UNIVERSITY OF HELSINKI REPORT SERIES IN PHYSICS

HU-P-D90

AB INITIO AND DFT DERIVED POTENTIAL ENERGY FUNCTIONS IN SIMULATIONS OF SELECTED POLYESTERS BASED ON ATOMISTIC MODELS

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ACADEMIC DISSERTATION

To be presented, with the permission of the Faculty of Science of the University of Helsinki, for public criticism in Auditorium E204 of the Department of Physics, on May 26th, 2001, at 10 o'clock.

Helsinki 2001

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ISBN 951-45-8947-5
ISBN (pdf version) 951-45-9929-2
ISSN 0356-0961
Helsinki 2001
Yliopistopaino

J. Blomqvist: *Ab initio* and DFT derived potential energy functions in simulations of selected polyesters based on atomistic models, University of Helsinki, 2001, 51 p. + appendices, University of Helsinki, Report Series in Physics, HU-P-D90, ISSN 0356-0961, ISBN 951-45-8947-5, ISBN (pdf version) 951-45-9929-2.

Classification (INSPEC): A3000, A3620, A3520P, A3120A, A6140
Keywords (INSPEC): atomic and molecular physics, macromolecules and polymer molecules, force fields, ab initio calculations, amorphous state

Abstract

This study focuses on atomistic simulations of polyesters, the main interest being in the performance of classical models. The Polymer Consistent Force Field (PCFF), developed for synthetic polymers, forms the basis for the simulations. The calculated properties of synthetic polymers depend strongly on the conformational statistics of the polymer chains, and the force field is, therefore, of crucial importance for the reliability of the simulations. Thus, the PCFF has been tested by comparing its results for model molecules of the polyesters studied with those of quantum mechanical *ab initio* and density functional theory (DFT) calculations regarding the rotational behaviour of typical bonds in these polyesters. The calculations showed that there were severe disagreements between the quantum mechanical and the PCFF studies, leading thus to re-optimisation of the particular torsion potentials of the PCFF. The quantum mechanical methods used were also compared, and though they gave mostly similar results, the DFT methods were found to underestimate some of the torsional barriers. The modified PCFF was shown to yield results in good agreement with experimental data for single chain properties of the selected polyesters (poly(methyl acrylate), poly(methyl metacrylate), poly(vinyl acetate) and some main chain polyesters having alkyl chains of various lengths between the carboxyl groups). The dependence of the RIS Metropolis Monte Carlo (RMMC) method, used for these property calculations, on different run parameters, such as cut-off for non-bonded interactions, was discussed in more detail. The RMMC method, using the original and modified PCFFs, was also used in studies on the flexibility of some polyesters, which are known to be biodegradable, i.e. of polylactic (PLA) and polyglycolic (PGA) acids and some of their copolymers. The original PCFF was found to reproduce the flexibilities of these polyesters in contradiction with the results obtained with the modified PCFF. Finally, the modified PCFF was applied to molecular dynamics simulations on the constructed amorphous models for PLA and PGA and some of their copolymers to study the probability for hydrolysis as the first stage of biodegradation.

The main conclusion of this study is, that re-optimisation of the torsion parameters was necessary to reproduce the torsional behaviour obtained by QM methods. The modified PCFF can, thus, be reliably used in single chain property calculations and in studies on bulk material properties of polyesters containing structural units studied in this work.

BRIEF DESCRIPTION OF PUBLICATIONS

This thesis is based on the following publications, which will be referred to by Roman numerals I-V:

I. J. Blomqvist, L. Ahjopalo, B. Mannfors and L.-O. Pietilä, Studies on Aliphatic Polyesters I: Ab Initio, Density Functional and Force Field Studies of Esters with One Carboxyl Group, J.Mol.Struct. (Theochem) 488 (1999) 247-262.

II. J. Blomqvist, B. Mannfors and L.-O. Pietilä, Studies on Aliphatic Polyesters. Part II. Ab Initio, Density Functional and Force Field Studies of Esters with Two Carboxyl Groups, J.Mol.Struct. (Theochem) 531 (2000) 359-374.

III. J. Blomqvist, B. Mannfors and L.-O. Pietilä, RIS Metropolis Monte Carlo Studies of Some Main Chain and Side Group Polyesters, Polymer 42 (2001) 109-116.

IV. J. Blomqvist, RIS Metropolis Monte Carlo Studies of Poly(L-lactic), Poly(L,D-lactic) and Polyglycolic Acids, Polymer 42 (2001) 3515-21.

V. J. Blomqvist, B. Mannfors and L.-O. Pietilä, Amorphous Cell Studies of Polyglycolic, Poly(L-lactic), Poly(L,D-lactic) and Poly(glycolic/L-lactic) Acids, submitted to Polymer.

In publications I and II quantum mechanical *ab initio* and density functional theory (DFT) calculations on selected model molecules for polyesters studied in this thesis are described. This work was done to test and improve the performance of the Polymer Consistent Force Field (PCFF) to yield the correct torsional behaviour for typical bonds in polyesters. Also the results obtained by *ab initio* MP2, and DFT B3-LYP and B-LYP methods were compared with each other to obtain the best reference method for computation of conformational properties of molecules. Especially the torsional behaviour and the conformational dependence of the valence co-ordinates and of the atomic charges were discussed. The first publication discusses esters with an isolated carboxyl group and the second one esters with two non-isolated carboxyl groups.

In publications III and IV the properties of single polymer chains were studied with the RIS (Rotational Isomeric State) Metropolis Monte Carlo (RMMC) method using the PCFF, as improved in papers I and II. In paper III the modified PCFF was applied to RMMC calculations on selected main chain and side group polyesters with isolated carboxyl groups to test the reliability of the modified PCFF and to study the performance of the RMMC method with different choices of run parameters. In paper IV the RMMC method was applied to investigate the flexibility of the chains of a few important biodegradable polyesters with non-isolated carboxyl groups (i.e. poly(L-lactic) (PLLA), poly(L,D-lactic) (PLLA/PDLA) and polyglycolic (PGA) acids). Comparisons between the results obtained with the original and modified PCFFs are shown in paper IV. In publication V amorphous state properties, i.e. solubility, free volume and pair correlation functions, of PLLA, PLLA/PDLA, PGA and PGA/PLLA were studied by the Amorphous Cell -method utilising the modified PCFF.

This thesis includes also some unpublished results.

Contents

ABBREVIATIONS

AM1	Austin Model 1
B-LYP	Becke–Lee-Yang-Parr
B3-LYP	Three parameter Becke–Lee-Yang-Parr
BO	Born-Oppenheimer
CFF	consistent force field
CHELPG	Breneman’s procedure for calculating electrostatic potential derived atomic charges
COMPASS	Condensed-phase Optimised Molecular Potentials for Atomistic Simulation Studies
D	Debye
DP	degree of polymerisation
DFT	Density Functional Theory
ESP	electrostatic potential
FF	force field
HF	Hartree-Fock
LJ	Lennard-Jones
MC	Monte Carlo
MD	molecular dynamics
MM	molecular mechanics
MP2	Møller-Plesset 2nd order perturbation (theory)
PCF	pair correlation function
PCFF	polymer CFF
PDLA	poly(D-lactic) acid
PES	potential energy surface
PGA	polyglycolic acid
PGA/PLLA	copolymer of L-lactic and glycolic acid
PLA	polylactic acid
PLLA	poly(L-lactic) acid
PLLA/PDLA	poly(L,D-lactic) acid
PMA	poly(methyl acrylate)
PMMA	poly(methyl metacrylate)
PVA	poly(vinyl acetate)
QM	quantum mechanics or quantum mechanical
RIS	rotational isomeric state
RMMC	RIS Metropolis Monte Carlo
rms	root-mean-square
rrms	relative root-mean-square
SCF	self-consistent field

1 Introduction

Development of the performance of computers and of the theory has made computational simulations an important tool also in materials science. Today increasingly accurate results can be obtained in a reasonable time for even large and complicated molecular systems. Still more reliable methods are, however, needed to obtain more realistic determinations of molecular properties to be utilised in different applications and to understand the physics of molecular systems. The basic question is how to describe real materials by simplified theoretical models. For example in a classical atomistic description, in which the detailed chemical structure of a molecular system is taken into account, still more reliable models have to be found to represent the interactions between atoms.[1]

One way to classify the most frequently used methods in molecular modelling is illustrated in Fig.1. The methods can roughly be divided into atomistic simulations, in which every atom is explicitly included, and non-atomistic simulations, in which groups of atoms, or entire chains, are collectively modelled.

According to the Born-Oppenheimer (BO) approximation[2] the motions of electrons and nuclei can be separated due to their different masses. Thus, quantum mechanical (QM) methods (*ab initio*, density functional theory (DFT) and semi-empirical)[3,4,5,6,7] are based on solving the time-independent Schrödinger equation for the electrons of a molecular system as a function of the positions of the nuclei. In classical atomistic simulations, instead, atoms are treated as basic units, and the interactions between the atoms are described by classical potential energy functions (force fields (FFs)). High-level *ab initio* and DFT calculations are computationally demanding. The computing time depends on the number of electrons, and therefore QM methods are usually limited to molecules and molecular systems consisting of less than about 30 non-hydrogen atoms. Classical FF methods, such as molecular mechanics (MM)[8,9] and molecular dynamics (MD)[9,10] methods, on the other hand, can be applied to much larger molecular systems containing thousands of atoms. The FF contains parameters, which are derived from QM and/or experimental data. These parameters and the functional forms of the energy terms determine the ability of the FF to describe the molecular system under investigation.

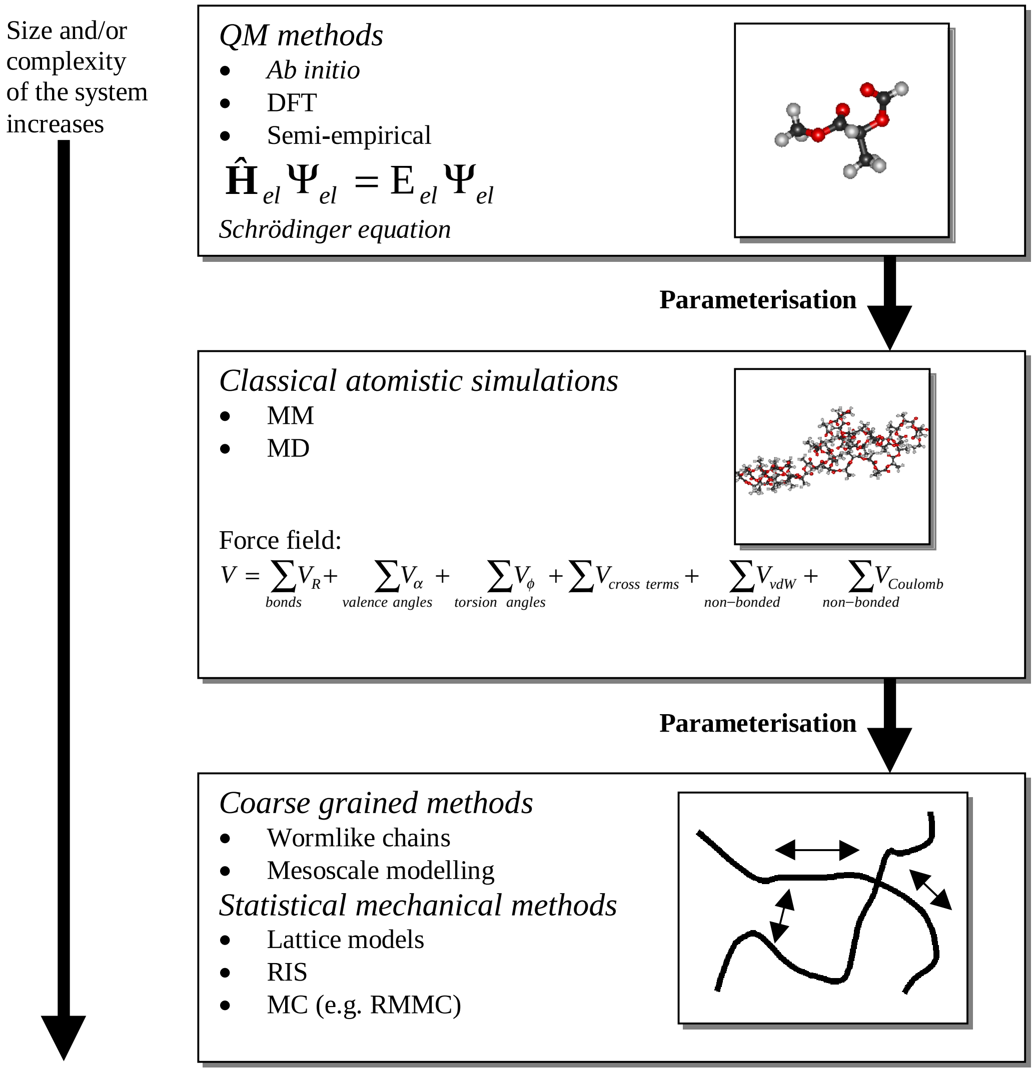

Fig. 1. The most frequently used methods in molecular modelling.

The microscopic details of the molecular behaviour are unnecessary to know, when the long time-scale motion of large molecular systems is considered. In these cases coarse grained methods, such as wormlike chain- or mesoscale models[11,12,13,14,15,16,17,18,19,20], or statistical mechanical methods, such as lattice models[21,22,23,24], Rotational Isomeric State (RIS) model[25,26,27] or Monte Carlo (MC) method[28], can be applied. In coarse grained molecular theories the motion of a polymer chain is simplified by describing it with parameterised models such as a bead and spring model[11,12,13,14] or as continuous wormlike chains[15,16,17,18].

The most frequently used lattice models of polymers, that also are parameterised models, are based on the Flory-Huggins mean-field theory[21,22,23,24] and typically used in modelling of polymer blends or polymer-solvent systems. Lattice models do not provide detailed information about the atomic-scale structure of polymer chains, and if this is needed, RIS models can be utilised. The RIS theory[25,26,27] is used especially in the calculations of statistical conformation-dependent properties of polymer chains under Θ-conditions, where the effective long-range intrachain interactions are neglected. In practice a Θ-state is achieved either in the melt or in a specific Θ-solution. Statistical weights, needed in the RIS theory, can also be used in a MC scheme, in which the polymer conformation is changed randomly according to certain rules, to generate independent chain conformations with the correct statistics (RIS MC[29]). One practical drawback of the RIS methods is that statistical weights must be derived for each possible minimum energy conformation of the polymer chain. However, in less complex cases RIS methods are preferred for calculation of single chain properties, due to their high computational efficiency. These methods can mainly be applied to homopolymers and polymers with small or stiff side groups. The RIS Metropolis Monte Carlo (RMMC) method[30] has similarities with the conventional RIS theory but is not a true RIS method despite its name. In the RMMC method, the conformational energies of the polymer chains are calculated directly from the selected FF. Since the bond rotation (torsion) angles are allowed to vary continuously in the RMMC method, RMMC can easily treat copolymers and polymer chains with flexible side groups. More detailed discussions of the coarse grained and statistical mechanical methods can be found in textbooks or publications in this field[11-29,31,32]. The RMMC method[30] is presented in more detail also in chapter 2.3 of this thesis.

To obtain reliable conformational statistics for polymer chains, the selected FF has to estimate the potential energy surface (PES) of the systems studied as realistically as possible. An accurate representation of the bond rotations in the chain is extremely important, since especially the properties of synthetic polymers depend highly on the conformational statistics of the polymer chains. As regards the conformational analysis of large molecules and polymers, the most important terms of the FF are torsion and non-bonded potentials, out of which the latter usually contains van der Waals and Coulomb interactions. Correlation between the parameters of the model function is a serious problem in derivation of FFs. The non-bonded parameters are strongly correlated with all other parameters of the FF. The torsional potential, on the other hand, is local in nature, and its parameters are strongly correlated with the non-bonded parameters. Due to correlations, FF parameters are usually not uniquely determined. Therefore, optimisation of only part of the parameters may improve some calculated results for molecular properties, though simultaneously new discrepancies are easily introduced in other properties. However, re-optimisation of torsion parameters does not significantly affect other molecular properties than conformational energy features of the concerned bonds. An incorrect torsional behaviour can, therefore, be corrected by re-optimising the torsion parameters. Although this re-optimisation may not be physically completely correct, it is technically the only easy way to safely improve the FF. It should, however, be noted that the need to re-optimise torsion potentials may also reflect inadequacies in other energy terms of the FF which the re-optimisation tries to compensate. An other notable point is that due to correlations, the parameters that are optimised for one FF are not directly transferable to other FFs. The reliability of the FF to be used should always be tested when studying new kinds of molecules. There exist no accurate universal FFs[8], and all commonly used FFs are optimised for special purposes.

In this study, interest is focused on the reliability and applications of the PCFF (Polymer Consistent Force Field)[33,34,35,36,37,38,39,40,41], which is a member of the CFF[42,43,44,45] family and optimised for synthetic polymers. In most FFs the parameters are optimised to reproduce QM and/or experimental data on various molecular properties. Compared with experiments, QM calculations have the advantage that they easily yield a consistent and a sufficient amount of data for determining the FF parameters. As regards the torsional behaviour, QM results are favoured in the test as well as in the re-optimisation of the torsion potentials, since in this way the entire rotational behaviour over the whole range of dihedral angles can be obtained. If the level of the QM method used is high enough and the basis set large enough the results that are to be used as reference data will be reliable. A flow chart picture showing the goal of this study is presented in Fig. 2.

Polymer chains can be thought to consist of smaller units. By investigating these units as neutral model molecules, information about the properties of the polymer chain can be obtained. In this thesis the conformational energy behaviour of the studied polymer chains was determined through QM studies carried out for selected model molecules (in this study esters) (see papers I and II). With the aid of these model molecules the reliability of the PCFF was then investigated. If the torsional behaviour of the QM and FF results disagreed, the torsion potential of the FF was modified. The reliability of the modified FF was further investigated by RMMC calculations on single chain properties for such polyesters for which

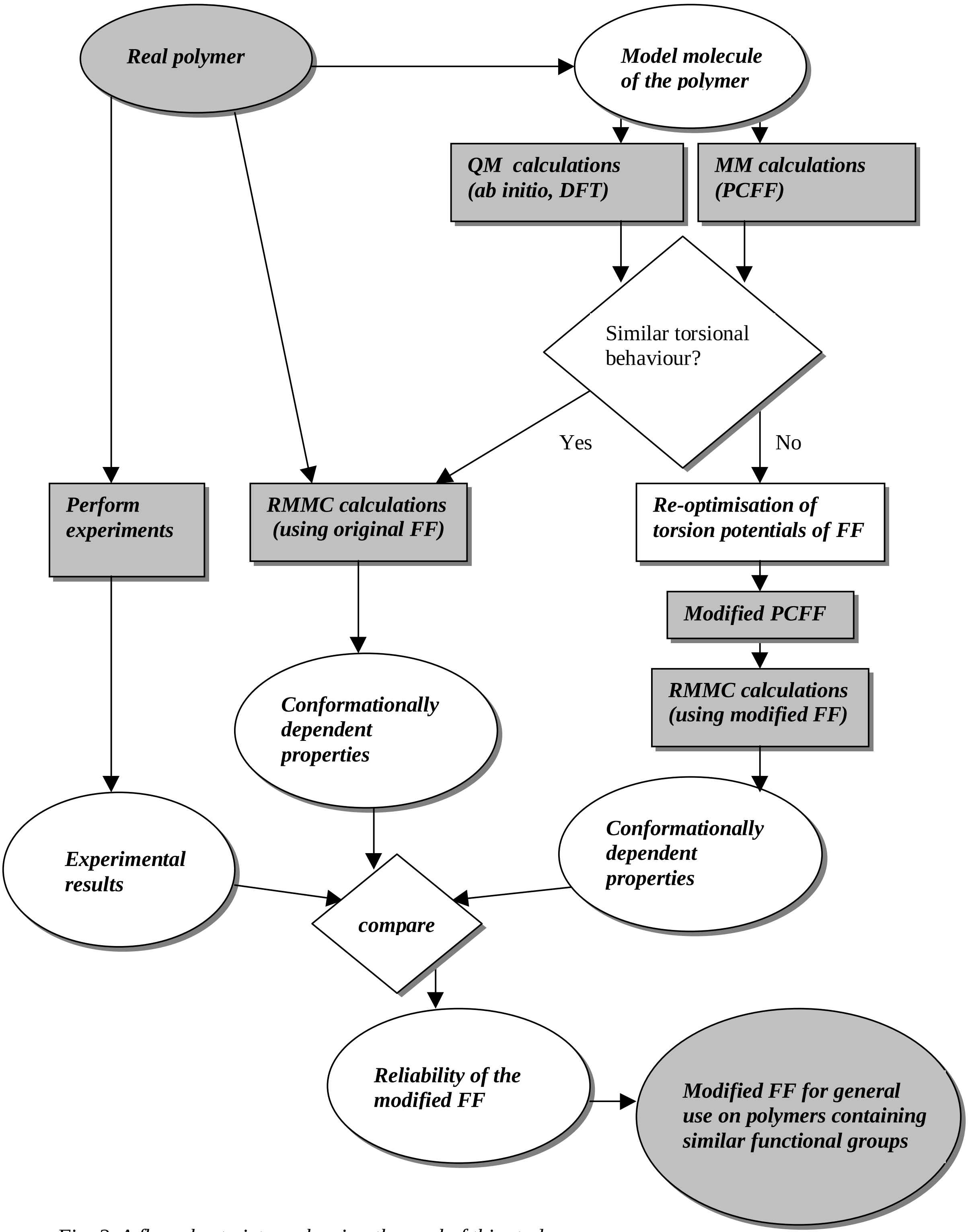

Fig. 2. A flow chart picture showing the goal of this study.

there was reliable experimental data available (paper III). In this work also the parameters which affect the RMMC results were studied. The modified PCFF was further applied to RMMC studies on the chain flexibility of a few polyesters known to be biodegradable (paper IV), and in amorphous phase studies of biodegradable polylactic and polyglycolic acids (paper V). The amorphous phase studies were carried out to find factors, which affect the biodegradability of the studied polyesters. The final goal is to obtain a PCFF for general use on polyesters.

The model molecules and polyesters studied in papers I-V are presented in Fig. 3. Esters A and B (molecules I and II in paper I) represent model molecules for aliphatic main chain and side group polyesters with isolated carboxyl groups, and esters A-E (molecules C-E are molecules I-III in paper II) model molecules for biodegradable polylactic and polyglycolic acids, which are polyesters with non-isolated carboxyl groups. Polylactic (PLA), polyglycolic (PGA) acids and their copolymers are used for example in paper coatings, food packaging and in biomedical applications, such as in surgical sutures, bone fixation devices and in drug delivery system in pharmacology[46,47,48,49,50]. The flexibility is of interest due to the possible applications of these biodegradable polyesters for example in packaging materials or baby diapers. The side group polyesters poly(methyl acrylate) (PMA), poly(methyl metacrylate) (PMMA) and poly(vinyl acetate) (PVA) were chosen for these studies because they have been very carefully studied and are widely used in many applications, PMA for example in packings, PMMA in paints and plastics and in a range of glazing applications and PVA in coatings and in adhesives[51].

2 Theoretical aspects

In the following, the theory related to the methods used in the calculations of this thesis is presented. Chapter 2.1 contains a brief review of the *ab initio* and DFT methods. The FF methods and especially the PCFF are presented in chapter 2.2. The RMMC method, which applies a FF in the calculations of single chain properties of polymers is presented in chapter 2.3. Properties of an amorphous polymer material were studied by the Amorphous Cell - method, which is described in chapter 2.4.

2.1 Quantum mechanical methods

Despite the fact that they are the most correct atomistic computational methods available, the QM methods use approximations and simplifications of the theory. In the following the main features of the QM methods used in this thesis are briefly presented. More detailed descriptions can be found in for example Refs. 3-7.

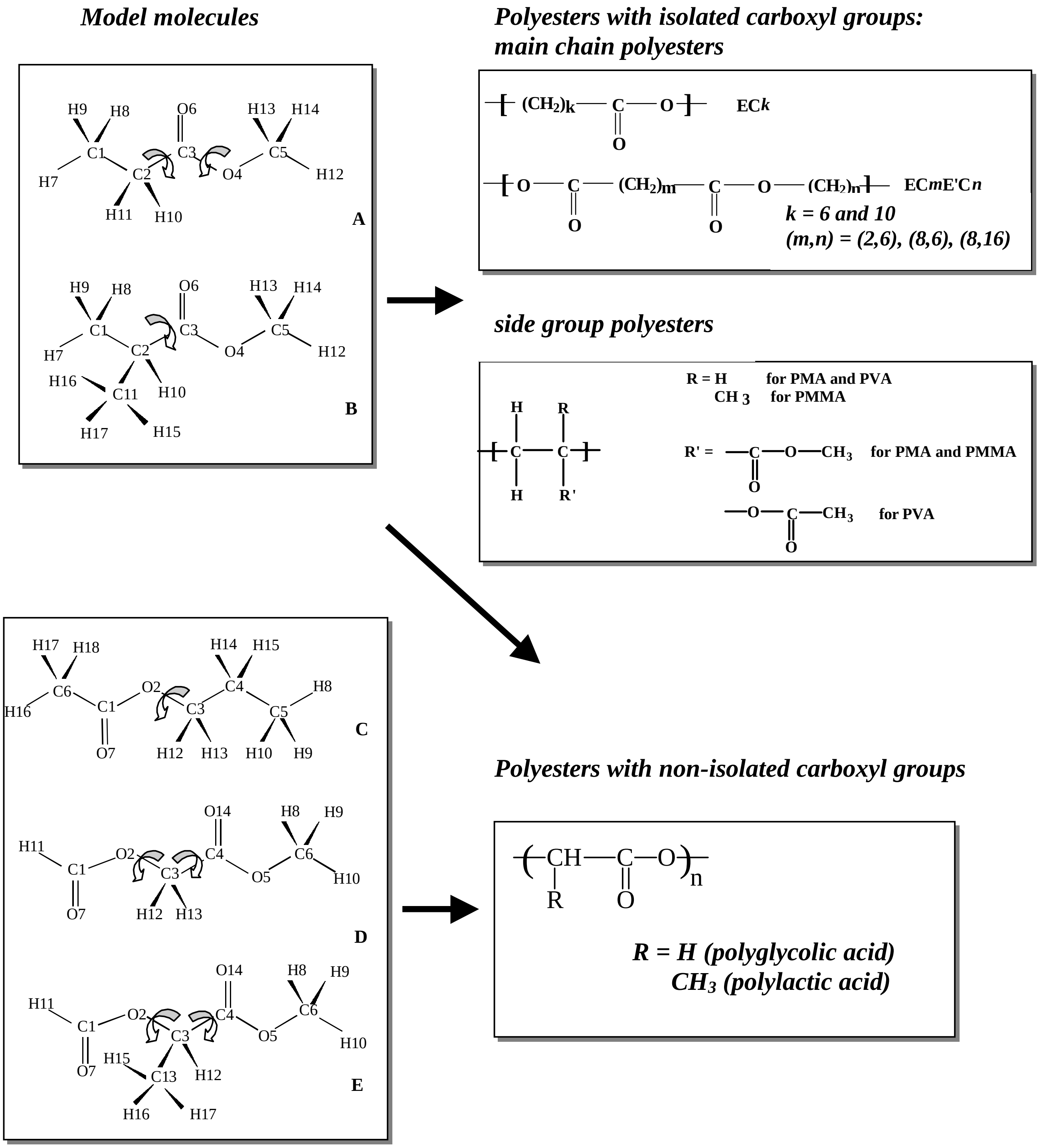

Fig. 3. Model molecules (including the numbering of the atoms) for studied polyester chains.

According to the BO approximation[2], motions of electrons and nuclei can in most situations be studied separately due to their different masses. Thus, QM (both *ab initio* and DFT) methods are based on solving the time-independent Schrödinger equation for the electrons of a molecular system

$$\mathbf{H}_{el}\Psi_{el} = E_{el}\Psi_{el}. \tag{1}$$

In eq. (1) $\mathbf{H}_{el}$ is the electronic Hamiltonian, Ψ_{el} is the electronic wave function and E_{el} is the total electronic energy of the molecular system for a given arrangement of the nuclei. The total energy $E_{tot}(\{\boldsymbol{R}\})$, in which $\{\boldsymbol{R}\}$ describes the co-ordinates of the nuclei, provides a multidimensional PES for nuclear motion. To simplify the equations all quantities in the following discussion will be in atomic units and $\mathbf{H}_{el}$, Ψ_{el} and E_{el} are given without a subindex since in this chapter only the electronic problem is considered.

The electronic Schrödinger equation of the many-electron problem can be solved using the Hartree-Fock (HF) approximation, in which the many-electron problem is replaced by a set of one-electron problems. The electron-electron repulsion is taken into account through an average potential. The HF equations comprise a set of independent equations for each one-electron orbital. For an orbital a it is

$$\left\{\mathbf{h}(i) + \mathbf{v}^{HF}\right\}\phi_a(i) = \varepsilon_a\phi_a(i). \tag{2}$$

The Hamiltonian is, thus, presented as an approximate Fock operator, which is a sum of one-electron operators $\mathbf{h}(i) = -\frac{1}{2}\nabla_i^2 - \sum_A \frac{Z_A}{r_{iA}}$ and $\mathbf{v}^{HF}(i) = \sum_{b\neq a}\left[\mathbf{J}_b(i) - \mathbf{K}_b(i)\right]$, in which Z_A is the charge of nucleus A, r_{iA} is the distance between electron i and nucleus A, $\mathbf{J}_b$ is a Coulomb operator and $\mathbf{K}_b$ an exchange operator. The effective one-electron potential $\mathbf{v}^{HF}$ describes the interaction of electron i in the spinorbital a with the average field formed by all the other electrons in spinorbitals b ($b\neq a$). In eq. (2) ε_a is the energy of the spin orbital $\phi_a(i)$ of electron i. The wave function of the electron has to satisfy also the anti-symmetry principle that is known as the Pauli exclusion principle. To solve the wave function from the HF equations, a molecular orbital, containing all the electron wave functions of the molecule, is usually written as a linear combination of atomic orbitals ϕ_j as follows

$$\Psi_i = \sum_{j=1}^{K} c_{ij}\phi_j. \qquad i, j = 1,2, \ldots, K \tag{3}$$

Here c_{ij} is the molecular orbital expansion coefficient. Substitution of eq. (3) into the HF equations and use of the variation principle gives the Roothaan-Hall equations, which can be solved iteratively by a Self-Consistent Field (SCF) method. The results of the Roothaan-Hall equations yield the HF wave function for the ground state of an N electron system as a

Slater determinant and the electronic energy in the field of M point charges (i.e. nuclei). By varying the co-ordinates of the nuclei a PES is obtained, and by minimising the energy the global minimum energy information of the molecule can be achieved. Due to computational reasons, the atomic orbitals ϕ_j are usually expressed as a linear combination of gaussian-type basis functions. This is utilised in the software package GAUSSIAN[52], which has been used in all QM calculations of this thesis.

Since the electron-electron correlation in the HF theory is taken into account only through an average potential, for example bond lengths and dissociation energies can be underestimated. In the Møller-Plesset perturbation theory this defect is corrected by treating the correlation energy as a small perturbation[53]. The Hamiltonian is

$$\mathbf{H}_\lambda = \mathbf{H}_0 + \lambda\mathbf{V}, \tag{4}$$

in which $\mathbf{H}_0$ is the approximate Fock operator of the HF method and $\lambda\mathbf{V}$ is a small perturbation applied to $\mathbf{H}_0$, in which λ is a parameter and $\mathbf{V}$ a perturbation operator. The perturbed wavefunction ψ_λ and energy E_λ are expressed in terms of the parameter λ:

$$\psi_\lambda = \psi^{(0)} + \lambda\psi^{(1)} + \lambda^2\psi^{(2)} + \lambda^3\psi^{(3)} + \ldots$$

$$E_\lambda = E^{(0)} + \lambda E^{(1)} + \lambda^2 E^{(2)} + \lambda^3 E^{(3)} + \ldots \tag{5}$$

The Møller-Plesset second order perturbation (MP2) theory has turned out to be the most satisfactory for most applications, when the computing times and the accuracy of the results are considered.[54] Computationally more inexpensive methods, which also take electron correlation into account, are the DFT methods based on the density functional theory for a uniform electron gas (local spin density approximation)[6,55,56]. The DFT methods have their origin in the Hohenberg-Kohn theorem[55] and are based on the knowledge that the electron density $\rho(r)$ determines the external potential and, thus all molecular properties. Electron correlation is calculated through general functionals of the electron density. It has been proved that the functionals satisfy the variational principle, and that the functional has a minimum at the right ground state density. From this general theory different approximate methods to calculate an electronic structure and a total energy of a molecule have been developed. In the Kohn-Sham equations the electronic behaviour of the molecules is described by a sum of exchange and correlation functionals. The electronic energy can be partitioned into different terms as follows

$$E = E_T + E_V + E_J + E_{XC}. \qquad (6)$$

Here E_T is the kinetic energy of the electrons, E_V is the potential energy of the nuclear-electron attraction and of the nuclear-nuclear repulsion, E_J is the electron-electron repulsion term and E_{XC} is the exchange-correlation term. The corrections due to the non-uniform electron density of molecules have been made to the exchange term (e.g. Becke's functional (B88 or B[57,58])) and/or to the correlation term (e.g. the functional by Lee, Yang and Parr (LYP[59])). Also hybrid methods have been developed, in which the exchange functional is replaced by the HF exchange term and by some density functional (e.g. Becke's 3-parameter model with the LYP-correlation functional, B3-LYP[60]). By including the HF term a hybrid method reduces the overestimation of bond lengths given by pure DFT methods.

In semi-empirical QM methods approximations are made to the overlap, repulsion and nuclear integrals by introducing empirical parameters and/or omitting terms. Though in paper I some semi-empirical calculations using the Austin Model 1 (AM1)[61] method were performed, further discussion of semi-empirical methods has been left out from this thesis. Semi-empirical methods are known to be uncertain in many cases[I,62,63,64] and special care has to be taken that they are applied to molecules similar to those for which the methods have been parameterised. Due to the smaller computing effort needed as compared with the *ab initio* methods, the semi-empirical methods are mainly utilised in studies of large molecular systems.

Atomic net charges are not QM observables, and they cannot be determined directly with QM calculations or by experiments. Different methods exist for the estimation of atomic charges of the molecular system[65]. Basically, the atomic charges are best derived by a least-squares fit to the electrostatic potential (ESP), calculated in a large number of points around the molecule of interest[66]. For example Sigfridsson and Ryde[67] have compared different QM methods for deriving atomic charges from ESPs. The CHELP[68], CHELPG[69] and Merz-Kollman[70,71] schemes are the methods included in GAUSSIAN[52]. They differ from each other mainly in the choice of the points where the ESP is calculated. In the CHELPG method, which also is used in the present studies, the points are selected on a regularly spaced cubic grid (with the distance of 0.3 Å between the grid points). All potential points that are not within the van der Waals radius of the atom are neglected, as well as all points that are farther than 2.8 Å from the nuclei. The point density is over 10 times higher than for the other two methods.[67] With the default settings of GAUSSIAN, Sigfridsson and Ryde noticed that the CHELPG scheme gave the most stable (atomic) charges. Wiberg and Rablen[72] have also noted that the CHELPG method best describes the non-bonded interactions compared to the other methods available in GAUSSIAN.

2.2 Force field methods

Compared to QM methods, the classical MM and MD methods[8,9,10], are computationally much faster, though more approximate ways to compute the molecular structures and energies. In these methods the nuclei are taken as interaction centres of the molecular system. With MM, minimum energy geometry structures, their energies and static properties are obtained. MD solves the classical set of equations of motion for a system of N interacting atoms and can be used to derive dynamic properties. The potential energy of the molecular system is described by a FF, which includes different parameterised energy terms to describe the interactions between atoms.

Several different FFs have been developed for various purposes. The best known ones are MM3 and MM4 by Allinger et al.[8,73,74,75,76,77,78,79], the CFF family by Lifson et al.[42-45] and Hagler et al.[80], CHARMM by Karplus et al.[81,82,83], AMBER by Kollman et al.[84,85,86], OPLS by Jörgensen et al.[87], MMFF by Halgren et al.[88,89] and GROMOS by van Gunsteren et al.[90]. Out of these FFs the PCFF (Polymer CFF)[33-41] and the COMPASS (Condensed-phase Optimised Molecular Potentials for Atomistic Simulation Studies) force field[91], belong to the CFF family and are especially developed for synthetic polymers. The main interest in this thesis is in the PCFF, though some calculations were also carried out using the COMPASS FF in paper I.

The general form of the potential energy given by a FF[8,92,93,94,95,96] is as follows

$$\begin{aligned} V = {} & \frac{1}{2}\sum_i \left[F_{ii}(q_i - q_{i0})^2 + F_{ii}{}^{(3)}(q_i - q_{i0})^3 + F_{ii}{}^{(4)}(q_i - q_{i0})^4 + \ldots\right] \\ & + \sum_{i<j} F_{ij}(q_i - q_{i0})(q_j - q_{j0}) + \sum V_{tor} + \sum V_{q,tor} \\ & + \sum V_{tor,\,tor} + \sum V_{nb}\,. \end{aligned} \tag{7}$$

In eq. (7) the first two sums comprise the valence part of the FF, and they describe the energy related to changes in valence co-ordinates. Here q_{i0} is the reference value of the valence co-ordinate q_i, F_{ii} is the harmonic diagonal force constant, $F_{ii}{}^{(k)}$ is the anharmonic diagonal force constant of order k and F_{ij} is the interaction force constant between the valence co-ordinates q_i and q_j. Regarding computation of polymer properties by MC methods, the bond lengths and valence angles usually are constrained, and then the valence terms of the energy function affect conformational properties of molecular systems only indirectly through the optimised geometry. The torsion potential V_{tor} (and its interaction terms) and the non-bonded potential V_{nb}, on the other hand, directly affect the conformational properties of system (direct effect on the population of the conformational states of molecules in MD and MC simulations), and are thus the most important potential energy terms as regards conformational analysis of molecular systems. In the PCFF and the COMPASS FF, the torsion potential V_{tor}, which describes rotations about chemical bonds in molecular systems, is expressed as follows

$$V_{tor} = \sum_{n=1}^{3} V_n (1 - \cos n\phi). \tag{8}$$

In eq. (8) n is the periodicity of the term related to a torsion co-ordinate ϕ and V_n is the corresponding torsion barrier parameter. $V_{q,tor}$ and $V_{tor,tor}$ in eq. (7) describe interactions between a valence co-ordinate q_i and a torsion co-ordinate ϕ or between two torsion co-ordinates, respectively. There exist more advanced representations for torsional behaviour, e.g. by Allinger et al. in the MM4[75-79] and by Mannfors et al. in the CFF [92,97,98]. Both these models contain a fourfold term and the latter an additional one-fold term ($1+\cos^m\phi$, m is an odd integer), which was needed to reproduce correctly the *ab initio* gauche conformation and its torsional frequency in 1,3-butadiene and in a few of its methyl substituted derivatives. The non-bonded potential V_{nb} describes interactions between atoms that are not chemically bonded to each other or to a common atom (1,4 and higher interactions). It is usually represented by a Lennard-Jones (LJ) type (long-range attractive and short-range repulsive) potential for the van der Waals interactions and a Coulomb potential for the electrostatic interactions. This is the representation also used in the PCFF and the COMPASS FF. For a LJ 9-6 potential V_{nb} has the analytic form

$$V_{nb}(r_{ij}) = E_{0,ij}\left[2\left(\frac{R_{0,ij}}{r_{ij}}\right)^9 - 3\left(\frac{R_{0,ij}}{r_{ij}}\right)^6\right] + k\frac{e_i e_j}{\varepsilon(r_{ij}) r_{ij}} \tag{9}$$

In eq. (9) r_{ij} is the distance between atoms i and j, $E_{0,ij}$ and $R_{0,ij}$ are parameters which depend on the type of atoms (i and j), e_i (e_j) is the partial charge of atom i (j), $\varepsilon(r_{ij})$ is the dielectric constant, that in some FFs is distance dependent, most often though taken as 1.0, and k is a constant. The LJ 9-6 potential has been found to give better results than the 12-6 potential[44,99], and it is also used in the PCFF and the COMPASS FF. As already mentioned, the electrostatic interactions in the PCFF, as well as in the most currently used FFs, are described by a Coulomb potential, i.e. as a fixed point charge model. More advanced electrostatic models have been developed, for example by Mannfors et al.[66,100] for the SDPFF (Spectroscopically Determined Polarizable Force Field). In addition to atomic charges the model includes atomic dipoles and is further enhanced by the possibility to explicitly account for polarisability in the form of induced charges and anisotropically induced atomic dipoles. Other models also exist in which polarisability is at least partly accounted for.[101,102,103,104,105] In still other electrostatic models charge and dipole changes as a function of geometry are taken into account.[106,107]

2.3 RIS Metropolis Monte Carlo (RMMC) method

In the RMMC method, which was developed by Honeycutt[30], conformations of polymer chains are generated with the MC technique[28] using potential energy functions (FFs) directly. The generated conformations of the polymer chains are then used to calculate average values for single chain properties such as characteristic ratio, radius of gyration and persistence length, i.e. properties, which can also be computed with the conventional RIS method.

In Ref. 30 and in paper III some of the main features and differences between the RMMC and conventional RIS methods are presented. Since the RMMC method uses continuous torsion co-ordinates it can easily be applied to, for example, copolymers and branched polymers with flexible side groups. The quality of the selected FF is, however, crucial for the RMMC method. In the RMMC method, as well as in the RIS theory, the bonds and valence angles are constrained, in the conventional RIS method to mean values and in the RMMC method preferably to values corresponding to the initially optimised minimum energy structure. In most QM or FF calculations such constraints are not used.

An RMMC simulation scheme is presented in Fig.4. The RMMC simulation of a polymer chain starts by choosing an arbitrary conformation for the chain. In a MC step a change is done to that conformation, and based on the temperature and the energy of the new conformation relative to the old one, it is decided whether this new conformation is accepted or not. This process is repeated several times in order to get a distribution of conformations which is characteristic for the studied chain at the specified temperature. Then conformational property calculations are carried out and running averages updated. The whole process is repeated until a sufficient number of iterations is achieved. The RMMC method is discussed in more detail in Papers III, IV and in Ref. 30.

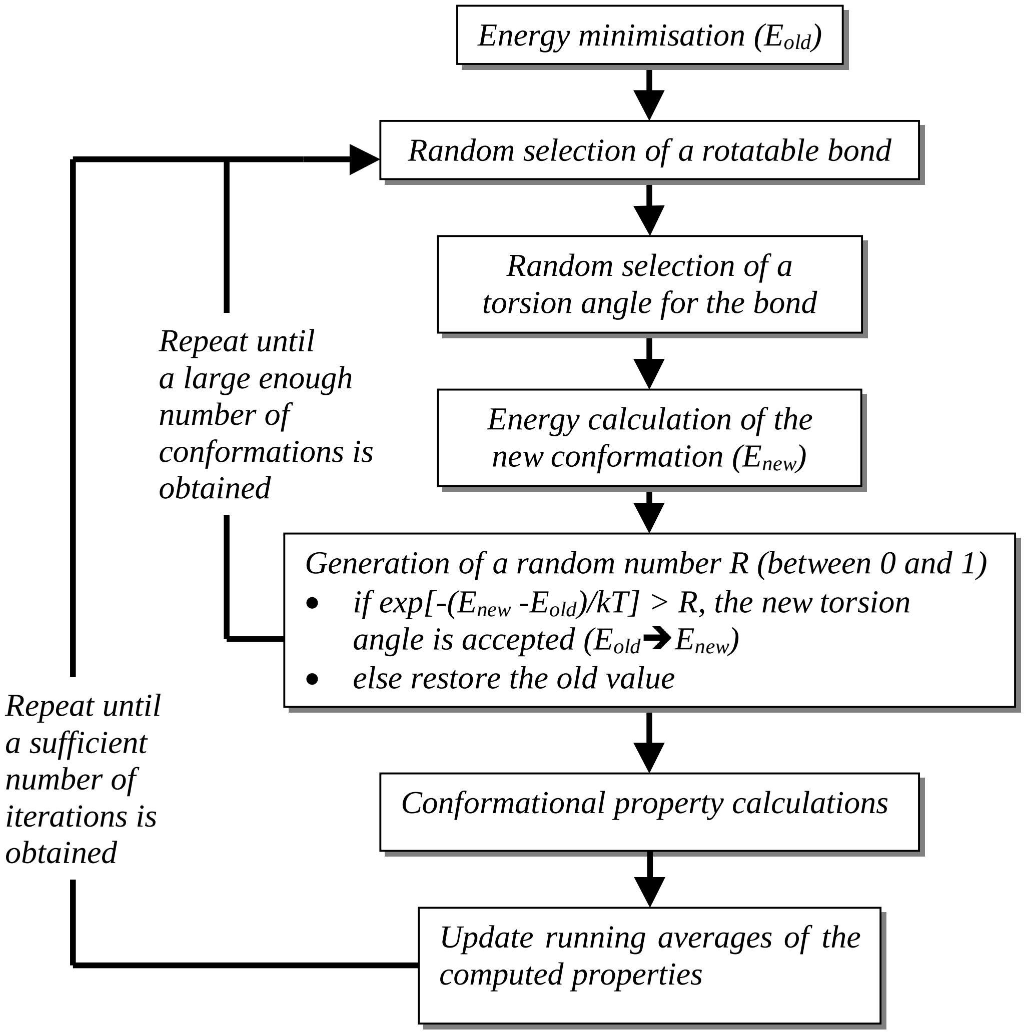

Fig. 4. The RMMC simulation procedure.

There is a number of parameters that significantly affect the results of a RMMC simulation, such as the parameters of the selected FF, the cut-off for non-bonded interactions and an effective dielectric constant. The energy terms of the selected FF considered in the RMMC simulation are the torsion and non-bonded potentials. For a polymer chain in Θ-conditions interactions between distant atoms along the chain vanish and, in order to simulate these conditions, a non-bonded cut-off has to be imposed. There are two methods to treat cut-off in the RMMC method. In the distance dependent method, interactions beyond the defined maximum distance between interacting atoms are not included. This treatment, however, allows non-bonded interactions also between distant atoms along the chain in flexible polymer chains. In the Max_Bonds method, instead, the non-bonded distance is determined between a minimum and maximum number of bonds along the chain. The latter method takes, thus, proper care that the non-bonded interaction is kept at a short range along the chain, as required for a Θ-state of a polymer chain. The Max_Bonds method, which is used to treat the cut-off in all RMMC studies of this thesis, is clarified in Fig. 5 in the case of PLLA, without and with charge groups, using Min_Bonds=3 and Max_Bonds=6.

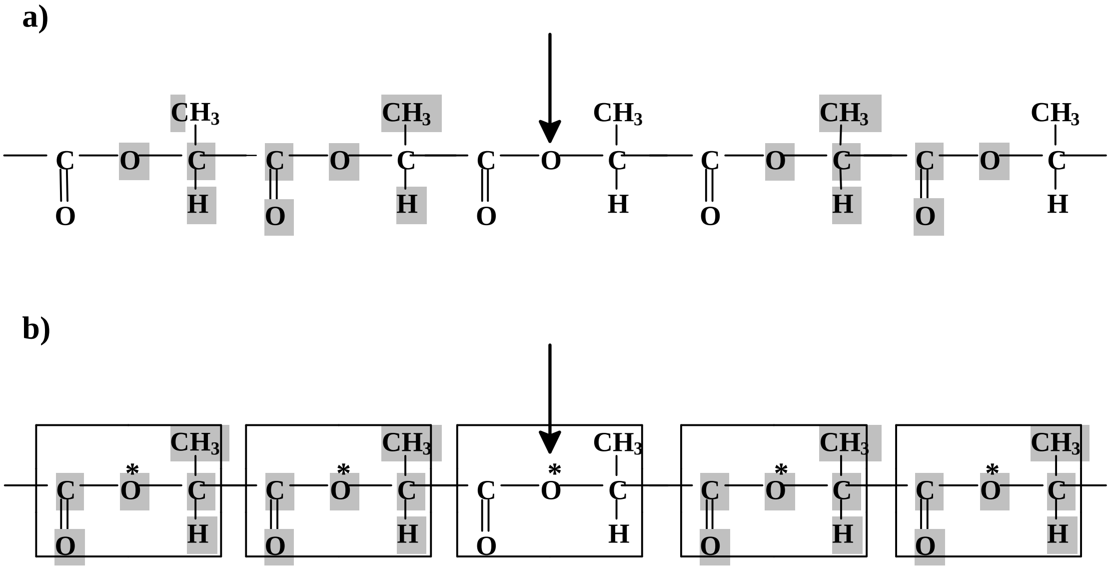

Fig. 5. The Max_Bonds method a) without and b) with electrically neutral charge groups in the case of PLLA. The minimum distance (Min_Bonds) is 3 bonds and the maximum distance (Max_Bonds) is 6 bonds. The non-bonded interactions are taken into account between all the atoms in shadowed boxes. The arrow marks the atom from which the count of the bonds is started. Each charge group contains an atom assigned as a switching atom (*) to define the starting point for counting the number of bonds.

If charge groups are not used, the Coulomb interactions may not be in balance (because of the cut-off). By dividing the polymer chains into neutral charge groups unbalanced Coulomb interactions can be avoided, as seen in Fig. 5 for PLLA. The choice of charge groups is discussed in more detail in paper III. As regards the parameter values, Min_Bonds is usually defined to be three bonds as the non-bonded interactions in most FFs are restricted to 1,4- and higher interactions. Max_Bonds typically range from 4 to 6[30,III,IV], but larger values may be required depending on the chain architecture. The effective dielectric constant ε_{eff} can be used to account for the chain's environment, but mostly it is taken as 1. The choice of the parameters is not *a priori* evident, and has to be based on careful tests for various types of polymer chains.

The most significant single chain property is the flexibility of a polymer chain**.** The characteristic ratio ($C_\infty = \lim_{n\to\infty} C_n$) is determined for flexible polymers as follows[25]

$$C_n = \frac{\langle r^2 \rangle}{n l_v^{\,2}}. \qquad (10)$$

In the above equation $<r^2>$ is the mean squared end-to-end distance of the chain, n is the number of bonds and l_v is the length of a real or a virtual bond. Virtual bonds are more commonly used for polymers having rigid units in the chain, and it is defined as a “bond” connecting the atoms on the opposite sides of a rigid unit.[25] As regards less flexible chains such as liquid crystals, a persistence length is a better measure of stiffness than the characteristic ratio. It can be defined in various ways. It may be defined as the average sum of the projections of all bond vectors onto the first bond of a chain. Alternatively, it may be defined as the projection of all succeeding bonds (including the bond itself) onto an internal bond of the chain. The persistence length is, thus, a measure of the distance over which a chain retains "memory" of its initial direction. The latter way is preferred in this thesis. A ratio of the mean squared end-to-end distance over the mean squared radius of gyration ($<r^2>/<s^2>$) can also be calculated. The theoretical value of this ratio is 6 for ideal random walk chains, which are chains that obey gaussian statistics. However, it is of no significant practical importance.

2.4 Simulations of amorphous polymers

In the following a simulation method available in an MSI (Molecular Simulations Inc.)[108] software package and used in this thesis to study the amorphous state of a polymer material is presented. First the construction and the refinement of the amorphous model is described, then the methods used for calculation of the properties of the constructed model are briefly presented. More details can be found in textbooks and research articles.[108,109,110,111,112,113]

Construction and refinement of the model

The Amorphous Cell -procedure is shown in Fig. 6.

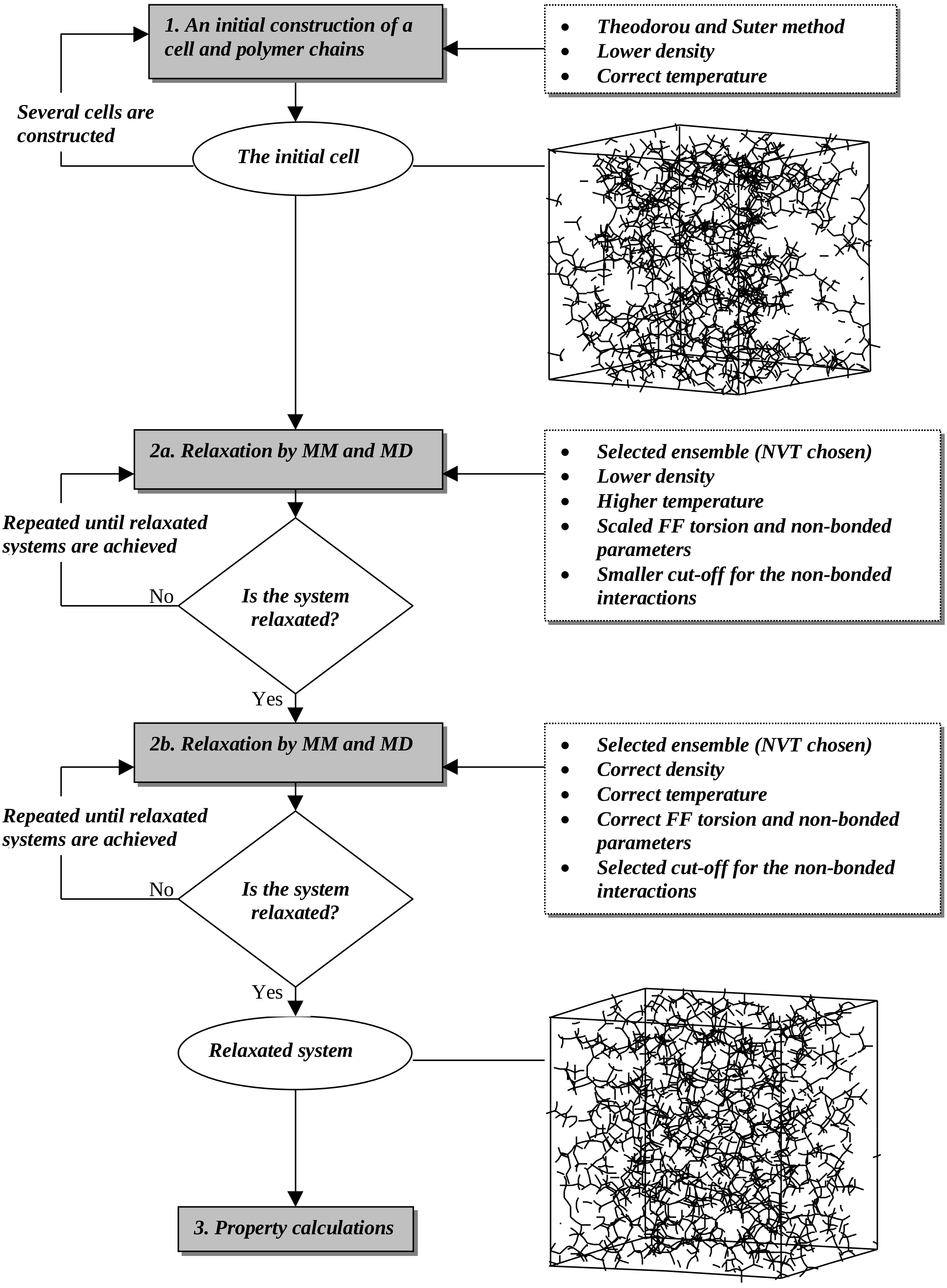

Fig. 6. The Amorphous Cell-procedure

The amorphous models were built in two steps: First, an initial structure was generated for the polymer chains in a box (or amorphous cell) using the Theodorou and Suter method (step 1 in Fig. 6). Second, the constructed structures (i.e. polymer chains in the cell) were optimised to obtain low-energy structures of the model (steps 2a and 2b in Fig. 6). In the Theodorou and Suter method, the three first backbone atoms together with the pendant atoms of the first two are placed in a box with periodic boundary conditions. Thereafter the chain is constructed stepwise so that one bond at a time is added to the chain. The torsion and the non-bonded potentials of the selected FF (or the statistical weights in the RIS method) determine the value of the dihedral angle of the added bond. The periodic boundary conditions and minimum image convention, used in calculations to avoid artificial surface effects, are shown in Fig. 7.

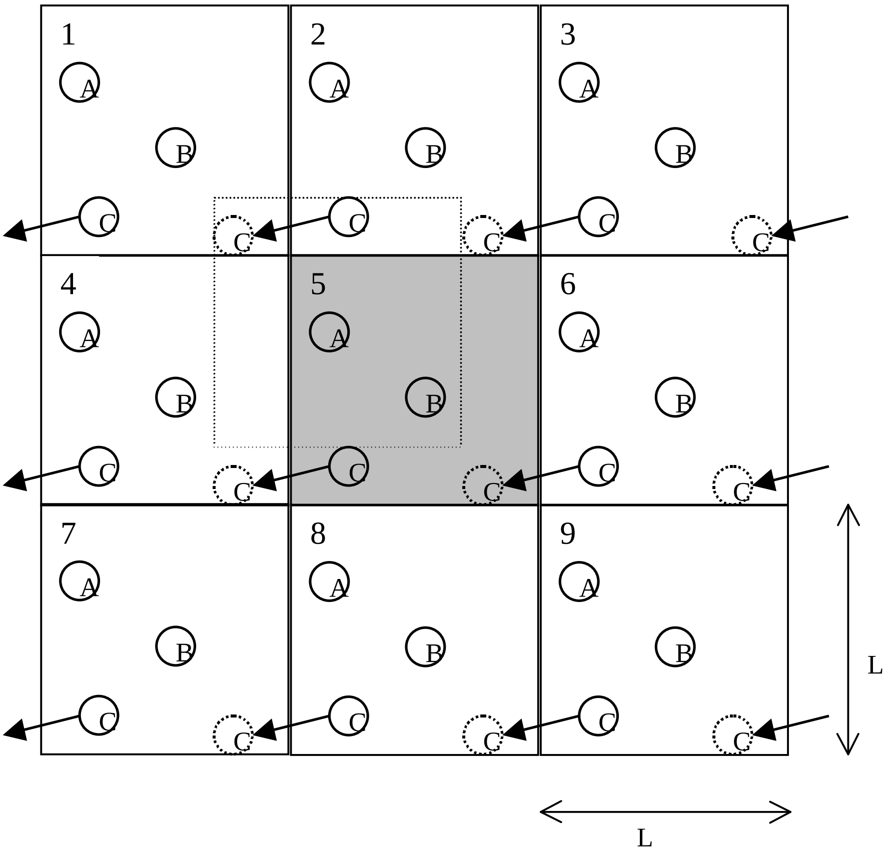

Fig. 7. A minimum image convention and periodic boundary conditions in a two-dimensional system. (L=the length of the cell edge). [9]

With the periodic boundary conditions, the system is considered to be surrounded by replicas of itself forming an infinite macrolattice. When a molecule moves in the original box, its periodic images in the neighbouring boxes move in the same way. When a molecule (C) leaves the central box, one of its images will enter through the opposite face, since there are no walls at the boundaries of the central box and no surface molecules. In the minimum image convention, only the shortest possible distances between the atom pairs, the lengths of less than half of the box edge length, are taken into account in the calculation of the forces between the atoms. For example, in the box constructed (dashed line) with molecule A_5 at its centre, the molecule A_5 interacts with all the molecules whose centres are inside the constructed box, i.e. with the closest periodic images of the other molecules (B_5 and C_2). Charge groups, as described in section 2.3, can be used also in the Amorphous Cell -procedure. The number of chains constructed and the degree of polymerisation (DP), i.e. the length of the chain, together with the density determine the size of the constructed cell. The FF and the temperature determine the conformational statistics of the chains. Lower density than the experimentally observed one can be used in the initial construction of the cells to facilitate the proper packing of the cells. The constructed initial model structure usually has a high potential energy, and the cell has regions in which the density fluctuates a lot (see Fig. 6). Several cells are required to obtain sufficient statistics for the conformational states of the polymer chains for averaging of the calculated properties.

The initial structures are then refined using repeated MM and MD steps to obtain low-energy cells. A canonical ensemble is selected. In this thesis, the relaxation was made in two steps (2a and 2b in Fig. 6) to facilitate the proper equilibration of the structures. In step 2a the densities of the cells were kept lower than the experimentally observed ones and a smaller cut-off value for the non-bonded interactions was used. The torsion and non-bonded parameters of the FF were scaled. MD steps with higher temperature than in the experimental studies were carried out to avoid the cells trapping into local high-energy minima, since MM energy minimisation always leads into the nearest downhill minimum. In a MD simulation the system can travel over potential energy barriers if the kinetic energy is large enough. In this way, the system can adopt conformations in the low-energy region, even when there are several barriers between the starting point and the low energy region. The systems were considered to be equilibrated when the cohesive energy densities of the cells did not grow further, the energies of the different cells were close to each other and the cells by visual inspection also seemed to be evenly distributed. After the first relaxation, the structures were optimised using the experimental conditions (the correct density and temperature) and realistic parameters (non-scaled torsion and non-bonded parameters and a cut-off value, which is less than half of the cell-edge length due to the minimum image convention used). Corrections to the energy and pressure (tail corrections[9]) were included in this work to compensate for the missing long-range part of the non-bonded potential. All atoms were, thus, explicitly taken into account. After the relaxation, the cells were ready for further analysis and for calculation of the properties of interest.

Calculation of properties

In this study, solubility parameters, free volumes and pair correlation functions were calculated. These static properties of the amorphous material, which are computed as mean values of several cells, can be obtained using the optimised structures.

The Hildebrand solubility parameter expresses the interactions between the polymer and the solvent, and is defined as[111]

$$\delta = (U_{coh}/V)^{1/2}. \tag{8}$$

Here $U_{coh} = U_{intra} - (U_{calc} + \Delta U_{tail})$ and V is the volume of the system. U_{intra} is the intramolecular energy of the constructed molecules, U_{calc} is the energy given by the simulation using the potential cut-offs and ΔU_{tail} is the correction for the non-bonded energy caused by the use of cut-offs.

The free volume can be studied by different methods. The Gusev and Suter method[110] calculates the Helmholtz free energy of the penetrant molecule at each point on a uniform grid. Each grid point is then assigned to the nearest local minimum and a graph of the size distribution of unoccupied sites is produced. In the Gusev-Suter method, the interaction energy between the polymer matrix and the penetrant molecules is calculated using a LJ 9-6 potential but the Coulomb interactions are neglected. The other method to study free volume is the Voorintholt method[112], which uses a geometric algorithm to calculate a value describing the distance of a probe molecule at a grid point from the nearest atom. Free volume distribution can also be estimated by constructing Voronoi tessellations. In the Voronoi method[108,113], a Voronoi polyhedron, identifying the available free space, is constructed around a centre atom, and a distribution of polyhedra with various shapes and sizes is generated. Thus, in the Voronoi method only the available free space, without penetrant molecules, is considered.

The pair correlation functions (PCFs) give a distribution of the atoms located at a distance r from the reference atom. They, thus, yield information about packing of the atoms in a cell. Intramolecular PCFs were used to study the structure of the polymers and intermolecular

PCFs to study the packing of the chains. The total PCF gives the sum of the intra- and intermolecular PCFs.

3 Computational details

3.1 Programs used

All the computational results were obtained using a CrayC94 or an SGI Power Challenge computer at CSC (Center for Scientific Computing Ltd., Espoo, Finland). The QM calculations of papers I and II were performed using GAUSSIAN 94/98 (Revisions B.1 and E.2)[52] and the FF calculations using the InsightII 3.0.0 and Discover 4.0.0P of MSI software packages[108]. The RMMC calculations of papers III and IV were performed using the RIS module and the amorphous phase calculations of paper V using the Amorphous Cell - module of the particular MSI software. In addition, an in-house code (written by Pietilä[114]) was used to calculate the distributions of the adjacent dihedral angle pairs of the constructed amorphous structures[V].

3.2 QM and FF studies

The QM methods used in papers I and II were *ab initio* MP2[53] and DFT with non-hybrid B-LYP[57-59] and hybrid B3-LYP[60] functionals. The semi-empirical AM1[61] method was also tested in paper I. The B-LYP and B3-LYP functionals were chosen because they are generally used and well studied functionals.[62,115,116] It has also been found that most molecular properties (such as geometries, conformational energy differences and vibrational frequencies) are not so sensitive to the correlation functional used in the DFT calculations but clearly sensitive to whether a non-hybrid or a hybrid method is used.[62] In paper I the polarised basis set 6-31G(d) and the diffuse basis set 6-31+G(d) were studied. The latter was tested because of the presence of the lone pair electrons on the oxygen atoms. In the 6-31G(d) basis set d-orbitals have been added to non-hydrogen atoms (here to the carbon and oxygen atoms), in addition to which diffuse functions (i.e. large-size versions of s- and p-type functions) are added to the heavy atoms in the 6-31+G(d) basis set. FFs chosen for the calculations were the PCFF and the COMPASS FF.

Constraints are necessary in the re-optimisation of the torsion parameters so that the studied rotation is not affected by the other torsions in a molecular system. To have compatible results for comparisons, the same constraints were used in QM and FF calculations. The neighbouring rotations for the studied rotation were constrained to trans (dihedral angle=180°) conformations. In the methyl groups, except the C13 methyl group in molecule E (see Fig. 3), one of the hydrogen atoms was constrained to the trans conformation with the backbone. In the C13 methyl group the H15 atom was fixed to the trans conformation with respect to the H12 atom. All dihedral angles containing the C=O bonds were constrained to the cis conformation along the backbone and all other C-O and C-C bonds to the trans conformation, when rotating either C-O or C-C bond. These constraints on the C-O and C-C rotations, instead of the real minimum energy conformations were chosen, since the minimum energy conformations in different molecules and/or methods studied may differ from each other.

Potential energy scans were carried out at all the chosen levels of theory by optimising the geometry at each fixed dihedral angle of the rotation under investigation and with the constraints explained above. The minima and maxima of the QM potential energy curves were separately determined and, in situations where difficulties arose with convergence, potential energy scans using smaller steps were carried out to locate the extrema. To find the potential energy minima in the FF studies of papers I and II the steepest-descents method was first used as a minimisation algorithm to locate the low-energy structures. The conjugate gradient method (Polak-Ribiere)[117,108] was then applied near the minima. The final minima were located using a quasi-Newton-Raphson method BFGS (Broyden-Fletcher-Goldfarb-Shanno)[117,108].

3.3 RMMC studies

The polyester chains of papers III and IV were constructed following the RMMC scheme presented in Fig. 4. The chains in paper III were constructed with two different chain lengths, DP=100 or 200, to study the effect of chain length on the results. In paper IV DP=50 or 100 were used to produce about the same number of rotatable backbone bonds as was used in paper III. All polymer chains were divided into electrically neutral charge groups (see Fig. 5), and the Max_Bonds=4, 5 and 6 were studied in paper III. In paper IV, the Max_Bonds=4 and 6 were used due to the different choice of charge groups. For PLLA also the Max_Bonds=9 was tested because of the large deviations between the different experimental results and to study the effect of longer-range interactions on the results. Coulomb potential was included and the dielectric constant was set to 1.0 in all calculations. The temperature was 298 K. The energy minimisation was carried out using a conjugate gradient method (Polak-Ribiere). In the RMMC studies of paper III, the number of equilibration and production steps were 800,000 and 3,000,000 for the 100 repeat-unit chains, and for the longer chains 1,500,000 and 5,000,000, respectively. The equilibration and production steps in the calculations of paper IV were 3,000,000 and 6,000,000. The results were updated every 600th step. All RMMC calculations were carried out using the modified PCFF and in paper IV for DP=100 also with the original PCFF. In this thesis, RMMC calculations using the original PCFF were carried out also for polyesters studied in paper III.

3.4 Amorphous phase studies

The amorphous polymer structures, studied in paper V, were constructed with the Amorphous Cell - procedure shown in Fig. 6. Several cells, which were cubes in this work, were built. For PLLA and PGA ten amorphous cells containing five identical chains with DP=50 were constructed. Since the differences in the final optimised cells of PLLA and PGA were small, only four cells containing five dissimilar chains were built for the copolymers; dissimilar chains were used to obtain sufficiently random structures. In steps 1 and 2a of Fig. 6 the densities of the cells were set to about 90% of the experimental value. In step 2b they were increased to the experimental ones, i.e. for PLAs 1.25 kg/m^3, [118] for PGA 1.50 kg/m^3, [119] and for PGA/PLLA 1.375 kg/m^3 (average of the first two). All constructed structures were fully optimised using a conjugate gradient method (Polak-Ribiere) with 1000 steps and with MD using the velocity Verlet algorithm[120] with 10000 steps. The time step in the MD calculations was 1 fs, and the NVT (constant volume and temperature) ensemble was used. For the relaxation in step 2a the temperature was raised to 500 K, the group-based cut-off value for non-bonded interactions was set to 7 Å, and torsion and non-bonded parameters were scaled by a factor 0.5. In step 2b the respective values were 298 K, 11 Å and 1.0 (non-scaled). Tail corrections were included in the final relaxations. Usually about 5-10 MM/MD cycles were needed to achieve statistically stable systems.

To study the effect of water molecules on the packing of the cells in the amorphous phase of the polyesters studied ten H_2O molecules were included in the final cells. Two cycles with 1000 MM and 15000 MD steps and a final energy minimisation were carried out to optimise the cells with the water molecules.

4 Main results and discussion

In the following the main results of papers I-V are discussed. In section 4.1 the conformational properties related to the studied rotations of the model molecules, calculated by the QM and FF methods in papers I and II, are considered. The reliability of the FF, modified in papers I and II, is investigated in section 4.2.1 by performing single chain property -calculations for the selected polyester chains. In section 4.2.2 the applications of the modified FF are considered.

4.1 Conformational properties of the selected model esters

In paper I, the rotations about the C(sp^2)-O(sp^3) and C(sp^3)-C(sp^2) bonds adjacent to the carbonyl C=O group were studied in esters A and B. In paper II the rotations about the neighbouring C(sp^3)-O(sp^3) and C(sp^3)-C(sp^2) bonds adjacent to the methylene CH_2 group in molecule D or the $CH(CH_3)$ group in molecule E were investigated. The C(sp^3)-O(sp^3) rotation of molecule C was studied as a reference for those in D and E. Molecules D and E represent the structural units of polyglycolic and polylactic acids. The ability of the PCFF, and in paper I also of the COMPASS FF, to reproduce the *ab initio* conformational behaviours of the C-O and C-C rotations in question was evaluated. As general results, both the PCFF and the COMPASS FF computations, especially for the C-C rotations, were in severe disagreement with the QM results. Since the COMPASS FF reproduced the C-O rotations of paper I even worse than the PCFF, the PCFF was chosen for re-optimisation and later for the calculations of papers III-V. Similar disagreements between the QM and PCFF results have been found also for esters with a tartaric unit.[121] The results of the semi-empirical AM1 method for the torsional behaviours presented in paper I were also in disagreement with the results of other more accurate QM methods, and the method was not considered in later studies. In paper I the results obtained with the basis sets 6-31G(d) and 6-31+G(d) were compared, but no significant differences between the results were obtained. Therefore in paper II the 6-31G(d) basis set was automatically chosen for the QM calculations. The Coulomb potential may strongly affect the conformational properties of esters, which are molecules with polar bonds. Therefore the conformational dependence of the ESP derived CHELPG atomic charges are also considered in section 4.1.2.

In the following the relevant QM and PCFF results of the model molecules studied in papers I and II are discussed in more detail.

4.1.1 Torsional behaviour

When a bond rotation is studied, the effects of other bond rotations on the studied one have to be eliminated. Therefore, excluding the rotated one, in papers I and II the bonds are constrained to allow a systematic comparison of the results with each other. The exact constraints are presented in section 3. These constraints are justified, which can be proved with the results of the 2D potential energy maps. The effect of neighbouring bond rotations on each other are shown in Figs. 7 and 8 of paper II for molecules D and E. The C(sp^3)-O(sp^3) and C(sp^3)-C(sp^2) bonds were rotated, while the rotations around the other bonds were kept fixed. The points of fully optimised minima (with no constraints), calculated by the PCFF, MP2 and B3-LYP methods and presented in Table 5 of Paper II, fall into the calculated minimum energy regions. These results are in agreement with the 1D results, and as examples the 1D C(sp^2)-O(sp^3) and C(sp^3)-C(sp^2) rotations of molecule A and the C(sp^3)-O(sp^3) and C(sp^3)-C(sp^2) rotations of molecule E are presented in Fig. 8.

The PCFF was found to give the C-O curves in reasonable agreement with the MP2 and DFT ones. In general, the C-O bonds were not so flexible as the C-C bonds. The C(sp^2)-O(sp^3) rotation of molecule A has a high barrier at about 80° (14.0 kcal/mol by the MP2 method) and a global minimum at 180° with all the selected methods. The C(sp^3)-O(sp^3) rotations of molecules C, D and E, as well, have high (cis) barriers (7.7 kcal/mol, 16.8 kcal/mol and 17.8 kcal/mol, respectively) and a smaller barrier at about 130°. Global minima were calculated to be at about 83°, 74° and –75° (E is not symmetric around the cis conformation), respectively. The C-C curves obtained with the PCFF were in total disagreement with the ones obtained by the QM methods. In fact, the PCFF C-C torsion profiles seem to be reversed in all the studied molecules as compared to the corresponding MP2 or DFT curves. The C(sp^3)-C(sp^2) rotation barriers of the PCFF were also calculated to be much higher than the barriers calculated by the QM methods (see e.g. Fig. 8). Re-optimisation of the torsion potential of the PCFF is, thus, definitely needed to correct the wrong torsional behaviour.

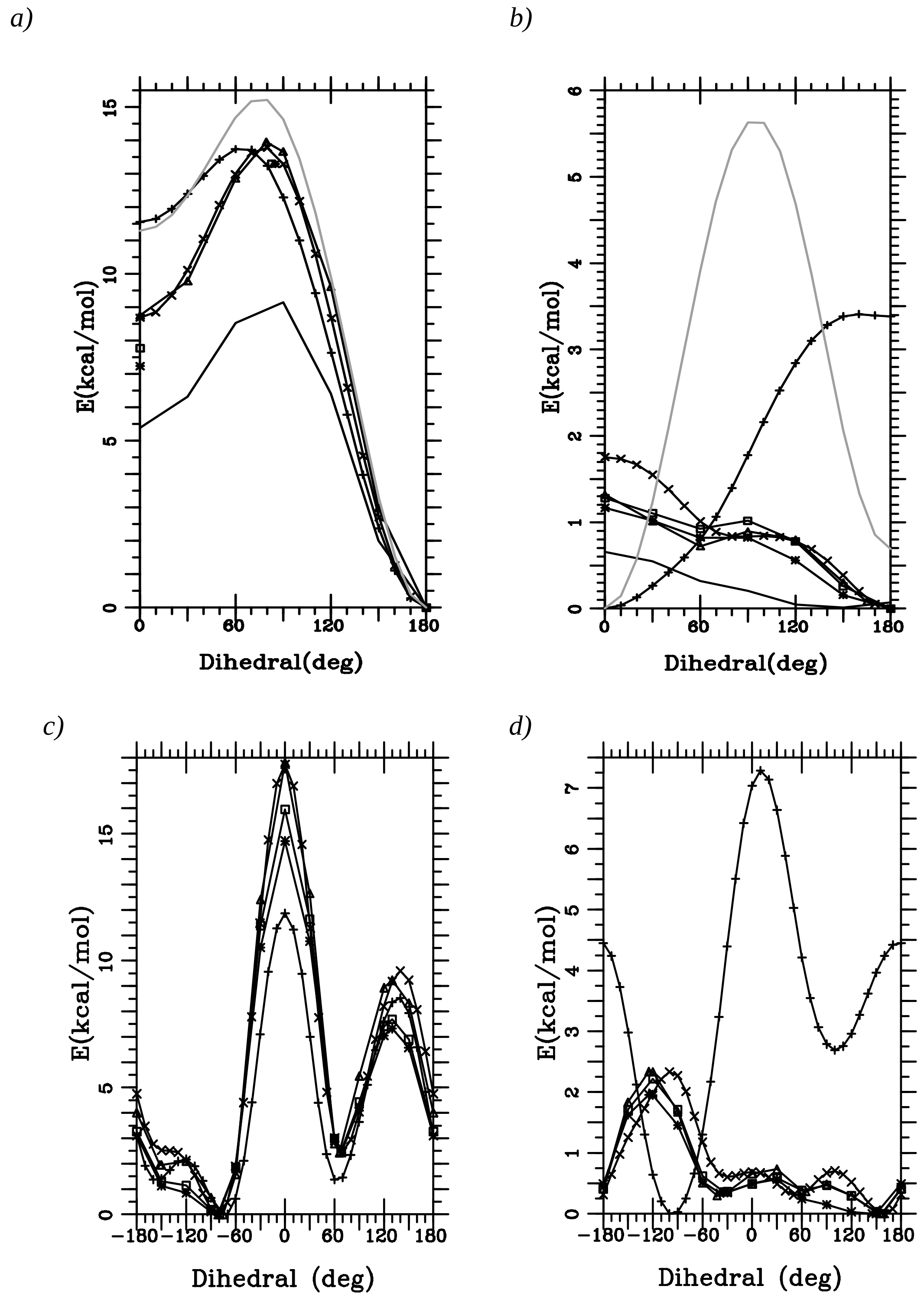

*Fig. 8. a) The C(sp^2)-O(sp^3) and b) C(sp^3)-C(sp^2) rotations of molecule A, and c) the C(sp^3)-O(sp^3) and d) C(sp^3)-C(sp^2) rotations of molecule E. In Fig. Δ: MP2/6-31G(d), *: B-LYP/6-31G(d), : B3-LYP/6-31G(d), +: the original PCFF force field, ×: the modified PCFF force field, black solid line: AM1, and grey solid line: COMPASS.* [I, II]

The torsional behaviours obtained by the *ab initio* (MP2) and DFT (B3-LYP, B-LYP) methods were also compared with each other in papers I and II. The curves were mostly in good agreement with each other. There were, however, some deviations between the MP2 and DFT results such as the cis-trans energy difference in the C-O rotations. The heights of barriers, calculated with the DFT methods, were also systematically smaller in the C(sp^2)-O(sp^3) and C(sp^3)-O(sp^3) rotations than those calculated with MP2 (0.7-1.5 and 0.5-3.1 kcal/mol, respectively). Locations of the energy minima and maxima were, though, close to each other with both methods. The MP2 results were chosen as a reference data, due to the better description of dispersive interactions by MP2 as compared with that of the DFT methods. [122]

The PCFF torsion parameters (V_1, V_2 and V_3 in eq. (8)) relevant to the studied rotations were re-optimised to reproduce the MP2 torsional behaviour. The non-bonded potential and the valence FF in the PCFF were not re-optimised. Thus, the O6=C3-O4-C5 dihedral angle for the C(sp^2)-O(sp^3) rotation and the C1-C2-C3=O6, C1-C2-C3-O4, H-C2-C3-O4 and H-C2-C3=O6 dihedral angles for the C(sp^3)-C(sp^2) rotation were optimised in paper I (see Fig. 3.). For all the other dihedral angles belonging to the particular C-O and C-C rotations the PCFF torsion parameters were not changed in order to retain the transferability between the parameters of molecules with corresponding functional groups. The re-optimised FF obtained in paper I was used as a starting point for the similar optimisation in paper II in which the C1-O2-C3-C4, C1-O2-C3-C13 and C1-O2-C3-H dihedral angles for the C(sp^3)-O(sp^3) rotation, and the O2-C3-C4-O5, O2-C3-C4=O14 and C13-C3-C4-O5 dihedral angles for the C(sp^3)-C(sp^2) rotation were optimised for molecules D and E. The original and the re-optimised results are presented in Table 8 of paper I and Table 4 of paper II.

The torsional behaviours obtained by the modified PCFF for the molecules A and E are also given in Fig. 8. The modified PCFF now reproduces the MP2 torsional behaviours of the studied rotations, though some minor differences can be seen. Further improvement would require re-optimisation of the non-bonded potential. This was not done, as already mentioned, due to the strong correlation of the non-bonded parameters with the other parameters of the FF. Since the differences are small, the present accuracy of the FF is sufficient for a reliable generation of chain conformations and further computation of polymer properties for polyesters containing the studied structural units.

4.1.2 Coulomb interactions

Electrostatic interactions in the PCFF and the COMPASS FF are represented as a Coulomb potential, i.e. as interactions between fixed point charges. An average set of charges is usually optimised for all conformations, assuming that the variation of charges due to changes in conformation is small. However, this assumption may not be valid for molecules with polar groups. Thus, in papers I and II ESP derived atomic charges were calculated for different conformations of the model molecules using the CHELPG method, as implemented in GAUSSIAN 94/98. It was found that the most significant atomic charges of the model esters as regards the ESP, depended only slightly on conformation (detailed results are in Tables 5-7 of paper I and in the supplementary material (Tables A-E) of paper II). The atomic charges of the less polar alkyl groups, however, were more sensitive to changes in conformation, especially during the C(sp^2)-O(sp^3) rotation. In total, the conformational changes in atomic charges were less than 0.2e. A large part of this effect on the conformational statistics is accounted for by the torsion parameters in the fitting procedure. Thus, the approximation of conformationally independent partial charges in the FF of the esters studied should be valid, as the polar carboxyl groups dominate the ESP. This is not always the case, and for example in esters with tartaric units also eletrically significant charges experience larger conformational changes.[121] As regards the performance of the different computational methods used, the absolute values of the most significant atomic charges at the global minima are about the same using the MP2 and B3-LYP levels of theory, whereas B-LYP usually gives smaller absolute values. The conformational dependence is however similar in all these methods. The conformationally independent PCFF charges, with a few exceptions, also are rather close to the QM atomic charges (see papers I and II).

The relative root-mean-square (rrms) deviations of the ESP charge fits at the different minima of model molecules were rather satisfactory. They were slightly better for the C-O rotations (9.0-16.6%) than for the C-C rotations (15.1-17.4%). The absolute root-mean-square (rms) deviations were in volts 0.04-0.07 for the C-O and 0.05-0.07 for the C-C rotations. The MP2 molecular dipole moments for the different minima were 1.5-4.3 D (Debye) for molecule A, 1.6-1.7 D for B, 1.6-1.9 D for C, 2.0-2.6 D for D and 2.2-2.6 D for E. The deviation between the dipole moments calculated using the optimised atomic CHELPG charges for each conformer and those calculated as expectation values of the dipole moment operator was 0.002-0.050 D at the MP2 level. Since also the changes in the ESP derived atomic charges due to conformation changes in the different rotations were small for electrically significant charges, a set of average values for the charge parameters should be appropriate to describe Coulombic interactions in a FF model in this case.

4.2 Properties of the polyesters studied

4.2.1 Reliability of the modified PCFF

The RMMC method is especially sensitive to the FF and cut-off for non-bonded interactions. Thus, the reliability of the PCFF, modified in papers I and II, was studied in paper III by performing single chain property calculations with the RMMC method for such polyesters for which there exists reliable experimental data. The effect of the choice of run parameters in the RMMC procedure, mainly the cut-off limit for non-bonded interactions and the chain length, on the results was also studied in more detail in paper III. The characteristic ratios, persistence lengths and ratios of mean squared end-to-end distance to the mean squared radii of gyration were calculated for a few side group polyesters, such as poly(methyl acrylate) (PMA), poly(methyl metacrylate) (PMMA) and poly(vinyl acetate) (PVA), as well as for a set of aliphatic main chain polyesters (see Fig. 3). For details about the calculations see section 3.3.

The ratios of mean squared end-to-end distance to the mean squared radii of gyration were close to the ideal value of 6 in all studied polyester chains. The calculated persistence lengths were much shorter than the contour lengths for each chain indicating the sufficiency of the selected chain lengths for reliable RMMC calculations. They were also found to follow the behaviour of the calculated characteristic ratios as a function of run parameters. Therefore, in the following only the characteristic ratios, which give the best measure for chain flexibility in the case of flexible polymer chains, are considered.

Some relevant results of paper III are presented in Table 1. There were no major differences between the results obtained with different chain lengths in the main chain polyesters, and a chain length of 100 repeat units was therefore considered to be large enough. The Max_Bonds value 4 was also found to be sufficient for main chain polyesters. The chain length of 200 repeat units was more recommendable for the side group polyesters and also a larger Max_Bonds value (5) was needed to properly account for the interactions between the bulky side groups.

Table 1. Characteristic ratios for the main chain and side group polyesters studied in paper III. The characteristic ratios calculated using the original PCFF are given in parentheses. (at=atactic, it=isotactic, st=syndiotactic) (See paper III for references.)

DP	**100**			**200**			
Max_Bonds	**4**	**5**	**6**	**4**	**5**	**exp.**	**QSPR**
Main chain polyesters							
EC6	5.89 ± 0.06 (5.05 ± 0.06)	8.70 ± 0.09	8.53 ± 0.09	6.03 ± 0.07	-	5.9	6.01
EC10	6.35 ± 0.06 (6.17 ± 0.06)	8.66 ± 0.09	8.27 ± 0.08	6.51 ± 0.07	-	5.1	6.54
EC2E'C6	5.50 ± 0.06 (2.69 ± 0.03)	9.54 ± 0.11	9.97 ± 0.12	5.67 ± 0.07	-	5.25	5.49
EC8E'C6	5.90 ± 0.06 (4.98 ± 0.05)	8.77 ± 0.09	8.31 ± 0.08	5.78 ± 0.07	-	5.8	6.18
EC8E'C16	6.42 ± 0.06 (6.33 ± 0.06)	9.01 ± 0.09	8.26 ± 0.08	6.60 ± 0.07	-	6.5	6.7
Side group polyesters							
PMA-at	7.59 ± 0.13	11.93 ± 0.19	-	7.78 ± 0.19	9.39 ± 0.23	8.4 - 9.4	-
PMMA-it	3.65 ± 0.09	8.77 ± 0.21	-	5.65 ± 0.18	11.67 ± 0.37 (11.04 ± 0.20)	9.4 - 10.8	-
PMMA-at	5.96 ± 0.14	8.66 ± 0.20	-	5.11 ± 0.16	8.64 ± 0.28 (9.03 ± 0.15)	6.05 - 9.0	-
PMMA-st	10.12 ± 0.22	10.22 ± 0.22	-	10.15 ± 0.27	10.07 ± 0.32 (6.62 ± 0.13)	7.3 - 9.8	-
PVA-at	6.15 ± 0.10	10.73 ± 0.17	-	6.19 ± 0.14	9.51 ± 0.22	9.0 -11.3	-

In Table 1 are also given the characteristic ratios calculated using the original PCFF for main chain polyesters with DP=100 and Max_Bonds=4 and for PMMAs with DP=200 and Max_Bonds=5. The characteristic ratios of PMMA as a function of chain tacticity are presented also in Fig. 9, calculated using the original and modified PCFFs with DP=200 and Max_Bonds=5.

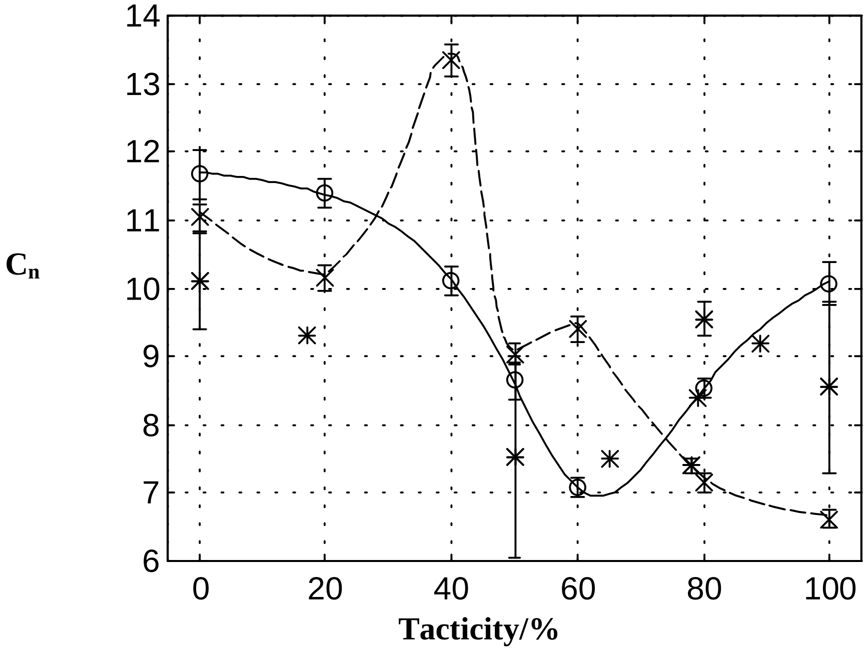

Fig. 10. The characteristic ratio C_n of ***PMMA*** *as a function of chain tacticity (in % of racemic dyads). The C_n calculated using the original and modified PCFFs (Max_Bonds=5 and DP=200) and the experimentally determined C_n (see Paper III for details) are expressed by* ×, ***O*** *and* *****, *respectively.*

The characteristic ratios of the main chain polyesters using the original PCFF differ much more from the experimental values than the ones obtained using the modified PCFF. For EC10 both calculated results differ from the experimental value. The fact that the experimental and calculated results are otherwise very compatible indicates that the experimentally determined characteristic ratio for EC10 may be inaccurate. The QSPR (Quantitative Structure Property Relationship) method, which is based on topological indices[111], gave similar results compared with the RMMC ones, also for EC10. As regards the side group polyesters, the RMMC results with the modified PCFF for PMMA agree with the experimental values which, however, partly deviate rather much from each other.[123,124] The respective calculations performed with the original PCFF give results that deviate much more from the experimental values, especially for tacticities of 40, 60 and 100%. This is as expected since the original PCFF could not produce the conformational states of the chains correctly, whereas the modified PCFF does, due to the re-parameterisation. The modified PCFF is, thus, able to give reliable results for polyesters with the structural units studied.

In RMMC calculations the bond lengths and valence angles are constrained to the values of a reasonable energy conformation, which is one without large repulsions. However, changes in conformation may significantly affect geometries especially in molecules with polar bonds. Therefore the conformational dependence of these co-ordinates was studied in papers I and II using the MP2, B-LYP and B3-LYP methods. There were no significant differences between the results of the different methods. It was found that in the model esters the conformational dependence of the bond lengths was small, the largest changes being 0.01-0.02 Å. Especially in the C-O rotations, conformational changes in the valence angles were large, up to 18°. These changes, however, occurred in high-energy and thus low-population conformations. The effect of the conformational changes of the valence angles on the RMMC results was thus in practice small. Errors in the RMMC results caused by small conformational changes in valence co-ordinates can be reduced by randomising the chain conformation prior to the energy minimisation of the chain, which is then used for the actual RMMC calculation.

4.2.2 Applications of the modified PCFF

4.2.2.1 Flexibility of the PLA and PGA chains

In paper III the RMMC method using the modified PCFF and with a correct choice of run parameters was found to be a reliable method for computing single chain properties also for polymer chains with side groups that are allowed to rotate. In paper IV the same approach was used for the RMMC studies on chain flexibility of selected biodegradable polyesters with strongly interacting polar carboxyl groups. The polyesters studied were poly(L-lactic) (PLLA), poly(L,D-lactic) (PLLA/PDLA) and polyglycolic (PGA) acids (Fig. 3). Because the exact chain configuration in the experimental studies of the copolymer of L-lactide and D-lactide units was not known,[125] calculations were carried out for a copolymer with alternating L-lactide and D-lactide units (alternating PLLA/PDLA) and for a copolymer with random combinations of L,D- and D,L-dyads (random PLLA/PDLA). Corresponding calculations were carried out also for a random combination of G,L- and L,G-dyads (random PGA/PLLA). For details about the calculations see section 3.3.

In general, the results for the characteristic ratios did not depend significantly on the chain length. The differences between the results with DP of 50 and 100 were small, though the results of DP of 100 were slightly closer to the available experimental values (only for PLLA and PLLA/PDLA). The chain length of 50 repeat units was thus considered large enough for all the studied polyester chains. The calculated characteristic ratios with DP=100 and Max_Bonds=4 or 6 are compared with the experimental values in Table 2. Details about the experimental results are given in Paper IV.

Table 2. The characteristic ratios of PLAs, PGA and PGA/PLLA with DP=100 and Max_Bonds=4 (6 in parentheses) using virtual bonds (See paper IV for references and details about the experimental values).

Polyester chain	Original PCFF	Modified PCFF	Exp.
PLLA	5.62 ± 0.13 (3.69 ± 0.05)	7.68 ± 0.16 (10.01 ± 0.21)	7.2, 2.0, 11.7
PLLA/PDLA (alternating)	7.98 ± 0.18 (9.22 ± 0.21)	6.49 ± 0.14 (6.64 ± 0.14)	4.0
PLLA/PDLA (random)	8.53 ± 0.20 (9.31 ± 0.22)	6.84 ± 0.15 (6.97 ± 0.15)	4.0
PGA	5.98 ± 0.12 (5.49 ± 0.11)	7.53 ± 0.13 (6.84 ± 0.12)	-
PGA/PLLA (random)	6.30 ± 0.13 (5.72 ± 0.12)	7.03 ± 0.14 (7.16 ± 0.14)	-

The characteristic ratios are given using virtual bonds (see section 2.3) determined from the generated polymer chains in the RMMC calculations. The virtual bonds are average values of all corresponding bonds in the chains, and are between 3.73-3.78 Å (see paper IV for details).

In general, the characteristic ratios increased as a function of the Max_Bonds value, except for the characteristic ratio of PGA. In the case of the PLLA chains, the characteristic ratio was strongly dependent on the Max_Bonds value, and the chain became less flexible, when the Max_Bonds value was increased from 4 to 6 (the characteristic ratio increased by 29-30%). The corresponding values obtained with the original PCFF showed a reverse trend (the characteristic ratio decreased by 34%). With the cut-off value of 9, the characteristic ratio of PLLA was clearly larger than with smaller cut-offs.

The experimental results, available for PLLA and PLLA/PDLA, vary a lot (see Table 2). Therefore, suggestions concerning recommendable cut-off values for the kind of polyesters studied, based on comparison of the experimental and calculated characteristic ratios, are difficult to make. More accurate measurements in the Θ-state would be needed for a better determination of this relation. However, the Max_Bonds value of 4, which was suggested also in paper III for main chain polyesters, gave also here results closest to the most reliable experimental results, i.e. 7.2 for PLLA and 4.0 for PLLA/PDLA. Thus, according to the

RMMC calculations of Papers III and IV, using the modified PCFF, it seems that for polyesters with small side groups the Max_Bonds value of 4 would be appropriate. On the other hand, for polyesters with larger side groups the value should be larger.

Due to its definition, a smaller characteristic ratio corresponds to a more flexible polymer chain. Based on the calculated characteristic ratios with the modified PCFF (DP=100 and Max_Bonds=4) the flexibility of the polyester chains studied is predicted to increase in the following order: PLLA, PGA, PGA/PLLA (random) and PLLA/PDLA (random, alternating). The differences between the characteristic ratios, however, are not large. The original PCFF predicted the flexibility to increase as follows: PLLA/PDLA (random, alternating), PGA/PLLA (random), PGA and PLLA, in contradiction with the results obtained with the modified PCFF. The differences between the characteristic ratios using the original PCFF are also larger than those obtained with the modified PCFF. The order in flexibility for PLLA and PGA calculated using the modified PCFF also agrees with the potential energy maps presented in Paper II, and with the results of other studies.[118,126]

The tacticity is known to affect on flexibility of the polyester chains. Thus, the effect of tacticity on the characteristic ratio was studied in PMMA, and the results are shown in Fig. 9. The characteristic ratio varies between the values 7.1 (for 60 % of racemic dyads) and 11.7 (for 0 % of racemic dyads). The various lengths of the alkyl chains between the carboxyl groups in the main chain polyesters, studied in paper III, were found to have practically no effect on the flexibility. The characteristic ratios of polyesters with isolated carboxyl groups were calculated to be 5.5-6.4 (with real bonds and the modified PCFF, Max_Bonds=4 and DP=100). The characteristic ratios for polyesters with non-isolated carboxyl groups (with real bonds and the modified PCFF, Max_Bonds=4 and DP=50) were close to these values, 6.1 for PLLA, 5.7 for PGA, 5.3 for PGA/PLLA and 4.6-5.1 for PLLA/PDLA. The flexibility of the polyester chains studied seems, thus, to be practically independent of the chemical environment of the carboxyl groups. It should be noted, however, that the large conformational changes in the valence co-ordinates are not explicitly taken into account and may have some effect on the calculated characteristic ratios.

4.2.2.2 Amorphous state properties

The amorphous state properties of PLLA, PLLA/PDLA, PGA and PGA/PLLA were studied in Paper V. The reason for these studies was that hydrolysis, as a first step of the biodegradation, first takes place in the amorphous phase of the polymer[48,49]: The polymer chains are broken by a random hydrolytic scission into shorter chains. After that a rapid metabolisation occurs, first in the non-ordered structures (the amorphous phase), and then in the more ordered structures (the crystalline phase), while the resistant material (highly ordered structures) remains unchanged. The final metabolisation depends on the temperature and other external conditions. Hydrolysis is, therefore, directly related to the biodegradability of the polymers, and the probability for hydrolysis gives estimates for the biodegradation probability, though no information is obtained concerning the dynamics of biodegradation. Amorphous Cell -models were therefore constructed to study the probability of these polyesters to hydrolyse. The properties of interest concerning the hydrolysability are the solubility parameters, the free volume and the pair correlation functions (PCFs). The ability of the polyesters in question to form hydrogen bonds with water molecules was studied by including water in the cells. For details about the calculations see section 3.4.

The x-ray scattering curves, calculated for PLLA, PLLA/PDLA and PGA to estimate how realistic the constructed models are, came out in agreement with the experimental curves (see Fig. 2 in paper V). The distributions of the adjacent dihedral angle pairs also give information about the reliability of the constructed structures. In Fig. 10 the adjacent $C(sp^3)$-$O(sp^3)$ and $C(sp^3)$-$C(sp^2)$ rotations are shown as an example for one cell of PLLA, PLLA/PDLAs and PGA.

The calculated distributions of the dihedral angle pairs of PLLA/PDLAs resemble more the distribution of PGA than that of PLLA. This is due to the fact that PLLA/PDLA consists of an alternating sequence of D- and L-lactide units, i.e. is syndiotactic with respect to the methyl group, while PLLA is regular consisting only of L-lactide units, i.e. is isotactic. The points of the dihedral angle pairs in Fig. 10 fall into the minimum energy regions of the 2D potential energy maps presented in Figs. 7 and 8 of Paper II for the model molecules of PGA and PLLA. The constructed models were, thus, accepted for further calculations.

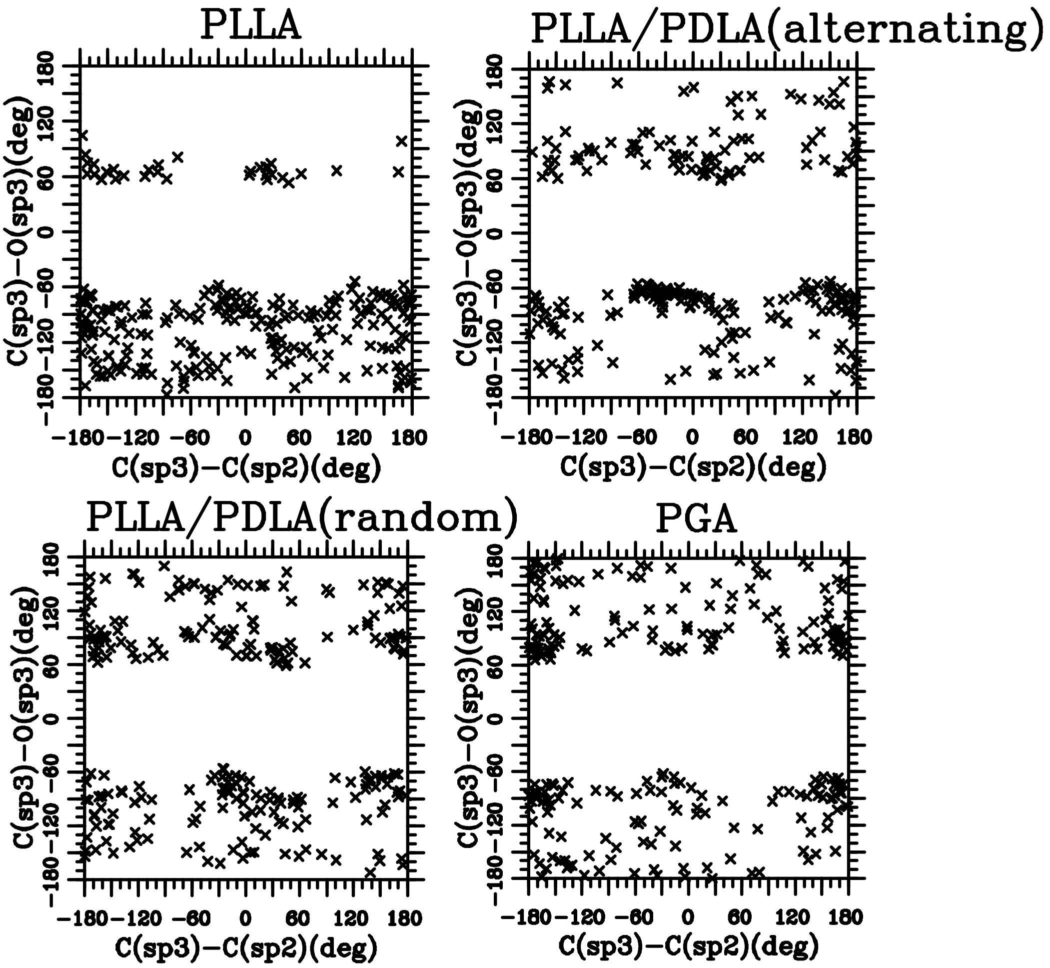

Fig. 10. The distributions of the adjacent dihedral pairs (C(sp^3)-O(sp^3) and C(sp^3)-C(sp^2) rotations) as an example for one cell of PLLA, PLLA/PDLAs and PGA.

Some of the main results and features of PLLA, PLLA/PDLA, PGA and PGA/PLLA regarding the hydrolysability of these polyesters are presented in Table 3.

Table 3. Some of the main results of PLLA, PLLA/PDLA, PGA and PGA/PLLA regarding hydrolysability in the amorphous state.

	PLLA	**PLLA/PDLA (alternating)**	**PLLA/PDLA (random)**	**PGA**	**PGA/PLLA (random)**
Solubility parameter (J/cm^3)^{½}	22.0	23.2	23.4	34.0	26.6
Free volume (Voronoi) (in 8.5-25.0 $Å^3$)					
• **% of the total free volume**	68.5	67.9	68.3	68.1	68.3
• **absolute amount ($Å^3$)**	5.65	5.23	5.34	4.45	5.30
PCF, hydrogen bonds (separation (Å), Intensity)	(1.95, 5.76)	(1.85, 7.79)	(1.85, 7.79)	(1.85, 3.95)	(1.85, 5.50)

As regards the solubility parameters, the most easily hydrolysable polyester is the one, which has its solubility parameter closest to that of water (about 40 $(J/cm^3)^{½}$). The degree of crystallinity should be low, since the non-ordered structures are known to hydrolyse and biodegrade more easily than the ordered part of the polymer. If enzymes take part in the biodegradation process, the polymer chains must also be flexible enough to fit into the active site of the enzyme. The solubility parameter of PGA (34.0 $(J/cm^3)^{½}$) was calculated closest to that of water. The respective parameters for the other polyesters were somewhat smaller but close to each other (from 22.0 of PLLA to 26.6 of PGA/PLLA). The reason for the better solubility of PGA is the larger amount of hydrophilic groups in PGA than in the PLAs.

The free volume calculations, which tell about the packing of the polymer, were carried out using the Voorintholt method[112] instead of the Gusev-Suter method.[110] The Voorintholt method was chosen, since the Gusev-Suter method was found not to be valid due to its approximations in some cases.[127] The free volume distributions were also estimated utilising Voronoi tessellations. The free volume is given for the PLAs, PGA and PGA/PLLA using the Voorintholt method in Fig. 11. The maximum radius of the probe molecule, in the case of water molecules as penetrants, was set to 1.0 Å. The size of the water molecule was taken to be smaller than the average dimension in different directions to take into account the flexibility of the penetrant molecule.

According to the Voorintholt free volume results the packing of the studied amorphous materials was somewhat different. All PLAs and PGA/PLLA had lots of small free sites, while PGA was the most tightly packed one. In the distributions of the Voronoi tessellations the free volumes with various shapes and sizes are taken into account, but the actual penetrant molecules are not considered. The Voronoi tessellations revealed that the packing of the studied polyesters was very similar, though PGA had less free volume as compared to the other polyesters. The largest fraction of polyhedra (Fig. 4 of Paper V) has sizes of 8.5-25.0 $Å^3$, which corresponds to the space in which water molecules fit well. About the same relative amount of the available free space of the PLAs, PGA and PGA/PLLA occurs in that particular region (about 68%, see Table 5), but the absolute amount is slightly smaller for PGA.

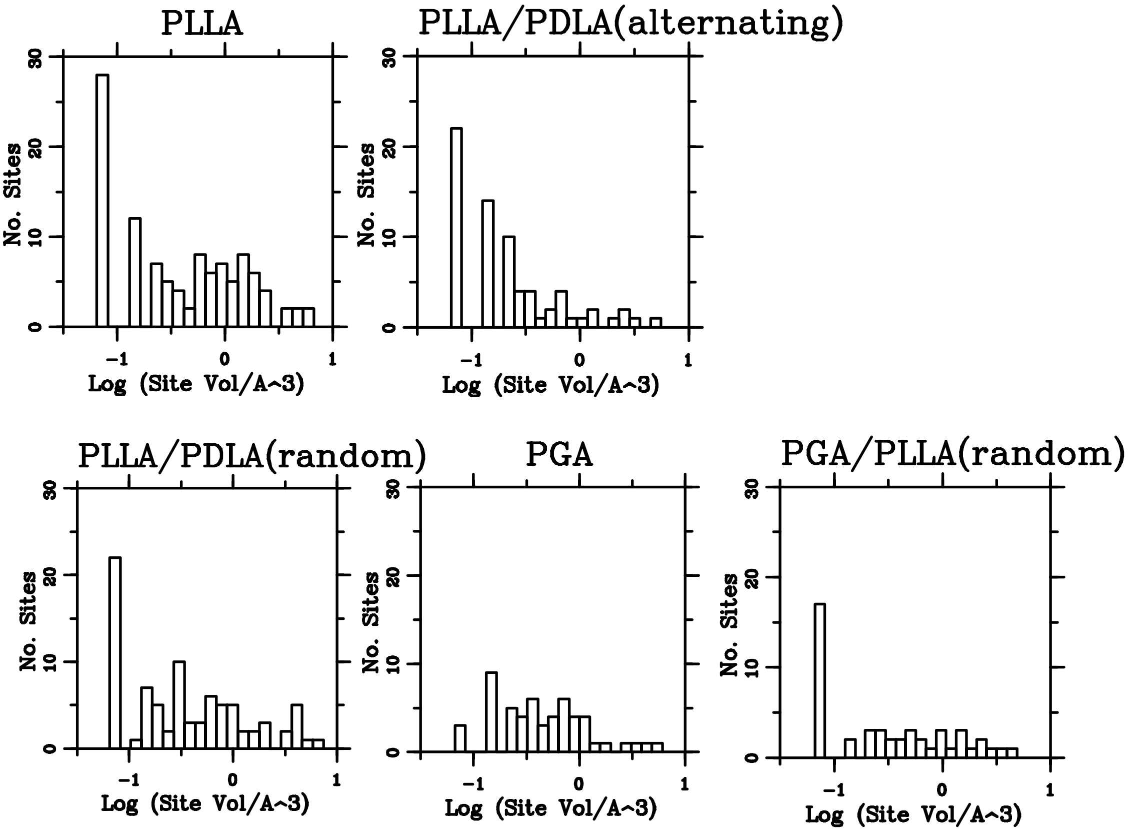

Fig.11. The free volume of the PLAs, PGA and PGA/PLLA using the Voorintholt method. [V]

According to the calculated PCFs (Paper V), there were no significant differences between the packing of the amorphous structures in the studied polyesters, at least before the water molecules enter the amorphous structures. The PCFs with water molecules in the cells, instead, revealed that there were slightly less hydrogen bonds formed between the hydrogen atoms of water and the carbonyl oxygen atoms in PGA than in the other polyesters (see Table 3). This can be due to the effect of hydrophobic methyl groups in PLAs that force the water molecules close to the carbonyl groups.

These studies show that the most significant differences between the amorphous state properties of the polyesters in question occur in the solubility parameter and in the PCFs when water molecules are included in the cells. Thus, the ratio of the amounts of hydrophilic and hydrophobic groups of the chains seems to be an important factor affecting the hydrolysis and, hence, biodegradability. Other factors that are significant for biodegradability are the degree of crystallinity of the polymeric material and the flexibility of the chains. The copolymers are usually introduced in biodegradable applications due to their more amorphous nature compared to the respective homopolymers. The degree of crystallinity of PLLA is typically about 40 % and that of PGA about 50%. The flexibilities of these polyesters according to our studies are close to each other, though the copolymers and PGA are calculated to be more flexible than PLLA.

5 Conclusions

In this study, the performance of the PCFF regarding the torsional behaviour of different type of bonds in selected polyesters was improved by re-optimising some of the torsion parameters. The ab initio (MP2) and DFT (B-LYP and B3-LYP) torsional behaviours were found to be close to each other, and both methods could thus be used in the (re-) parameterisation of the torsional potential. However, the MP2 method was chosen as a reference method due to its better description of dispersive interactions.[121] The MP2 and original PCFF C-O torsional behaviours were in reasonable agreement with each other, but the C-C curves were in total disagreement. These disagreements between the MP2 and PCFF torsional behaviours could here be reduced by re-parameterisation of the torsional potential. Further improvements of the torsion potentials would require a re-optimisation of the non-bonded potential, which cannot be performed without re-optimisation of the whole FF, due to strong correlations with the other terms of the FF. The quality of the non-bonded potential should be improved in the future, however, for better estimation of polymer properties, such as solubility parameters or other properties that depend on molecular packing.

The RMMC method was used in single chain property calculations on selected main chain and side group polyesters to test the reliability of the modified PCFF and to study the performance of the RMMC method with different choices of run parameters. The results obtained with the modified PCFF agreed well with the experimental ones. For main chain polyesters the combination of DP=100 and Max_Bonds=4 as a cut-off for non-bonded interactions was found to best reproduce the experimental values. For the side group polyesters, DP=200 and Max_Bonds=5 were more favourable.

In studies on the flexibility of biodegradable PLAs, PGA and PGA/PLLA, the RMMC results were found to be extremely sensitive to the selected FF model. Re-optimisation of the pertinent torsion potentials, to avoid incorrect conformational statistics of the polymer chains, was shown to be absolutely necessary for a realistic prediction of the chain flexibility with the RMMC method. The amorphous state properties of PLAs, PGA and PGA/PLLA were studied by the Amorphous Cell -method. The probability of hydrolysis was estimated by calculating solubility parameters, free volumes and PCFs (with and without water molecules in the cells). The most significant differences in the properties of the amorphous models studied were found in the solubility parameters and in the PCFs when water molecules were included in the cells. The ratio of the amount of hydrophilic/hydrophobic groups was found to be an important factor affecting the hydrolysability and, thus, the biodegradability. Also the degree of crystallinity in the amorphous material is known to affect the hydrolysability, since the biodegradation starts in the amorphous state. Therefore, the more amorphous copolymers are preferred over the respective homopolymers in biodegradable applications. Flexibility of the polymer chain also makes biodegradation easier, and of the polyesters studied the copolymers and PGA were found to be the most flexible ones with almost equal flexibility. Thus, according to this study the ratio of the amounts of hydrophilic/hydrophobic groups and the flexibility of the chains affect the biodegradability of these polyesters.

For the polyesters studied in this thesis, the re-optimisation of the torsion parameters of the PCFF to correct the wrong conformational statistics led to very successful results as regards the conformation-dependent properties. However, a mere re-optimisation of the torsional potential may not necessarily be a sufficient correction for all polymers, when the conformational statistics is not reproduced well. Better FF models are needed, and, for example, the non-bonded potential has also a large impact on the conformational properties especially, when the system studied contains strong steric or electrostatic interactions.

Acknowledgements

This thesis is based on research carried out at the Accelerator Laboratory of the Department of Physics, University of Helsinki, during the years 1997-2001. I wish to thank the head of the Department, Professor Juhani Keinonen, for the opportunity to work there.

I want to express my deep gratitude to my supervisor Dr. Berit Mannfors for guiding my studies. Her encouragement, valuable comments and interest in my work during these years of my studies have been invaluable. I also want to thank Dr. Lars-Olof Pietilä for advising me, especially during these years Berit has worked at the University of Michigan. I am very grateful to him for numerous useful discussions. I wish to thank Professor Dan Olof Riska for all his valuable advice and help. I am grateful to Professor Franciska Sundholm and Dr. Niklas Meinander for their valuable comments and inspiring discussions. I wish to thank all my colleagues and co-workers for pleasant collaboration. Especially, I wish to thank M.Sc. Virpi Korpelainen, my closest co-worker, for valuable discussions. I also want to express my gratitude to Dr. Kim Palmö from the University of Michigan for his help and interest in my work. Thanks are also due to Professor Folke Stenman, Professor Keijo Kajantie and Dr. Tom Sundius for their kind interest in my work.

I thank the CSC (Center for Scientific Computing) and the Physics Computing Unit for computational resources. Thanks are especially due to Dr. Kimmo Mattila, Dr. Tuija Raaska and Dr. Maija Lahtela-Kakkonen from CSC, as well as the personnel of the Physics Computing Unit, for their help in technical problems during my calculations.

I want to thank my parents, Sinikka and Tapio Seppä, for encouraging me to study physics and for all the support they have given me. I also want to thank my sister, my grandparents, my parents-in-law and all my other relatives and friends who have supported me in so many ways during the writing of this thesis.

My dearest thanks are reserved for my husband Anssi for his love, support and understanding. I am very grateful to Anssi for all his help.

Financial support from the Neste Foundation and the Magnus Ehrnrooth Foundation is gratefully acknowledged.

Helsinki, February 2001
Johanna Blomqvist

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