compared to the previous one. The required information (e.g. entropy of fusion, molar volume and quantitative solubility data for four solvents) for the implementation of this method often cannot be easily given by the engineer. As a result an application of the solftware to a given process would require much effort and time.

As already mentioned we decided for the implementation of Hansens 'Radius of Interaction' method into the concept. It is easy to implement and gives acceptable estimation results. On the following pages we are explaining the exact method of calculation.

2. Hansens Radius of Interaction

Hansens model consists of three solubility parameters for each substance::

- the factor accounting for dispersive forces, δ_d
- the factor accounting for polar forces, δ_p

- and the factor for hydrogen bonding forces, δ_h

The closer the solubility factor of one substance to another, the higher is the solubility. Distance of solubility parameters can be measured using an Euclidean distance metric. For two molecules A and B the distance R between their solubility parameter is given by:

$$R(A,B) := \sqrt{(\delta_d^A - \delta_d^B)^2 + (\delta_p^A - \delta_p^B)^2 + (\delta_h^A - \delta_h^B)^2} \tag{4.4}$$

where	R	is the Radius of Interaction,
	δ^A	are the solubility parameters for molecule A and
	δ^B	are the solubility parameters for molecule B.

A and B are therefore two points in $\Re^3$ with the coordinates $A = \{\delta_d^A, \delta_p^A, \delta_h^A\}$ and $B = \{\delta_d^B, \delta_p^B, \delta_h^B\}$. The larger R the less soluble is substance A in B. δ_d, δ_p and δ_h values for many liquids and solvents are listed in [7]. For calculating the solubility parameters of the solute and solvents which are not listed, we use the estimation techniques described in [7]. Various methods to determine each solubility parameter are given there, either based on molecular physical properties or structural contribution. The last method is simple to include in the software and the user will not have difficulties in searching for special molar physical properties. With the help of table 4.1 the factor δ_d^Z for a substance Z can be calculated according to this method as following:

$$\delta_d^Z = \frac{1}{V^Z} \sum_{i=1}^{n} F_{d,i}^Z, \tag{4.5}$$

where	n	is the number of functional groups and
	$F_{d,i}^Z$	is the Dispersion Molar Attraction Factor for the functional group i of substance Z [-].
	V^Z	is the molar volume of Z [cm^3/mol]

The molar volume of a substance Z is defined as:

$$V^Z = \frac{\mathrm{mw}^Z}{\rho^Z} \tag{4.6}$$

where	mw^Z	= molecular weight of Z $[g/mol]$
	ρ^Z	= density of Z $[\frac{g}{cm^3}]$

Structural group	F_d $\frac{\sqrt{J \cdot cm^3}}{mol}$	F_p $\frac{\sqrt{J \cdot cm^3}}{mol}$	$-U_h$ $\frac{J}{mol}$
-cyclohexyl(-C_6H_{11})	1620	0	0
-phenyl(-C_6H_5)	1430	110	0
-(o-,m-,p-)-phenylene(-C_6H_4-)	1270	110	0
-CH_3	420	0	0
=CH_2	400	0	0
-CH_2-	270	0	0
=CH-	200	0	0
$> CH$-	80	0	0
=$C <$	70	0	0
$> C <$	-70	0	0
-F	220	460	0
-Cl	450	550	400
$> Cl_2$	0	360	720
-Br	550	610	2100
-I	0	665	4000
-CN	430	1100	2500
-OH	210	500	20000
-O-	100	400	3000
-COH	470	800	4500
-CO-	290	770	2000
-$COOH$	530	420	10000
-COO-	390	490	7000
-NH_2	280	610	8400
-NH-	160	210	3100
-NO_2	500	1070	1500
-$N <$	20	800	5000
-S-	440	0	0
=PO_4	740	1890	13000

Table 4.1: Group Molar Hansen Parameters for disperse, polar and hydrogen bonding effects according to [7]

Similarly we can calculate the polar factor δ_p^Z:

$$\delta_p^Z = \frac{1}{V^Z}\sqrt{\sum_{i=1}^{n} F_{p,i}^Z} \tag{4.7}$$

where $F_{p,i}^Z$ is the Polar Molar Attraction Factor for the functional group i.

Values for $F_{p,i}$ are listed in table 4.1, so that δ_p^Z can easily be calculated. A special condition has to be made for δ_p: If a molecule has two identical polar groups and in addition is symmetrical, the polar force of the molecule decreases. To account for this decrease the parameter is multiplied by a factor:

- 0.5 for one plane of symmetry
- 0.25 for two planes of symmetry
- 0 for more planes of symmetry

The hydrogen bonding parameter is calculated slightly differently from the two previous parameters. Instead of the molar attraction constant F^Z for a substance Z we use the hydrogen bonding cohesive energy U_h^Z:

$$\delta_h^Z = \sqrt{-\frac{1}{V^Z}\sum_{i=1}^{n} U_h^Z} \tag{4.8}$$

Values for U_h^Z can be found in table 4.1.

Different sources and slightly deviating values for F_d, F_p and U_h can be found in literature. To assure that the solubility parameters harmonize with each other we take the values given by van Krevelen and Hoftyzer [8], who are the only ones to present values for all three molar attraction constants. If values for some functional group are missing we take values from other sources (see [7]).

To illustrate the calculation of solubility factors we take the example given in table 4.2. The required input is the molar volume and the molecular structure of diacetone to select the attraction factors according to the functional groups.

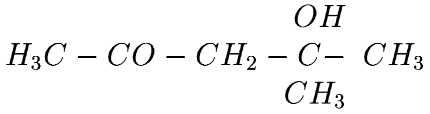 $\overset{OH}{\underset{CH_3}{H_3C-CO-CH_2-C-\ CH_3}}$			V = 123.8 cm^3/mol
Group i	$\sum_{i=1}^{z} F_{d,i}$ $\frac{\sqrt{J\cdot cm^3}}{mol}$	$\sum_{i=1}^{z} F_{p,i}^2$ $\frac{J\cdot cm^3}{mol^2}$	$-\sum_{i=1}^{z} U_{h,i}$ $\frac{J}{mol}$
3 $(-CH_3)$	1260	0	0
-CH_2-	270	0	0
$>C<$	-70	0	0
-CO-	290	593000	2000
-OH	210	250000	20000
total	1960	843000	22000
	$\delta_d = \frac{1960}{123.8}$ MPa$^{1/2}$ $= 15.8$ MPa$^{1/2}$	$\delta_p = \frac{\sqrt{843000}}{123.8}$ MPa$^{1/2}$ $= 7.4$ MPa$^{1/2}$	$\delta_h = \sqrt{\frac{22000}{123.8}}$ MPa$^{1/2}$ $= 13.3$ MPa$^{1/2}$

Table 4.2: Solubility parameter calculation for diacetone according [8]

As a result we obtain the following solubility parameters for diacetone:

$$\delta_d = 15.8\ \sqrt{MPa},\quad \delta_p = 7.4\ \sqrt{MPa},\ \delta_h = 13.3\ \sqrt{MPa}$$

For further calculating the Radius of interaction between Diacetone and any solvent, solubility parameters for the solvent have to be calculated and the solubility parameters of both substances are inserted in (4.4). In most solvent-solute combinations the radius R lies between 0 and 30 (see next subsection).

In the case that more substances should be soluble in a solvent, the radius of interaction R_z has to be calculated separately for each substance z and we use the arithmetic mean:

$$\overline{R} = \frac{1}{n}\sum_{z=1}^{n} R_z \tag{4.9}$$

The number of soluble substances should be limited to a maximum of three since the more solutes are included the less importance is given to a single solute. As a result an insoluble substance has too little weight in the mean value $\overline{R}$.

3. Absolute solubility

Hansens radius of interaction itself only presents relative solubilities, i.e. it gives results which solvent from a solvent list dissolves a substance best. But it does not show the absolute solubility: In a solvent database of three solvents there is always a best-soluting solvent for a substance, but still the substance may be insoluble in all three solvents. In order to obtain absolute solubilities we create three categories 'soluble', 'slightly soluble' and 'insoluble' and relate them to R with the help of literature:
In [9] Scheflan lists many organic substances plus their solubility in several solvents. He gives six categories of solubility:

> infinitely soluble, very soluble, soluble, slightly soluble, very slightly soluble and insoluble

We reduce them to three since Hansens model is not a very precise model (see discussion of solubility models above). For estimation of the upper and lower bound of each category we calculate the radius of interaction for several solvent-solute combinations given in [9] and and compare them with Scheflans categories.

For infinitely soluble to soluble solvent-solute combinations we obtain the following table:

infinitely soluble, very soluble and soluble combinations according to [9]		
solute	solvent	R
Acetaldehyde	Acetone	5.21
Acetaldehyde	Benzene	16.71
Acetaldehyde	Ethanol	11.98
Acetic Acid	Benzene	13.52
Acetic Acid	Ethanol	6.41
Acetic Anhydride	Ethanol	11.11
Acetone	Ethanol	12.55
Acetylchloride	Acetone	3.26
Acetylchloride	Benzene	14.01
Acrylonitrile	Acetone	6.37
Acrylonitrile	Benzene	17.38
Acrylonitrile	Methanol	16.75
Acrylonitrile	Ethanol	15.42
Acrylonitrile	Toluene	15.99
Allylmethylether	Ethanol	14.5

contd...

solute	solvent	R
Allylthiocyanate	Ethanol	12.14
tert-Amyl Butyrate	Ethanol	14.56
Amylnitrile	Ethanol	12.64
sec-Butylether	Ethanol	16.61
NN-Dibutylaniline	Acetone	7.42
NN-Dibutylaniline	Benzene	4.61
1.2-Dichlorobenzene	Benzene	5.88
NN-Dibutylaniline	Benzene	4.61
Diethanolamine	Ethanol	5.35
Methanol	Ethanol	4.60
Octylamine	Ethanol	13.32
1.5-Pentanediol	Acetone	14.44
1.5-Pentanediol	Ethanol	5.54
1.5-Pentanediol	Methanol	9.52
4-Amino-2-Butanol	Acetone	10.36
4-Amino-2-Butanol	Benzene	17.35
4-Amino-2-Butanol	Methanol	6.7
1-Amino-2.3-Propanediol	Ethanol	7.64
Benzedrine	Ethanol	12.7
1-Bromo-2-propanone	Benzene	12.74
Butylethanollamine	Acetone	8.89
Butylethanollamine	Benzene	12.17
Butylethanollamine	Methanol	12.26
1.3-Butanediamine	Acetone	6.12
1.3-Butanediamine	Benzene	13.96
1.3-Butanediamine	Methanol	10.3
2-Chloro-1-propanol	Ethanol	4.07
1-Chloro-2-propanone	Ethanol	14.41
Cyanopropionic Acid	Ethanol	8.85
Diamylbenzene	Acetone	12.24
Diamylbenzene	Benzene	2.65
NN-Diethyl-1.3-Propanediamine	Acetone	4.60
NN-Diethyl-1.3-Propanediamine	Benzene	12.57
NN-Diethyl-1.3-Propanediamine	Methanol	14.38
Di-sec-Butylamine	Acetone	9.54
Di-sec-Butylamine	Benzene	4.17
Di-sec-Butylamine	Methanol	21.12

contd...		
solute	solvent	R
Nonylbenzene	Acetone	12.24
Nonylbenzene	Benzene	2.51
Octylamine	Acetone	6.73
Octylamine	Benzene	6.89
Octylamine	Methanol	17.48
Triamylamine	Acetone	9.44
Triamylamine	Benzene	3.69
μ		11.55
σ		4.68

For slightly to very slightly soluble combinations we obtain:

slightly and very slightly soluble combinations according to [9]		
solute	solvent	R
1-Bromo-2-iodobenzene	Ethanol	12.59
1-Bromo-2-propanone	Ethanol	12.98
Butyltoluene	Ethanol	21.08
Caprinitrile	Ethanol	15.98
1.2-Dichlorobenzene	Ethanol	17.93
Diethanolamine	Ethanol	19.65
Diethylene Glycol	Ethanol	12.08
2.4-Dimethylhexane	Ethanol	21.33
2-Ethyl-2-methylpentane	Ethanol	21.43
Nonanenitril	Ethanol	21.15
μ		20.37
σ		3.73

And for insoluble combinations we get:

insoluble combinations according to [9]		
solute	solvent	R
Diamylbenzene	Methanol	25.31
1-Amino-2.3-Propanediol	Benzene	26.12
Nonylbenzene	Methanol	25.31
1.5-Pentanediol	Benzene	17.92
Triamylamine	Methanol	21.16
μ		25.31
σ		3.52

Comparing the median μ for all categories we see a clear tendence: with decreasing solubility we obtain higher values for R, i.e. there is a correlation of Hansens 'Radius of Interaction' to Scheflans solubility categories.
To fix the upper and lower bound for each category we assume gauss distributions and calculate the median $\mu_{cat1,cat2}$ of the medians μ_{cat1} and μ_{cat2} of adjecting categories. Subsequently we get the bounds in weighting the obtained medians according to the variances of the adjecting categories.
The lower bound of the category 'soluble' is set to 0 and the upper bound of the category 'insoluble' is set to infinity in order to cover all possible values for R. As a result we obtain the following bounds:

solubility status	Radius of Interaction, R	
	lower bound	upper bound
soluble	0	16.45
slightly soluble	16.45	17.75
insoluble	17.75	infinity

Table 4.3: Categories of solubility

As can be seen, the range for slightly soluble substances is very small. This is justifiable since, according to fuzzy logic, a solvent is either soluble or insoluble and by introducing the third category we simply soften the bound between them.

While conducting the comparison between Hansens radius and Scheflans categories we found that water has totally deviating solubility values from other solvents and consequently it cannot be included in the concept presented above. A possible reason for this is the strong hydrogen-bonding and polar effect of water which leads to significantly higher values for R. As a result we obtain a very large radius R for nearly every water-solute combination compared to other values of R, even if water dissolves the substance better than solvents with lower R.

For infinitly to soluble substances in water we can calculate the following Rs:

infinitly soluble, very soluble and soluble substance-water combinations according to [9]	
solute	R
Acetaldehyde	33.15
Acetic Acid	30.37
Acetone	35.74
Diethanolamine	24.37
Methanol	20.35
1.5-Pentanediol	26.02
4-Amino-2-Butanol	26.4
1-Amino-2.3-Propanediol	18.09
1.3-Butanediamine	30.48
Butylethanollamine	31.4
1-Chloro-1-propanol	27.87
1-Chloro-2-propanone	37.11
Cyanopropionic acid	30.43
NN-Diethyl-1.3-Propanediamine	34.46
Di-sec-Butylamine	40.73
μ	30.43
σ	6.16

For slightly soluble substances we obtain:

slightly soluble substance-water combinations according to [9]	
solute	R
Allylisocyanide	37.03
Allylmethylether	38.48
Allylthiocyanate	35.80
tert-Amyl Butyrate	38.49
Amylnitrile	36.15
Benzedrine	36.65
1-Bromo-2-propanone	35.66
sec-Butylether	40.52
Octylamine	37.29
μ	37.03
σ	1.58

And for insoluble substances we get the following values of R:

insoluble substance-water combinations according to [9]	
solute	R
1-Bromo-2-Iodobenzene	36.41
Butyltoluene	45.02
Caprinitrile	39.92
Diamylbenzene	45.09
2.4-Dimethylhexane	45.23
2-Ethyl-2-methylpentane	45.29
NN-Dibutylaniline	39.64
Nonanenitrile	39.57
Nonylbenzene	45.08
Triamylamine	40.83
μ	42.93
σ	3.29

Comparing the median of water-solubility to the median of the other solvents for each category, we again find very large distances for R (11.72 to 18.88). In literature too, a considerable variation in the Hansen parameters is reported for water (see [7]).

If we look at the variances and medians of water we can see that although the values for water do not fit with the values for ordinary solvents, a correlation between Hansens Radius and solubility categories is obtained: the smaller the radius R the more soluble is the substance in water. As a result it is indeed possible to implement the solvent 'water' in our concept.

We calculate special bounds for the solubility in water according to the bound calculation of usual solvents:

solubility status	Radius of Interaction, R	
	lower bound	upper bound
soluble	0	35.68
slightly soluble	35.68	38.94
insoluble	38.94	infinity

Since we are ranking the solvents according their solubility and reactivity at the end of the performance test and therefore include the Radius of Interaction into the concept, we have to take special measures to include the solubility of water: we multiply the Radius of Interaction for water with a special downscale factor, which is a function of the Radius itself and which sets the bounds for water in proportion to the bounds for usual solvents.

After discussing the estimation of solubility of solute-solvent-combinations we look at the second important constraint for the solvent function 'reaction medium', the reactivity.

4. Reactivity estimation

The National Fire Protection Agency has defined various parameters to estimate the danger of fire and explosion in a chemical plant. One of these standardized parameters is the *reactivity value* N_R (range: 0 to 4). Since it gives a clear distinction of grades of reactivity and is easy to handle and obtain we include this value as the second constraint in the solvent function 'reaction medium'. Because of its relevance as an important environmental constraint, its definition and context is explained in the subsection "Fire and Explosion" of chapter 4.2.3.

5. Score calculation

Every solvent function has at least one performance constraint. In order to compare solvents according to their overall performance in a process, a total score S_T^z has to be calculated for every solvent z consisting of all relevant performance constraints. In the case that a solvent should work as a a reaction medium, the two constraints solubility and reactivity have to be included.
To obtain the total score we normalize the single raw scores C_i^z using the following function:

$$C_{i,n}^z = \frac{C_i^z}{C_i^{max}} \tag{4.10}$$

where	$C_{i,n}^z$	is the normalized score of constraint i for the actual solvent z,
	C_i^{max}	is the highest score within the tested solvents for constraint i and
	C_i^z	is the score of constraint i for the actual solvent z,

This function simply translates all values onto a 0 to 1 range.
As example we want to show the calculation of solubility normalisation:

$$C_1^z = R_n^z = \frac{R^z}{R^{max}} \tag{4.11}$$

R^{max} is the largest radius of interaction for all conducted solvent-solute combinations and R^z is the radius for the actual combination solvent-solute. In all combinations the solute is the same.

Usually not every constraint is equally important, therefore a weight w_i is given for each constraint i according to its importance. In the case 'reaction medium' we fix a weight $w_1 = 4$ for solubility and $w_2 = 1$ for reactivity since a high solubility is the essential property of the solvent which should work as a reaction medium.

The total score S_T^z is obtained by multiplying each constraint score with its related weight and adding all these weighted scores:

$$S_T^z = \sum_{i=1}^{n} C_{i,n}^z \cdot w_i \tag{4.12}$$

where S_T^z is the total score for solvent z
n is the number of important performance constraints
w_i is the weight of constraint i

i.e. for a total score for solvent z in the case 'reaction medium' we can calculate:

$$S_T^z = R_n^z \cdot 4 + N_{R,n}^z \cdot 1 \tag{4.13}$$

The best solvents are the ones with the lowest score.

4.2.3 Environmental Test

There are many sources of pollution and the effects on nature are also manifold. A distinction can be made between long-term and short-term hazards. Long-term hazards, e.g. ozone depletion cause poisoning only after a longer span of time, e.g. years, while on the other hand the effect of short-term hazards, e.g. an explosion in a chemical plant, can be seen shortly after or during exposure. A second distinction can be made for the range of pollution: Some hazards may only influence the surrounding of the process, e.g. a leakage in a pipe which leads to poisoning of ground waters, while others have much farther importance. These may pose a harm within a wide or global range, e.g. the release of global warming gases which cause a change in the world climate. To cover all these cases and to obtain the least impact of the solvents on the environment, we included the following aspects in the solvent selection concept:

- global impact:
    - ozone depletion potential (ODP)
    - global warming potential (GWP)

- plant safety:
  - danger through fire
  - danger through explosion

  Both aspects are covered in DOWs 'Fire and Explosion Index' which calculates the potential harm through fire and explosion of a process when detailed description of the process and of the handling of material is given. It is the most widely used hazard index.

- toxicity for man and nature:
  - biological oxygen demand in 5 days (BOD_5)
  - toxicity (N_H)

The following chapters give an overview over each environmental hazard, its mode of operation, its effects and how to obtain or calculate values and thresholds, which make a quantitative or qualitative comparison of the degree of harm on the environment possible.

Global Hazards

1. Ozone Depletion Potential (ODP)

ODP is the ratio of impact on ozone of a chemical compared to the impact of a similar mass of CFC-11 (Trichlorofluoromethane). Thus, the ODP of CFC-11 is defined to be 1.0. Other Chlorofluorocarbons (CFCs) and Hydrochlorofluorocarbons (HCFCs) have ODPs that range from 0.01 to 1.0. Halons, containing bromine among other substances, have ODPs ranging up to 10. For a detailed list of ODP-values see [10].

Over the last 50 years, CFCs were thought of as miracle substances. They are stable, nonflammable, low in toxicity, and inexpensive to produce. Over time, CFCs were used as refrigerants, solvents and in many other applications. But CFCs have atmospheric lifetimes long enough to allow them to be transported by winds into the stratosphere, 12-50 km above the ground. Most of the atmospheric ozone which protects the earth from ultraviolet light is concentrated exactly in this layer. CFCs, HCFCs, halons and several other industrially used compounds which reach the stratosphere are very stable under normal condition. Only if they are exposed to strong UV radiation they decompose and release atomic chlorine or bromine. Exactly this occurs in the stratosphere since the ozone, which is located there, has not filtered UV radiation coming from the sun yet. As a consequence the chlorine or bromine radicals react with ozone and decompose it. One chlorine may lead to destruction of over 100000 ozone molecules. The net effect is that ozone is destroyed faster than it is naturally created and ultraviolet light which is not filtered anymore by the ozone may lead to skin cancer, cataract rates and crop damage.

The Montreal Protocol (founded 1987) on substances that deplete the Ozone Layer and its amendments control the phaseout of production and use of ozone depleting substances (ODS). Under the protocol several international organizations report on the science of ozone depletion, implement projects to help move away from these ozone depleting substances and provide a forum for policy discussions. A lot of governments signed the protocol to defeat the global harm.

Since ozone depletion therefore is an important global hazard and the problem is internationally acknowledged, we will include the ODP-values into the environmental test.

There are only few substances which are stable enough to be transported into the stratosphere and which in addition cause ozone depletion. These are:

- CFCs, HCFCs, Halons, Methyl Chloroform, Carbontetrachloride and Methyl Bromine

Therefore the easiest way to estimate the harm is to directly include the names and ODPs of the relevant substances in the program logic.

Furthermore the number of these substances is very small compared to the number of available solvents: with 1.1.1-Trichloroethane only one ODS is placed in the 15 top-most used solvents-list, see [11]. As a result substitutes for ozone depleting substances may be easily found. To contribute to the Montreal Protocol we therefore set a threshold of $ODP = 0$ for the solvents in our software:

$\Longrightarrow$ Threshold ODP = 0

2. Global Warming Potential (GWP)

The global warming potential GWP is the ratio of warming caused by a substance to warming caused by a similar mass of carbon dioxide (CO_2). Thus the GWP of CO_2 is defined to be 1.0. Various HCFCs and HFCs (Hydrofluorocarbons) have GWPs ranging from 93 to 12100.

Certain gases in the atmosphere, e.g. water, carbon dioxide, methane, nitrous oxide, CFCs and others absorb infrared light that would otherwise escape to space, radiating it back towards the planet's surface. These "greenhouse gases" have always played a critical role in determining the temperature of the Earth's surface and to the livability of the planet. Now with the

amount of CO_2 and other greenhouse gases increasing in the atmosphere due to human activities, the possible implications to climate are subject to much research. At Aeronomy Laboratories, researchers are conducting laboratory experiments and theoretical research to determine the infrared properties and atmospheric lifetimes of molecules that may contribute to the greenhouse effect.
At the time of this thesis only few substances are known that cause global warming. They and their related GWPs are listed in [10].
While looking at the substances which are known for causing global warming we found that the substances correspond with the ozone depleting substances plus HFCs, PFCs (Perfluorochlorides), CO_2, CH_4 and N_2O . With the same argument as above the substances with GWP > 0 are environmentally not acceptable in our solvent selection concept.

$\Longrightarrow$ Threshold GWP $= 0$

Fire and Explosion

1. DOWs Fire and Explosion Index (F&E-Index)
The F&E-Index is a direct method for providing a relative ranking of the risks in a chemical process plant [12]. It assigns penalties and credits based on plant features. Penalties are given to process materials and conditions that can contribute to an accident and credits are assigned to plant safety features that can mitigate the effects of an accident. These penalties and credits are combined to derive an index that is a relative ranking of the plant risk. Estimates of consequences in terms of cost and outage time can also be included in the evaluations. In our concept we develop a model of a storage tank to estimate the fire and explosion hazards deriving from the solvent. DOWs F&E-Index ranges with its related degree of hazard is shown in table 4.4. Solvents with light (0-60) and moderate (61-96) hazards are acceptable. Values above 97 give evidence of a dangerous and here environmentally not acceptable solvent. As a result we set the threshold for F&E-Index to 96.

$\Longrightarrow$ Threshold F&E-Index $= 96$

2. Calculation of the Fire and Explosion Index
2.1 Model

a) 120000 kg storage tank

F&E-Index	degree of hazard
0-60	light
61-96	moderate
97-127	intermediate
128-158	heavy
> 158	severe

Table 4.4: Fire and Explosion Index [12]

b) location: outside the process area in a warehouse

c) maximum storage temperature: 323 K

d) storage pressure: atmospheric

e) special safety measures: none

to a)
We assume a solvent demand of 500 l/h in the manufacturing plant. If the plant operates 24 h/day and the storage tank is refilled regularly after 10 days the tank needs a volume of 120 cubicmeters. Since most of the solvents have a density between 0.8 $\frac{g}{cm^3}$ and 1.2 $\frac{g}{cm^3}$ we take a mean density of 1.0 $\frac{g}{cm^3}$ to estimate a virtual mass of stored solvent, i.e. the storage tank holds 120,000 kg solvent.

to b)
Large storage tanks are normally located outside the process area in warehouses to avoid interference during accidents in the process area.

to c)
Surrounding temperatures vary from < 273 K in cold climate zones to 323 K in tropical countries. The higher the storage temperature the higher the reactivity of the solvent, i.e. the maximum hazard arises at 323 K, which we therefore take for our model.

to d)
If not recommended otherwise, liquids are stored at atmospheric pressure. Since this pressure is therefore common storage pressure, we will adopt this property in our concept.

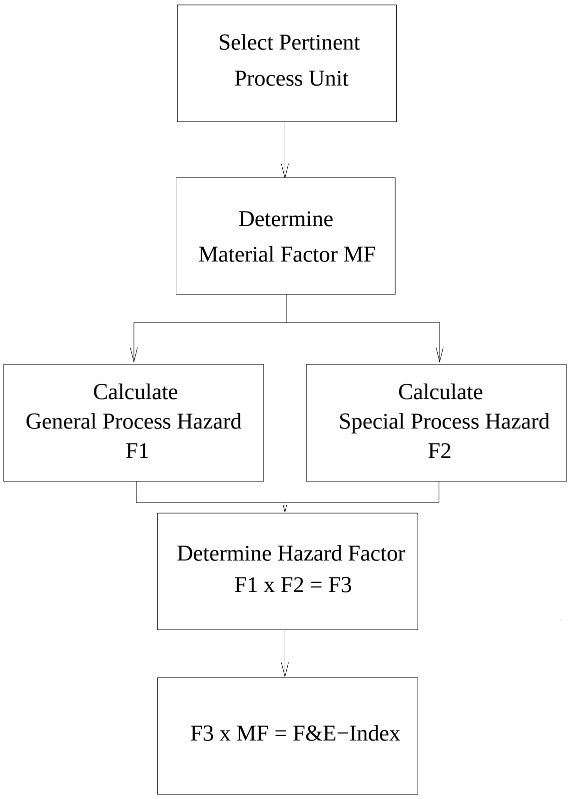

Figure 4.1: steps in F&E-Index calculation [13]

to e)
Special safety measures like correct diking and in-rack sprinklers are not included since the risk and hazard deriving from the tank should be estimated.

2.2 The Calculation
There are three factors that influence the F&E-Index according to figure 4.1:

- The *Material Factor MF*
- The *General Process Hazards Factor F1*
- The *Special Process Hazards Factor F2*

Material Factor MF
The MF is a measure of the intrinsic rate of potential energy release from fire and explosion produced by combustion or other chemical reactions. The

National Fire Protection Agency (NFPA) has specified standard values for the Material Factor, which can be found in [12], [14] and in DOWs Hazard Classification Guide. If the value of MF is not readily available, it can be easily calculated from flammability and reactivity indices N_F and N_R respectively (see table 4.5). N_F and N_R can be obtained from Material Safety Data Sheets (available for free in various databases on the Internet, e.g.[15]) and in the NFPA-standards 325M and 49.

N_R N_F	0	1	2	3	4
0	1	14	24	29	40
1	4	14	24	29	40
2	10	14	24	29	40
3	16	16	24	29	40
4	21	21	24	29	40

Table 4.5: Determination of the Material Factor through N_F and N_R

N_R is based on the following consideration [12]:

N_R	Reactivity
0	Substance is completely stable, even when heated under fire conditions
1	Mild reactivity upon heating with pressure
2	Significant reactivity, even without heating with pressure
3	Detonation possible with confinement
4	Detonation possible without confinement

The flammability value N_F is directly connected to the flash point [13]:

Flash point FP	N_F
none	0
FP $>$ 366 K	1
366 K $> FP >$ 311 K	2
311 K $> FP >$ 291 K	3
FP $<$ 291 K	4

General Process Hazard Factor F_1

The general process hazard is the sum of all the individual penalties for each category plus a base factor 1. Depending on whether the solvent is flammable, combustible or not combustible we obtain different results for F_1, ranging from 1.2 to 3.75. The exact calculation for these cases can be seen in table 4.6.

	solvents: category	flammable	Penalty	combustible	Penalty	not combustible	Penalty
1	exothermic chemical reactions	no	0	no	0	no	0
2	endothermic chemical reactions	no	0	no	0	no	0
3	loading or unloading involving flammable liquids with flash point < 311 K	yes	0.5	no	0	no	0
4	centrifiges, batch reactions or batch mixing	no	0	no	0	no	0
5	warehouse or yard storage	yes	0.85	yes	0.25	no	0
6	liquids are stored on racks without in-rack sprinklers in a warehouse/yard	yes	0.2	yes	0.2	no	0
7	dust filters	no	0	no	0	no	0
8	enclosed or indoor process units	no	0	no	0	no	0
9	bad access for emergency equipment	yes	0.2	yes	0.2	yes	0.2
10	no adequate drainage and spill control for liquids with flash point < 333.15 K	yes	1.0	yes	1.0	no	0
	$\sum Penalty$		2.75		1.65		0.2
	F_1		3.75		2.65		1.2

Table 4.6: Calculation of the General Hazard Factor F1

Special Process Hazard Factor F_2

The special process hazard is the sum of all individual penalties for each category plus a base factor 1. Depending on whether the solvent is flammable, combustible or not combustible, on N_F, N_H, i.e. the NFPA health value, and the specific heat of combustion H_C we obtain different results. Explanation and an exact definition of N_H is given in the next subsection and in table 4.8. The specific heat of combustion has to be converted in BTU according

to table 4.7 so that the individual penalty connected to the BTU can be obtained from figure 4.2.
Table 4.7 guides in calculating the individual special hazard factor for each solvent.

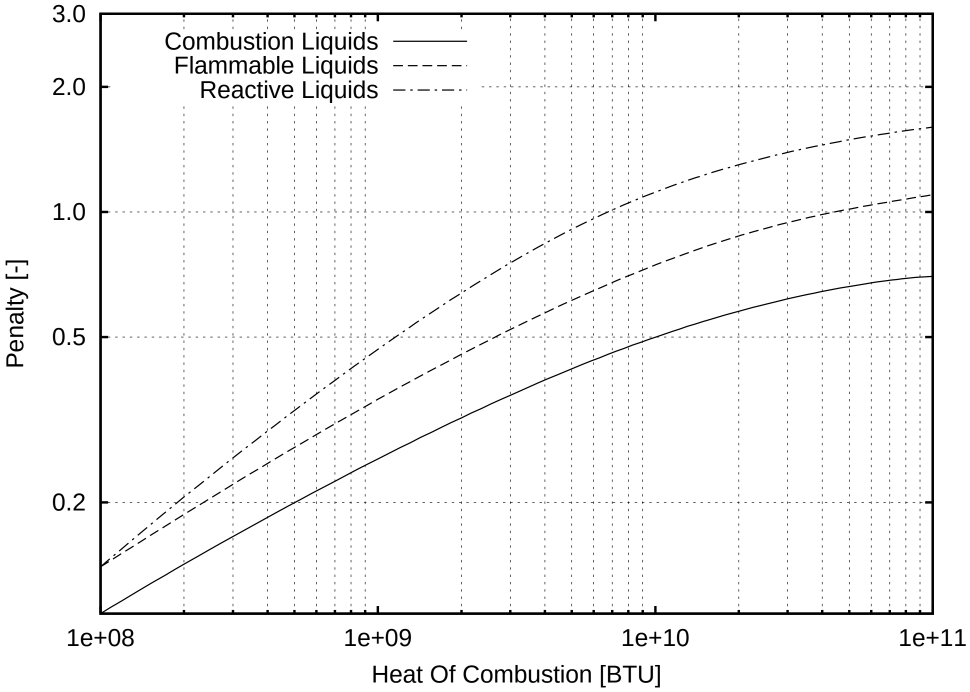

Figure 4.2: Penalty factor for quantity of reactive, flammable or combustible liquids, see [12]

Unit Hazard Factor F_3
The Unit Hazard Factor F_3 is the product of the General Process Hazard Factor F_1 and the Special Process Hazard Factor F_2:

$$F_3 = F_1 \cdot F_2 \tag{4.14}$$

The product is used rather than the sum since the "contributing hazards" included in F_1 and F_2 are known to have a compounding effect on each other. In the case that $F_3 > 8.0$, we use a maximum of 8.0.

Ultimately we receive the Fire and Explosion Index by multiplicating the two factors F_3 and MF:

$$\text{F\&E-Index} = F_3 \cdot MF \tag{4.15}$$

	solvents:	flammable		combustible		not combustible	
	category		Penalty		Penalty		Penalty
1	sub-atmospheric pressure <66.66 kPa	no	0	no	0	no	0
2	dust explosion possible	no	0	no	0	no	0
3	relief pressure possible	no	0	no	0	no	0
4	low temperature which may damage steel	no	0	no	0	no	0
5	corrosion or erosion	no	0	no	0	no	0
6	pumps, gland seals, compressors, flange joints (leakage)	no	0	no	0	no	0
7	sight glasses, bellows assemblies, expansion joint, abrasive slurry, thermal and pressure cycling	no	0	no	0	no	0
8	fired heaters	no	0	no	0	no	0
9	hot oil exchange systems	no	0	no	0	no	0
10	rotating equipment (pumps, mixers,...)	no	0	no	0	no	0
11	process equipment or process storage tank in flammable range	no	0	no	0	no	0
12	processes or operations in flammable range						
13	air can be breathed in a tank with flammable liquid during pump out or sudden cooling	yes	0.5	no	0	no	0
14	toxic material	Penalty = 0.2 $\cdot N_H$					
15	quantity of reactive, flammable or combustible liquids in a storage tank	if N_R >1: Penalty see fig. 4.2 else if flammable: Penalty see fig. 4.2 else if combustible: Penalty see fig. 4.2 1 BTU = $\frac{H_C\ [J/kg]}{2326\ J \cdot lb/(kg \cdot BTU)} \cdot \frac{120000\ kg}{0.4535\ lb/kg}$					
	$\sum Penalty$	0.5+ Pen.14 + Pen.15		Pen.14 + Pen.15		Pen.14 + Pen.15	
	F_1	1.0 + $\sum$ Penalty		1.0 + $\sum$ Penalty		1.0 + $\sum$ Penalty	

Table 4.7: Calculation of the Special Hazard Factor F2

Hazards for Man and Nature

1. Biological Oxygen Demand in 5 days (BOD_5)

The BOD_5 is the amount of oxygen used by microorganisms within 5 days in the process of decomposing organic matter in water. The more organic matter there is (e.g. in sewage) the greater the number of microbes. The more microbes there are, the greater is the need of oxygen they consume. Consequently, less oxygen is available for higher animals such as fishes. The BOD_5 is therefore a reliable gauge of organic pollution in water. One of the main reasons for treating sewage or waste water prior to its return to a water resource is to lower its BOD_5, i.e. to reduce its need of oxygen for decomposing and thereby lessen its demand from the rivers into which it is released. Industrial sewage may have BOD_5 levels many times that of domestic sewage, therefore special care has to be taken of this factor.
According to [16] we assume a threshold of $BOD_5 = 2$.

$\Longrightarrow$ Threshold $BOD_5 = 2$

2. Toxicity for Man and Animals

There are different methods to estimate the toxicity of a material for man and animals. Not every method is general enough to cover the different ways of poisoning which could be oral, cutan and through the respiratory tract or short term and long-term. For example the often cited LD_{50} covers only the short-term, oral case: the LD_{50} value is the amount of solid or liquid material that is needed to kill 50% of test animals in one dose. Poisioning at low concentrations over a long period (long-term poisoning) or short-term exposure by breathing are not considered. On the other side thresholds like the MAK (maximum concentration at the working place) cover only the long-term respiratory poisoning. Therefore we decide to take the NFPA-value N_H, since it covers the main aspects previously mentioned. According to its definition in table 4.8 substances are categorized in five groups, beginning with harmless substances which cause no harm ($N_H = 0$) over temporary incapacitation ($N_H = 2$) until major injury or death ($N_H = 4$) when exposed for a small period of time. Since the threshold for the F&E-Index already decreases the probability of an accident with the tested solvent, a higher toxicity value N_H is tolerable. A solvent with N_H=3 causes serious temporary injury. In contrast to this a solvent with $N_H = 4$ causes death or major injury also if only a short exposure is given. Therefore we can take $N_H = 3$ as the upper threshold for acceptable solvents.

$\Longrightarrow$ Threshold $N_H = 3$

N_H	Hazard
0	No hazard beyond that of ordinary combustibles
1	Only minor residual injury is likely
2	Prompt medical attention required to avoid temporary incapacitation
3	Materials causing serious temporary or residual injury
4	Short exposure causes death or major injury

Table 4.8: Definition of the N_H value from the NFPA 704

Acceptability and Grades

If the values of all the previously discussed environmental constraints are below their thresholds, the tested solvent is judged as environmentally acceptable. Still these environmentally acceptable solvents may have some, but less bad impact on the enviroonment. In order to estimate the rest hazard deriving from the acceptable solvents a grade is given according to the following table:

N_H	F&E-Index	grade/rest impact
0-1	$x \leq 60$	low
0-1	$60 < x \leq 96$	middle
2-3	$x \leq 60$	middle
2-3	$60 < x \leq 96$	high

Table 4.9: grades for environmentally acceptable solvents

The smaller N_H is, the less poisoning is the substance. An equally important factor is the F&E-Index. Solvents with F&E-Indices ≤ 60 are characterized as light hazards. If these solvents also have a N_H-value of 0 or 1, they are definitely more environmentally acceptable and preferable to others with higher values, e.g. water ($N_H = 0$; F&E-Index = 1.2) compared to 2-ethylhexanol ($N_H = 2$; F&E-Index = 16.8).

4.3 Software

The development of software for Solvent Selection is subject to the same principles as the previously presented one for Waste Minimization:

- In chapter 3.3 we already explained the need for software which helps the chemical process industries or research facilities to apply environmental ideas easily and in a short amount of time to an existing process.
- Furthermore we implemented calculations which require only basic input information about the process and materials like in the concept for Waste Minimization.
- The same ideas as in the development of the software for waste minimization apply here and the software is written in the standardized and internationally well-known programming language 'C'.

The number of solutes, their basic material data and basic process settings have to be given and as a result the software estimates which solvent is most suitable for the process and in addition is environmentally acceptable. Furthermore the twenty best performing solvents are presented with the obtained performance score and an explanation is given to each solvent, including:

- If a solvent is not environmentally acceptable, the criteria which it did not match are given and explained.
- If it is environmentally acceptable, the impact that still remains on the environment according to table 4.9 is given and explained.

In addition the user is informed about the solubility of each solvent-solute combination of the twenty best performing solvents according to table 4.3. As a special function the user may test any favorized chemical for suitability as a solvent for her process. In this case the user will be asked for more environmental and material data.

The second requirement for the execution of the software is the setup of a solvent database. The database we developed is small and representative and includes material data needed for performance and for environmental tests. We set a high value upon extensibility since the database may be further enlarged by increasing the number of solvents or the number of solvent properties for implementation of further solvent functions or environmental constraints.
For easy handling and clear structuring we split the database in two parts, respectively for the environmental and performance test data.

Subsequently we discuss the content of the database:
The solvents chosen belong to the most-often used solvents and material data is obtained from [11] and [15]. Furthermore they belong to different chemical

groups of solvents, e.g. organic, inorganic, alcoholic and chlorinated, so that the most important effects like nucleophilia or electrophilia are covered. The chosen solvents are:

- Acetone, Benzene, N-butylacetate, 1-Butanol, 1.2-Dichloroethane, Dimethylsulphoxide, Ethanol, 2-Ethylhexanol, Hexane, Methanol, Methylethylketone, 2-Propanol, Propylene Glycol, Toluene, 1.1.1-Trichloroethane, Water and Xylene

Xylene exists in three isomers: ortho-, metha- and para- Xylene. Since companies usually take different mixtures of all three substances, we assume a mixture where each isomer is included in the same proportion and we therefore take mean values of material data.

For the environmental test the following material constraints have to be included in the database:

- ODP, GWP, BOD_5, NFPA-values N_R, N_F and N_H, flashpoint and heat of combustion.

Since the environmental test is independent from the given process and solutes, i.e. only a function of the solvents, the environmental results for test-runs with the same solvents and solvent data are always the same.
In the performance test the following parameters are included into the database:

- Hansens solubility values δ_d, δ_p and δ_h, boiling point, solidification point and for further solvent functions: viscosity and surface tension.

To illustrate the previously explained ideas we give parts of the output of a test-run for Dimethylsulfate:

```
*****************************************************************
This program optimizes your process towards pollution prevention
through solvent substitution !
* Spent solvents constitute a major source of pollution in the
chemical and pharmaceutical industries. Much of this pollution
can be prevented by choosing solvents which are good envi-
ronmentally compatible or possess a high performance thus  re-
ducing the amount used.
* The program contains a solvent-database from which the best
solvents are selected according to environmental and performance
constraints. With the given obligatory data the program will
 start calculating and propose a list of acceptable solvents
```

```
 for your process.
***
RESULTS OF THE PERFORMANCE RATING
*The solvent should work as a REACTION MEDIUM.
The database is now searched for suitable solvents
high solubility is needed: weight = 5
low reactivity,i.e. low NFPA-reactivity is needed: weight = 1
recovery constraints (boiling point) are less important
at the moment: weight = 0
surface tension and viscosity are less important: weight = 0
*******************************************************************
The following list of solvents has been tested as a reaction medium
for dimethylsulfate:
(only the 20 best solvents are printed! score should be as small as possible)
***
position 1 (score = 1.80569): acetone   acceptance:  n
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is very soluble in acetone
position 2 (score = 1.90158): 2-ethylhexanol    acceptance:  y
         damage: m
        ** dimethylsulfate is very soluble in 2-ethylhexanol
position 3 (score = 1.94575): 1-butanol acceptance:  n
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is very soluble in 1-butanol
position 4 (score = 2.08215): 2-propanol        acceptance:  n
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is very soluble in 2-propanol
position 5 (score = 2.23453): methylethylketone acceptance:  n
         biological oxygen demand too high (bod5 = 2.24)
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is very soluble in methylethylketone
position 6 (score = 2.47998): n-butyl-acetate   acceptance:  n
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is very soluble in n-butyl-acetate
position 7 (score = 2.55826): 1,2-dichloroethane        acceptance:  n
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is very soluble in 1,2-dichloroethane
position 8 (score = 2.81117): dimethylsulfoxide        acceptance:  y
         damage: l
        ** dimethylsulfate is very soluble in dimethylsulfoxide
position 9 (score = 2.92235): ethanol   acceptance:  n
         danger through fire or explosion too high (F&E-Index = 124.072)
        ** dimethylsulfate is very soluble in ethanol
```

```
position 10 (score = 3.50974): 1,1,1-trichloroethane    acceptance:  n
         global warming potential too high (gwp = 140)
         ozone depletion potential too high (odp = 0.11)
        ** dimethylsulfate is soluble in 1,1,1-trichloroethane
position 11 (score = 3.84664): xylene(mix)      acceptance:  n
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is soluble in xylene(mix)
position 12 (score = 3.89133): water    acceptance:  y
         damage: l
        ** dimethylsulfate is soluble in water
position 13 (score = 4.05322): toluene  acceptance:  n
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is soluble in toluene
position 14 (score = 4.18277): methanol acceptance:  n
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is soluble in methanol
position 15 (score = 4.22757): propylene_glycol acceptance:  y
         damage: l
        ** dimethylsulfate is soluble in propylene_glycol
position 16 (score = 5): hexane acceptance:  n
         biological oxygen demand too high (bod5 = 2.21)
        ** dimethylsulfate is soluble in hexane
position 17 (score = 99): benzene       acceptance:  n
         the process-temperature is lower than the solidification point
         or higher than the boiling point!
         Therefore score is set to 99
         danger through fire or explosion too high (F&E-Index = 128)
        ** dimethylsulfate is soluble in benzene

OUT OF THE FIRST TEN SOLVENTS WE RECOMMEND:
-------------------------------------------
- 2-ethylhexanol (position 2)   rating: m
- Dimethylsulfate (position 8)  rating: l
All other solvents, which are listed under the first ten positions
before, have a bad environmental impact!
Under the recommended environmental friendly solvents
again there has been a rating:
IMPACT:   l = light ; m = middle; h = heavier
The solvents with 'l' are preferable!
```

4.4 Summary and Outlook

In this chapter we discussed a method for preventing pollution in chemical processes by selecting solvents which have good environmental behaviour in addition to good performance. We developed software which examines solvents according to their behaviour in the process and the environment respectively. The first test is a performance test and searches within a solvent database for solvents working at a given process temperature and fulfilling the selected task as a solvent. Solubility of solvent-solute combinations are calculated and the reactivity is estimated. In a second step the same solvents are tested for important environmental characteristics like global warming, ozone depletion, risk of fire and explosion, BOD_5 and toxicity. Estimation of the risk of fire and explosion is done by implementing a model for solvent storage in the calculation of the well known DOWs Fire and Explosion Index. Solvents passing both tests will enhance the productivity of the tested process since they are optimized towards efficiency and furthermore need less treatment when disposed.
Since only a small amount of basic data has to be given (number, molecular weights, densities and functional groups of the substances to be dissolved; process temperature) the software is easy to handle and can be applied with negligible expenditure of time. It can be applied in various stages of the development of the process (laboratory scale, pilot plant,...) or at chemical plants in production. The software can be used as a standard software for every existing and newly developed process with reaction in order to select a more efficient and environmental acceptable solvent for a chemical process and therefore prevent pollution.

However, although it can already be applied to chemical process industries in which solvents are used as reaction medium, there are more cases where a solvent may be needed: Liquid-liquid extraction, solid-liquid extraction or e.g. solvents as a direct or an indirect heat transfer media. These additional functions can easily be included in the software since the basic functionality has been developed: the material properties which are required in addition to the standard properties have to be included in the solvent database and the importance of various performance constraints has to be expressed by weighting them for calculation. A further advantage for complicated solvent applications will be to expand the softwares flexibility by permitting selection of more than one solvent task and implementing the setup of solvent blends which combine characteristics of diverse solvents in a way that the benefits sum up.

Since the main focus of this thesis is the development of a working concept for solvent selection, only a small database was established consisting of 17 of the most frequently used solvents. As a result extension of the number of solvents in the database is recommended in order to enhance the range of environmentally and good performing solvents.

It is furthermore recommended to include one more environmental constraint which has been neglected until now: the cancerous property of a solvent. A parameter which characterizes cancerous solvents has to be searched for in literature and the respective value for each solvent has to be included in the environmental database.

Chapter 5

Ranatidine - a Case Study

5.1 Introduction

As already mentioned in chapter 3.2.2 pharmaceutical products are known for their excessive consumption of raw material during manufacturing, originating in a complicated way of reaction (many reaction steps, ...). Therefore these processes represent good examples to demonstrate the two previously shown methods.

We choose the production of the drug Ranatidine, which is a top selling drug from the pharmaceutical company Glaxo Ltd. Ranatidine is known as a histamine blocker or an H_2-receptor blocker and is used to treat ulcers and heartburn. To manufacture this drug, the intermediate NMSM (1-methylamino-1-methylthio-2-nitroethylene) is needed. It is produced in a small scale in batches and uses the following chemical reaction:

$$\mathrm{CH_3NO_2} + \quad 2\ \mathrm{CS_2} + \quad 2\ \mathrm{KOH} \quad \rightarrow \quad \underset{\text{Dipotassiumsalt}}{\mathrm{(KS)_2C{=}CHNO_2}} + \quad \mathrm{H_2O} \tag{5.1}$$

$$\begin{aligned} &\mathrm{(KS)_2C{=}CHNO_2} + \mathrm{CH_3NH_2} + \mathrm{(CH_3O)_2SO_2} + \mathrm{H_2O} \\ &\qquad \rightarrow \underset{\text{NMSM}}{\mathrm{C_4H_8N_2SO_2}} + \mathrm{CH_3OH} + \mathrm{H_2S} + \mathrm{K_2SO_4} \end{aligned} \tag{5.2}$$

5.2 Waste Minimization

Table 5.1 shows the input of reactants and additional agents into the process and the output of product. Just by looking at the total material streams one can see that the process needs a lot of input to get little product: 1300 kg input to obtain 57 kg NMSM, i.e. $BA = 4.4\%$.

material	kg input	products	kg output
CH_3NO_2	80	NMSM	57
CS_2	150		
KOH	180		
$(CH_3O)_2SO_2$	234		
CH_3NH_2	20		
additional agents	636		
total	1300	total	57

Table 5.1: in- and output of the actual Ranatidine process

material	kg input	products	kg output
CH_3NO_2	80	NMSM	63
CS_2	150		
KOH	180		
$(CH_3O)_2SO_2$	187		
CH_3NH_2	16		
additional agents	632		
total	1245	total	63

Table 5.2: in- and output of the improved Ranatidine process

Realizing this the manufacturing industry changed the amount of input streams of various reactants and as a result they slightly raised the productivity to $BA = \frac{63}{1245} = 5.1\%$, as can be seen in table 5.2.
Still this value needed improvement, i.e. a cooperation between the manufacturing company and a chemical research institute was made. As a result they developed a completely different chemical reaction to obtain the drug intermediate. The following chemistry was chosen:

$$\mathrm{CH_3NCS + CH_3NO_2 + KOH} \rightarrow \underset{\text{Potassiumsalt}}{\mathrm{HNO_2C{=}C(SK)(NHCH_3)}} \tag{5.3}$$

$$\mathrm{C_3H_4KN_2O_2S + (CH_3O)_2SO_2} \rightarrow \underset{\text{NMSM}}{\mathrm{C_4H_8N_2SO_2}} + \mathrm{KCH_3SO_4} \tag{5.4}$$

Laboratory scale experiments obtained the results presented in table 5.3. With 0.449 kg input they obtained 0.1 kg NMSM. Compared to the two previous methods this way produces 4 times more NMSM.

material	kg input	products	kg output
CH_3NCS	0.078	NMSM	0.1
CH_3NO_2	0.090		
KOH	0.085		
$(CH_3O)_2SO_2$	0.170		
additional agents	0.026		
total	0.449	total	0.1

Table 5.3: in- and output of the new Ranatidine process

Applying the balance yield calculation to these three different processes in order to check for each grade of optimization, we obtain the results shown in table 5.2.
Discussion of the results:

- Because of the same chemical reaction of process 1 and 2 they present the same values for the theoretical balance yield BA_{TH} (=36.5%). The newly developed reaction in contrast has a 10% absolute higher BA_{TH}, i.e. the chemical reaction uses more efficiently the single reactant atoms.

- The relative yield of all three processes differs. Comparing the value of process 1 and the improved industrial process we can make out a large improvement. The relative yield of the new process is significantly lower. A possible explanation for this occurence is that the reaction until now is only carried out in laboratory scale, which means it is still in the beginning stage. A lot of optimization can be done in the actual plant or pilot plant to obtain the best reaction temperature and the most effective catalyst.

- The factor concerning the excess, the MA_{TR} is very low for both industrial processes (around 35%). Compared to this the new chemical reaction has a very high yield of 92% which needs no improvement anymore (improving this value would be very difficult and may lower also other productivity factors).

- Like the MA_{TR}, the EA_P (use of additional agents) for the new process is much higher than the values of the industrial processes:
  92% for the new process compared to approximately 50% for the industry processes.

	current industrial process	improved industrial process	new process
BA_{TH}	36.5%	36.5%	46.8%
RA	61.7%	84.5%	54.8%
MA_{TR}	38.0%	33.5%	92.1%
EA_P	51.1%	49.2%	94.2%
BA	4.4 %	5.1%	22.3%

Table 5.4: productivity and productivity factors of the Ranatidine processes

- As a result out of all four factors we obtain the following productivities BA:
  4.4 % for the first process, 5.1% for the improved chemical process and 22.3% for the new process. As can be seen, the BA of the third process is more than four times more productive. It should be preferred by the manufacturing industry.

5.3 Solvent Selection

After looking at the waste minimization aspect we want to check the processes for the best performing solvents with environmentally acceptable behaviour. As already discussed there are three ways to manufacture the Ranatidine-intermediate NMSM: two industrial processes which are based on the same chemical equation and one newly developed process with a different chemical reaction. For application of the solvent substitution concept on these processes only material data, the solvent function and the process temperature is needed. Since both industrial processes have exactly the same input data, we obtain the same results for the optimization, i.e. only two cases have to be discussed in the following chapters:

- the industrial process and
- the newly developed process.

The solvent selection will take place within the solvent database with the 17 solvents (see chapter 4.3):

- Acetone, Benzene, N-butylacetate, 1-Butanol, 1.2-Dichloroethane, Dimethylsulfoxide, Ethanol, 2-Ethylhexanol, Hexane, Methanol, Methylethylketone, 2-Propanol, Propylene Glycol, Toluene, 1.1.1-Trichloroethane, Water and Xylene.

5.3.1 Industrial process

The industrial process is based on the chemical equations (5.1) and (5.2). Six reactants and one intermediate react to one product plus four byproducts. These chemicals have different densities and are partly not soluble into each other. To carry out the reaction we therefore need a solvent which works as a reaction medium, i.e. dissolves the reactants and helps adjusting the required concentrations of each reactant in the reactor.
Since the byproducts and product are not necessary to carry out the reaction they do not need to be soluble. Furthermore products and byproducts which are not dissolved have the advantage that they are much easier to withdraw from the reactor and will not disturb the reaction by influencing the equilibrium or cause side-reactions. As a result the following substances, which are reactants, should be soluble to carry out the manufacturing of NMSM:

- CH_3NO_2, CS_2, KOH, $(KS)_2C{=}CHNO_2$, CH_3NH_2, $(CH_3O)_2SO_2$ and H_2O.

Refering to chapter 4.2.2 we limit the number of soluble substances to a maximum of three since the more solutes are included in the performance test the less importance is given to a single solute. As a result, an insoluble substance has too little weight in the mean value $\overline{R}$. To compensate the neglect of the reactants which are not included, we check for the solubility of these substances in the chosen solvents afterwards.

Hansen developed his solubility method mainly for organic reactions since inorganic chemicals often decompose to ions in a solution, i.e. different solution concepts have to be considered, and furthermore it is difficult to include the solubility of metal and especially heavy metal salts. As a result the solubility of inorganic substances, e.g. salts, cannot be estimated with Hansens method and the reactant KOH is not an appropriate candidate for the test. Its solubility in the recommended solvents has to be estimated subsequently. Furthermore the intermediate $(KS)_2C{=}CHNO_2$ should be definitely included as input since it is the most complex molecule of the seven substances and the more complex the molecule is, the more difficult is it to estimate its solubility in the solvent. Secondly it is the most valuable substance in the list of reactants since it is the product of the first reaction and therefore much energy, effort and material has to be inserted in the process to obtain it.

From the five remaining reactants CH_3NO_2, CS_2, CH_3NH_2, H_2O and $(CH_3O)_2$-SO_2 we choose CH_3NO_2 and CH_3NH_2 for the application of the software and will afterwards calculate the solubility of H_2O, CS_2 and $(CH_3O)_2SO_2$ to some solvents chosen by the test.

The reaction takes place at a process temperature of 273 K to 283 K. We therefore take the mean process temperature of 278 K as input temperature.

In order to calculate the solubility parameters, the molecular weight, density and functional groups have to be given as input:

	CH_3NO_2	CH_3NH_2	$(KS)_2C{=}CHNO_2$
Molecular Weight [g/mol]	61.04	31.06	213.36
Density [g/cm^3]*	1.14	0.9	1.0
Functional groups	$-CH_3$,$-NO_2$	$-CH_3$, $-NH_2$	=CH-, =C<, $-NO_2$, 2 -S-

The calculation is done according to (4.5)-(4.8). The solubility parameters obtained are:

$$\begin{array}{llll} \delta_d = 17.18 & \delta_p = 19.98 & \delta_h = 5.29 & \text{for } CH_3NO_2 \\ \delta_d = 20.28 & \delta_p = 17.68 & \delta_h = 15.60 & \text{for } CH_3NH_2 \\ \delta_d = 7.73 & \delta_p = 5.02 & \delta_h = 2.65 & \text{for } (KS)_2C{=}CHNO_2 \end{array}$$

Solubility parameters for the solvents are listed in the solvent database[†]. For each solute-solvent combination we calculate a radius of interaction according to (4.4) and can approximate the solubility status using the estimation given in table 4.3:

---

[*] specific gravities of many organic substances are given in [9]

[†] Solubility parameters of many solvents and organic liquids are listed in [7]

solvent	CH_3NO_2	CH_3NH_2	$(KS)_2C{=}CHNO_2$
Acetone	**soluble**	**soluble**	**soluble**
Benzene	insoluble	insoluble	soluble
n-Butyl-acetate	soluble	slightly soluble	soluble
1-Butanol	insoluble	soluble	soluble
1,2-Dichloroethane	**soluble**	**soluble**	**soluble**
Dimethylsulfoxide	soluble	soluble	slightly soluble
Ethanol	insoluble	soluble	insoluble
2-Ethylhexanol	insoluble	soluble	soluble
Hexane	insoluble	insoluble	soluble
Methanol	insoluble	soluble	insoluble
Methylethylketone	**soluble**	**soluble**	**soluble**
2-Propanol	insoluble	soluble	soluble
Propyleneglycol	insoluble	soluble	insoluble
Toluene	insoluble	insoluble	soluble
1.1.1-Trichoroethane	soluble	insoluble	soluble
Water	slightly soluble	soluble	insoluble
(o-, m- and p)-Xylene	insoluble	insoluble	soluble

As can be seen, the solvents Acetone, 1,2-Dichloroethane and Methylethylketone give the best solubility results and most probably dissolve all three substances.

For each solvent we have to calculate the mean radius $\overline{R}$ according to (4.9) and normalize it using (4.10). By adding the normalized N_F-value of each solvent we obtain the resulting scores listed in table 5.5.
The seventeen solvents are ranked with a score from 0.0 to 5.0, with the exception of Benzene. We set the Benzene score to 99 since Benzene does not fulfill the temperature condition '$T_{Solidification} < T_{Process}$' with $T_{Solidification}$ = 279.15 K and $T_{Process}$ = 278 K.

The solvents that obtain the best scores are Dimethylsulfoxide, Acetone and Methylethylketone which are followed by the rest of the solvents after a gap of 0.45. Water is on position 11 since it has a bad score, which can be explained by the low solubility to the intermediate $(KS)_2C{=}CHNO_2$.

After checking the performance we are looking at the environmental constraints. According to chapter 4.2.3 we have to estimate the global hazard (ODP and GWP), the fire and explosion hazards ($F\&E$-Index) and the hazard to Man and Nature (BOD_5 and N_h) for every solvent. The necessary data is given in the database and after calculation of the $F\&E$-Index and the acceptability we obtain the results given in table 5.6.

position	solvent	score
1	Dimethylsulfoxide	2.64
2	Acetone	2.92
3	Methylethylketone	3.13
4	1.2-Dichloroethane	3.58
5	n-Butylacetate	3.83
6	1.1.1-Trichloroethane	4.00
7	2-Ethylhexanol	4.13
8	1-Butanol	4.13
9	2-Propanol	4.15
10	Ethanol	4.28
11	Water	4.38
12	(o-,m- and p-)Xylene	4.58
13	Methanol	4.58
14	Toluene	4.59
15	Hexane	4.86
16	Propylene Glycol	5.00
17	Benzene	99 ($T_{Solidification} > T_{Process}$)

Table 5.5: Performance scores for the Industrial Process

Only four substances pass the environment-test, all the other solvents are either too toxic, too flammable or explosive or harm the climate or ozone layer. These four substances are:

- Dimethylsulfoxide, 2-Ethylhexanol, Propyleneglycol and Water.

Dimethylsulfoxide and 2-Ethylhexanol are placed within the first ten best performing solvents (see above), i.e. they are environmentally acceptable and give a good performance. Dimethylsulfoxide has a light rest-impact according to the definition given in table 4.9 while 2-Ethylhexanol is slightly more harmful (rest-impact = middle). Both solvents seem to be acceptable as solvents for manufacturing of NMSM in the presented process.

Water and Propyleneglycol are on position 11 and 16 of the performance ranking and should not be considered as solvents when no special performance enhancer is added, since they have a bad solubility or reactivity.

Before we finally decide for the best solvent we have to look at the solubility of the reactants which have not been tested yet and hence calculate the Radius of Interaction R for each combination H_2O, CS_2 and $(CH_3O)_2SO_2$

solvent	ODP/GWP	$F\&E$-Index	BOD_5/N_h	acceptability
Acetone	0.00/0	128	0.69/1	no
Benzene	0.00/0	128	0.00/2	no
n-Butyl-acetate	0.00/0	128	1.02/1	no
1-Butanol	0.00/0	128	1.50/1	no
1,2-Dichloroethane	0.00/0	128	0.00/2	no
Dimethylsulfoxide	**0.00/0**	**5**	**0.00/1**	**yes**
Ethanol	0.00/0	124	0.93/0	no
2-Ethylhexanol	**0.00/0**	**17**	**0.00/2**	**yes**
Hexane	0.00/0	91	2.21/1	no
Methanol	0.00/0	128	0.76/1	no
Methylethylketone	0.00/0	128	2.24/1	no
2-Propanol	0.00/0	128	1.29/1	no
Propyleneglycol	**0.00/0**	**23**	**0.96/0**	**yes**
Toluene	0.00/0	128	1.23/2	no
1.1.1-Trichoroethane	0.11/140	26	0.00/3	no
Water	**0.00/0**	**1**	**0.00/0**	**yes**
(o-, m- and p)-Xylene	0.00/0	128	1.25/2	no
Thresholds	**0.00/0**	**96**	**2.00/3**	

Table 5.6: Results of the Environmental Test

in the two recommended solvents. Applying the classification in solubility categories according to table 4.3 we obtain the following results:

	Solvents	
Solute	Dimethylsulfoxide	2-Ethylhexanol
H_2O	**soluble**	**soluble**
CS_2	insoluble	soluble
$(CH_3O)_2SO_2$	**soluble**	**soluble**

As can be seen both solvents dissolve Water and $(CH_3O)_2SO_2$, but whereas CS_2 is soluble in 2-Ethylhexanol, it is not soluble in Dimethylsulfoxide. As a result neither Dimethylsulfoxide nor 2-Ethylhexanol nor any other solvent in the database can be directly recommended without performance enhancer. This fact may change if we enlarge the database to more than 17 solvents in order to increase the probability of finding a solvent which dissolves all substances. Anyway, it is a very difficult task to dissolve seven chemicals in one solvent when the chemicals have very different properties and solubility forces.

In the actual process the chemical industry uses water as a solvent since it is cheap, available in high amounts, does not require special safety measures in the process and can safely be disposed without treatment if it is not polluted by other substances. In order to enhance the solubility to the intermediate and other substances, the companies add a phase-transfer-catalyst.

5.3.2 Newly Developed Process

The newly developed process is based on the chemical equations (5.3) and (5.4). The possible choices for the solutes in the software are:

- CH_3NCS, CH_3NO_2, KOH, $HNO_2C{=}C(SK)(NHCH_3)$, $(CH_3O)_2SO_2$

Out of these a maximum of three substances has to be selected as solutes. KOH as an inorganic salt is not acceptable (see 5.3.1). With four substances left and the maximum of tested solutes is three we choose CH_3NCS, CH_3NO_2 and the intermediate $HNO_2C{=}C(SK)(NHCH_3)$ and afterwards will test the last solute, Dimethylsulfide, for solubility in the selected solvent.

Process temperature varies between 273 K and 283 K, so that we take the mean Process temperature 278 K as input in the software.

Molecular weight, density and functional groups of all three substances are required for solubility calculation:

	CH_3NCS	CH_3NO_2	$NO_2HC{=}C(SK)(NHCH_3)$
Molecular Weight [g/mol]	73.11	61.04	172.25
Density [g/cm^3][‡]	1.07	1.14	1.0
Functional groups	$-CH_3$, -N<, =C<, -S-	$-CH_3$, $-NO_2$	$-CH_3$, =CH-, =C<, -NH-, NO_2, -S-

The obtained Hansen solubility parameters for dispersion, polar and hydrogen bonding forces are:

$\delta_d = 13.90$ $\delta_p = 11.71$ $\delta_h = 8.55$ for CH_3NCS
$\delta_d = 17.18$ $\delta_p = 19.98$ $\delta_h = 5.29$ for CH_3NO_2
$\delta_d = 10.39$ $\delta_p = 6.33$ $\delta_h = 5.17$ for $HNO_2C{=}C(SK)(NHCH_3)$

Solubility calculation and subsequent estimation of the solubility status according to table 4.3 give the following results:

[‡] specific gravities of many organic substances are given in [9]

solvent	CH_3NCS	CH_3NO_2	$HNO_2C{=}C(SK)(NHCH_3)$
Acetone	**soluble**	**soluble**	**soluble**
Benzene	soluble	insoluble	soluble
n-Butyl-acetate	**soluble**	**soluble**	**soluble**
1-Butanol	soluble	insoluble	soluble
1,2-Dichloroethane	**soluble**	**soluble**	**soluble**
Dimethylsulfoxide	**soluble**	**soluble**	**soluble**
Ethanol	soluble	insoluble	soluble
2-Ethylhexanol	soluble	insoluble	soluble
Hexane	soluble	insoluble	soluble
Methanol	soluble	insoluble	insoluble
Methylethylketone	**soluble**	**soluble**	**soluble**
2-Propanol	soluble	insoluble	soluble
Propyleneglycol	soluble	insoluble	insoluble
Toluene	soluble	insoluble	soluble
1.1.1-Trichoroethane	**soluble**	**soluble**	**soluble**
Water	soluble	slightly soluble	slightly soluble
(o-, m- and p)-Xylene	soluble	insoluble	soluble

As we can see there are six solvents which dissolve all three substances:

- Acetone, n-Butyl acetate, 1.2-Dichloroethane, Dimethylsulfoxide, Methylethylketone and 1.1.1-Trichloroethane

This number is larger than in the industrial process and suggests the conclusion that the reactants in this process are easier to dissolve.

Calculating the mean radius for every solvent and normalizing it according to (4.10) leads to the solubility score. By adding the reactivity score we obtain the total performance scores shown in table 5.7, ranging from 0.0 for the optimum performance to 5.0 for the worst performance.
Like in the performance test of the industrial process we set a total score of 99 for Benzene, since it does not fulfill the temperature conditions: the process temperature (278.0 K) is below the solidification point of Benzene (279.15 K), i.e. the solvent is in a frozen state.
The lowest score obtained is 1.73 (for Acetone), followed by the score for Methylethylketone (1.99) and Dimethylsulfoxide (2.40), i.e. there are three solvents with scores below 50% of the maximum score 5.0. In contrast there is not a single solvent in the previous test of the industrial process with a score below 2.5. It is therefore more difficult to obtain a good performance

position	solvent	score
1	Acetone	1.73
2	Methylethylketone	1.99
3	Dimethylsulfoxide	2.40
4	1.2-Dichloroethane	2.66
5	n-Butylacetate	2.79
6	1.1.1-Trichloroethane	3.05
7	2-Ethylhexanol	3.29
8	1-Butanol	3.55
9	2-Propanol	3.61
10	(o-,m- and p-)Xylene	3.70
11	Toluene	3.72
12	Hexane	4.02
13	Ethanol	4.04
14	Water	4.55
15	Methanol	4.62
16	Propyleneglycol	5.00
17	Benzene	99 ($T_{Solidification} > T_{Process}$)

Table 5.7: Performance scores for the New Ranatidine Process

for the industrial process with the given solvents than for the newly developed process.

For the exact results of the conducted environmental test we refer to table 5.6 since the same solvents are tested for environmental acceptability in the industrial process and therefore the same results are obtained. The solvents which passed the environmental test are:

- Dimethylsulfoxide, 2-Ethylhexanol, Propyleneglycol and Water.

Dimethylsulfoxide is on position 3 in the performance test and 2-Ethylhexanol on position 7. Both passed the environmental and performance test, i.e. they are environmentally acceptable and give a good performance in the newly developed manufacturing process for NMSM. Dimethylsulfoxide has a light rest impact according to the definition given in table 4.9 while 2-Ethylhexanol is slightly more harmful (rest impact = middle).

Water and Propyleneglycol are on position 14 and 16 of the performance ranking. They should not be considered as solvents when no special performance enhancer is added, since they have a bad solubility or reactivity.

Before we finally decide for the best solvent we have to look at the solubility of the reactant $(CH_3O)_2SO_2$ in the two recommended solvents, since this reactant has not been tested yet. Calculating the Radius of Interaction for each $(CH_3O)_2SO_2$-(recommended solvent) combination and applying the classification into solubility categories according to table 4.3 we obtain the following results:

	Solvents	
Solute	Dimethylsulfoxide	2-Ethylhexanol
$(CH_3O)_2SO_2$	**soluble**	**soluble**

As can be seen, both solvents dissolve the reactant $(CH_3O)_2SO_2$. Since Dimethylsulphate obtains a better score in the performance test and has less rest impact on the environment (see table 4.9), the first choice for solvent selection should be **Dimethylsulfoxide**.

The actual used solvent is Dimethylsulfoxide, which is also recommended as the best solvent in the software, followed by 2-Ethylhexanol. For the process the best solvent was chosen and there is no need of improvement in the process concerning the choice of the solvent.

Chapter 6

Summary

In this thesis two important aspects of pollution prevention have been looked at. Software for waste minimization and solvent substition is developed, in which chemical process industries and related research institutes can examine already developed processes or processes in work for their degree of optimization towards pollution prevention. Only basic information is required and the handling is very easy so that results and suggestions for improvement can be obtained very quickly.

In the waste minimization part we compare input and output flows of processes and their composition in order to calculate the excess of reactants, the relative yield, the use of additional agents and the efficiency of the chemical reaction itself. As a result we can identify possible weak points of the process and can locate input material which is not used efficiently. As an example which is typical for the material inefficiency and low productivity in most pharmaceutical and fine chemicals industries, we examined three manufacturing processes of the Ranatidine-intermediate NMSM: while two processes obtain a very low productivity and as a result high consumption of resources and production of waste, a newly developed process based on different chemical equations has a much higher productivity by recycling solvents, using reactants in less excess and producing less byproducts per product. By using concepts of this thesis we therefore could locate a process which leads to pollution prevention via waste reduction.

In the solvent optimization part we developed a method for preventing pollution in chemical processes by selecting solvents which have good environmental behaviour in addition to good performance. The software examines solvents from an attached solvent database for behaviour in the process and environment by conducting solubility calculations and other required property estimations which are related to the solvent function, and by checking for the influence on important environmental dangers ranging from global threats like ozone depletion to local harms. We tested the software on the manufacturing processes for NMSM. While in the first two processes too many substances have to be dissolved and therefore a solvent could not be found soluting all of them, the software obtained exactly the same solvent for the newly developed process that is already used in the process. The software therefore justifies the usage of exactly this solvent in the process.

Additionally we discussed possible and profitable extensions and improvements of each concept, that will further enhance the flexibility and application to diverse processes and cases. Especially the application of the last method on processes will grow in importance as the number of solvents in the database is extended and more solvent functions are offered.

Appendix A

Zusammenfassung

Im Rahmen dieser Diplomarbeit wurden zwei Konzepte zur Optimierung chemischer Prozesse hinsichtlich Umweltverträglichkeit entwickelt und diese als Software implementiert: die Reststoffminimierung, basierend auf Analysen der Massenströme eines Prozesses und daraus ableitbarer Einsparungen an Einsatzstoffen, und die Selektion umweltverträglicher und leistungsstarker Lösungsmittel anhand von ausgewählten und repräsentativen Kennwerten für das Lösungsmittelverhalten in der Umwelt bzw. der Lösungsmittelfunktion im Prozeß. Beide Konzepte inklusive ihrer zugehörigen Software sind Erweiterungen des produktionsintegrierten Umweltschutzes und können sowohl von Forschungsinstituten als auch von der chemischen Industrie eingesetzt werden unabhängig davon, in welchem Stand der Entwicklung sich ein Verfahren befindet.

Die **Minimierung der Reststoffmenge** basiert auf der Produktivitätskennzahl BA, die die Masse an Produkten zu der der Einsatzstoffe in Relation setzt. In BA fliessen die Produktivitätsterme BA_{TH} (theoretische Bilanzausbeute, basierend auf dem Syntheseweg), RA (relative Ausbeute), MA_{TR} (Grad der Vermeidung an Eduktüberschüssen) und EA_P (primärer Einsatzstoffanteil) ein, diese sind systematische Gegenüberstellungen von theoretisch notwendigen zu tatsächlich eingesetzten Stoffströmen. Die einzelnen Faktoren wurden auf ihre Auswirkungen auf Prozeß und Reststoffmenge und auf mögliche Maßnahmen zur Verbesserung des Optimierungsgrades hin untersucht. Die hiernach entwickelte Software berechnet für ein gegebenes Verfahren den Grad der Optimierung jedes Terms und diskutiert bei Unterschreiten eines definierten Schwellenwertes die Verfahrensmodifikationen zur Anhebung des Faktors.
Eine Anwendung des Konzeptes auf verschiedene Herstellungsverfahren des pharmazeutischen Zwischenproduktes NMSM zeigte Schwachstellen der Ver-

fahren auf, und durch den Vergleich der jeweiligen Kennzahlen konnte das materialeffizienteste Verfahren gefunden werden.

Eine Verringerung des negativen Einflusses von Lösungsmitteln auf die Umwelt läßt sich sowohl qualitativ durch Auswahl eines weniger schädigenden Lösungsmittels, als auch quantitativ durch Reduktion der Lösungsmittelmenge, also durch Wahl eines leistungsfähigeren Lösungsmittels erreichen. Beide Ansätze sind in das Konzept der **Selektion von Lösungsmitteln** integriert. Zusätzlich wurde eine Datenbank aufgesetzt, die die meistgenutzten Lösungsmittel für die Software zur Verfügung stellt und die zur Berechnung benötigten Stoffwerte enthält. Als Kriterien für umweltschonendes Verhalten wurden Materialkennwerte integriert, die globale oder lokale Auswirkungen beschreiben: Ozonzerstörungspotential (ODP), Klimaerwärmungspotential (GWP), DOWs F&E-Index zur Abschätzung der Feuer- und Explosionsgefahr, der biologische Sauerstoffbedarf (BSB_5) und die Toxizität (N_H). Jedem dieser lösungsmittelspezifischen Werte wird ein maximal zu tolerierender Grenzwert gegenübergestellt, der auf der Abschätzung zu erwartender Schäden basiert; erfüllt das Lösungsmittel eines der Kriterien nicht, so ist es nicht akzeptabel. Zur Charakterisierung der Leistungsfähigkeit eines Lösungsmittels in einem Prozeß wurden, neben generellen Temperaturbeschränkungen für dessen Einsatz, spezifische Lösungsmittelfunktionen aufgestellt. Anhand dieser konnten wichtige Kriterien für eine gute Funktionsfähigkeit im Prozeß ausgemacht werden, wie z.B. hohe Löslichkeit und niedrige Reaktivität für Lösungsmittel, die als Reaktionsmedium dienen. Für diese Lösungsmittelfunktion wurden Löslichkeitsberechnungen nach Hansen und Reaktivitätsabschätzungen in Konzept und Software integriert.
Die Anwendung des Konzeptes auf die Darstellungsprozesse von NMSM führte zu verschiedenen Ergebnissen. Im Fall des neuesten Verfahrens z.B. zeigte sich eine Übereinstimmung des aktuell verwendeten mit dem durch die Software selektierten Lösungsmittel, es ist damit optimal gewählt und zeichnet sich sowohl durch hohe Leistungsfähigkeit als auch hohe Umweltverträglichkeit aus.

Sowohl das Konzept zur Minimierung der Reststoffmengen als auch das Konzept zur Lösungsmittelselektion sind derart als Software implementiert, daß nur grundlegende, dem Anwender bekannte Eingabedaten zur Ausführung der einfach bedienbaren Software benötigt werden.

Abschließend wurden, zur Steigerung der Flexibilität und Vergrößerung der Anwendungsmöglichkeiten der Software auf diverse Prozesse und Fälle, mögliche und sinnvolle Erweiterungen und Verbesserungen für beide aufgestellten Konzepte diskutiert. Insbesondere die Anwendung des Lösungsmittelkonzeptes auf chemische Prozesse wird stark an Bedeutung gewinnen, sobald die Anzahl an Lösemitteln in der Datenbank erhöht und mehr Lösungsmittelfunktionen, wie z.B. Lösungsmittel als Extraktionsmittel, integriert werden. Zusätzlich ist eine Erweiterung der betrachteten Kriterien für umweltschonendes Verhalten durch Einbeziehen eines Materialkennwertes für Cancerogenität sinnvoll.

Appendix B

Symbols

A	Molecule	[-]
B	Molecule	[-]
BA	Balance yield	[-]
BA_{SP}	Specific balance yield	[-]
BA_{TH}	Theoretical balance yield	[-]
BOD_5	Biological oxygen demand in five days	[-]
C	Single raw score for one constraint	[-]
C^{max}	Highest single raw score for one constraint	[-]
C_n	Normalized single score for one constraint	[-]
EA_P	Additional agents factor	[-]
F_d	Dispersion molar attraction factor	$[\frac{\sqrt{J \cdot cm^3}}{mol}]$
F_p	Polar molar attraction factor	$[\frac{\sqrt{J \cdot cm^3}}{mol}]$
F_1	General process hazards factor	[-]
F_2	Special process hazards factor	[-]
F_3	Unit hazards factor	[-]
$F\&E$-Index	DOWs Fire and Explosion Index	[-]
FP	Flash point	[K]
GWP	Global warming potential	[-]
H_c	Specific heat of combustion	[J/kg]
MA_{TR}	Reactant excess factor	[-]
MF	Material factor	[-]
N_F	NFPA fire parameter	[-]
N_H	NFPA health parameter	[-]
N_R	NFPA reactivity parameter	[-]
$N_{R,n}$	Normalized NFPA reactivity parameter	[-]
ODP	Ozone depletion potential	[-]
ODS	Ozone depleting substance	[-]

R	Radius of Interaction	$[\mathrm{MPa}^{1/2}]$
$\overline{R}$	Mean radius of Interaction	$[\mathrm{MPa}^{1/2}]$
R^{max}	Maximum radius of interaction	$[\mathrm{MPa}^{1/2}]$
R_n	Normalized radius of interaction	[-]
RA	Relative yield	[-]
S_T	Total performance score	[-]
$T_{Boiling}$	Boiling temperature	[K]
$T_{Process}$	Process temperature	[K]
$T_{Solidification}$	Temperature of solidification	[K]
U_h	Hydrogen bonding cohesive energy	$[\frac{J}{mol}]$
V	Molar volume	$[\mathrm{cm}^3/\mathrm{mol}]$
Z	Substance	[-]
i	counter	[-]
j	counter	[-]
m_{In}	Input of raw material	[kg]
$m_{P,act}$	Actual output of desired product(s)	[kg]
$m_{R,act}$	Actual input of reactants	[kg]
$m_{R,act,stoich}$	actual amount of stoichiometrically added reactants	[kg]
$m_{P,th}$	Theoretical output of desired product(s)	[kg]
$m_{R,th}$	Theoretical input of reactants	[kg]
mw	Molecular weight	[kg/mol]
$mw_{R,i}$	Molecular weight of reactant i	[kg/mol]
$mw_{P,j}$	Molecular weight of product j	[kg/mol]
n	Number of functional groups	[-]
$n_{R,act,stoich}$	is the actual amount of stoichimetrically added reactants	[mol]
$n_{P,j}$	Number of mols of product j	[mol]
$n_{R,i}$	Number of mols of reactant i	[mol]
$n_{R,th}$	Theoretically necessary amount of reactants	[mol]
w_i	Weight for constraint i	[-]
z	Number of reactants or products	[-]
δ_d	Dispersion solubility parameter	$[\mathrm{MPa}^{1/2}]$
δ_p	Polar solubility factor	$[\mathrm{MPa}^{1/2}]$
δ_h	Hydrogen bonding solubility factor	$[\mathrm{MPa}^{1/2}]$
μ	mean value of Radius of Interaction	$[\mathrm{MPa}^{1/2}]$
ν_P	Stoichiometric coefficient of product	[-]
ρ	Density	$[\frac{g}{cm^3}]$
σ	variance	$[[\mathrm{MPa}^{1/2}]$
ξ_P	Turnover rate of product	[-]
$\xi_{R_{lim},act}$	actual turnover rate of limiting reactant	[-]
$\xi_{R_{lim},max}$	maximum turnover rate of limiting reactant	[-]

Appendix C

Attachment CD-ROM

Content:

- Diploma Thesis in ps- and pdf-format
- Software

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