

*“Wer nicht in Lachen ausbricht,
wenn er auf seine blossen Füße hinunterschaut,
der hat entweder keinen Sinn für Humor
oder keinen Sinn für Symmetrie.”*

R. Descartes (Mathematiker und Philosoph, 1596-1650)

Chapter 1

Introduction

1.1 Homochirality in Nature

All living beings from the human being to the paramecium, from the tree to the microbe are based on proteins and genes. Both, proteins and genes, consist of structural elements with spatial asymmetric conformations. In proteins the so-called α -helix is a dominant structural element, while the DNA (Desoxyribonucleinacid) - the substance carrying the genetic information - forms a double helix. The reason for these helical structures is the asymmetry of the elements of which these macro molecules are constructed, see figure 1.1. Proteins are composed of amino acids that exist in nature only in the so-called left-handed L-form (from Latin *laevus* = left). The backbone of the DNA double helix consists exclusively of a right-handed monosaccharide, the D-form (from Latin *dexter* = right) of desoxyribose. The left- and right-handed form (D- and L-Form) of a molecule are, as our left and right hand, mirror images of each other, yet they are not identical. These molecules possess the so-called handedness or, as Lord Kelvin introduced in 1884 [1], *chirality* (from Greek $\chi\epsilon\acute{\iota}\rho$ = hand). Left- and right-handed forms of a chiral molecule form a pair of so-called *enantiomers*. Enantiomers may experimentally be differentiated by their ability to rotate the polarization vector of light. They rotate the vector by the same rotational angle but in opposite directions. This behaviour, called *optical activity*, was discovered in 1815 by Biot when he shined linear polarized light through a water solution of sugar. The molecular structural source of chirality was found in 1874 independently by Van't Hoff and le Bel [2]. Especially, Van't Hoff's idea [3] that four different substituents of a carbon atom forming a tetrahedron could be arranged such that two different spatial forms of identical constructed molecules are formed – which behave like mirror images of

each other – can be considered to be the basis of the *stereochemistry* [4]. In 1954, Prelog *et. al.* introduced a general nomenclature for stereoisomers [5, 6]. For his research in the field of the stereochemistry of organic molecules and reactions Prelog was awarded the Nobel Prize in Chemistry in 1975 [7].

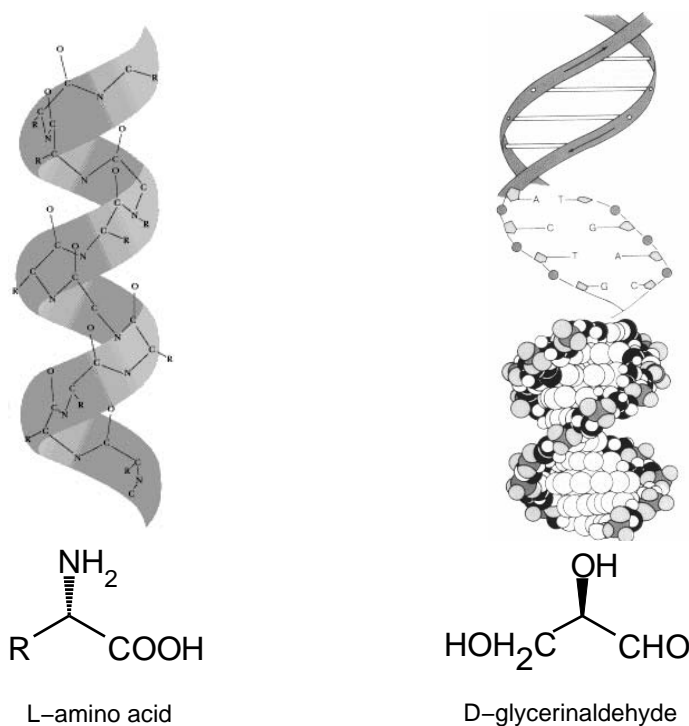


Figure 1.1: Homochirality of life: The α -helix of a protein (left) and the double-helix of DNA (right) are constructed exclusively of *L*-amino acids and *D*-monosaccharides (here the simplest one, *D*-glyceraldehyde, is shown), respectively.

The biomolecular homochirality in nature, i.e. the preference for *L*-amino acids and *D*-monosaccharides in all living beings, has been of decisive importance for the evolution of life on earth three and a half billion years ago [8]. Although there exists many theories for the origin of biomolecular homochirality on earth, e.g. meteorites as extraterrestrial source of homochiral biomolecules [9], it is indisputable that chirality is a critical factor for the functionality of life. All living organisms produce normally only one enantiomer of a certain organic compound. The reason is the chirality of the enzymes that are responsible for the production. These enzymes functioning as receptors are, in turn, capable to differentiate between both enantiomeric forms of a physiological active substance, known

as the “key and lock” principle proposed by Fischer [10].¹ Thus, the spatial conformation of a single functional group may have a drastic effect on the mode of functioning of a chemical compound.

An example of the drastic physiological effect due to the “wrong” handedness of a chemical group is the sedative and barbiturate Thalidomid (trade name Contergan) that was put on the market by the company Grünthal, Aachen, in 1956. Thalidomid resulted in malformation of extremities or death in cases of more than 10 000 infants [11]. While the (R)-enantiomer of the molecule had the desired sedative effect the (S)-form caused the mentioned results on foeti.² The teratogenic effect of (S)-Thalidomid was realized too late. Contergan consisted of a 1:1 mixture of both enantiomers, a so-called *racemate*, of the substance Thalidomid (Figure 1.2).³

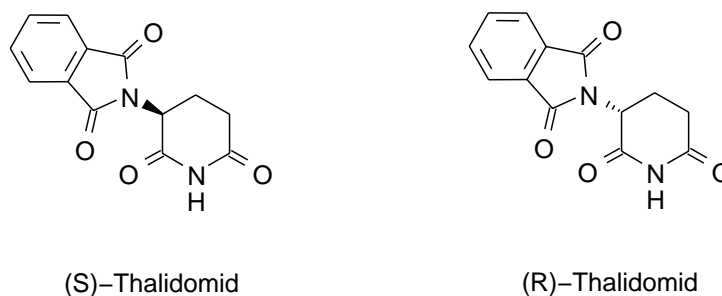


Figure 1.2: Enantiomeric forms of the active agent Thalidomid in Contergan

Contergan is just one example of many chiral molecules whose enantiomers have different biochemical properties. Especially for drugs, but also for insecticides, fungicides, herbicides, food additives or simply for odorous substances it is of great importance to produce pure enantiomeric chemicals. However, the chemical synthesis of pure enantiomeric substances is difficult. Starting from achiral educts only a 1:1 mixture of both chiral forms, a racemate, is produced. In 1848 Louis Pasteur managed to separate mechanically a racemic mixture of tartrate crystals into its optical antipodes discovering molecular chirality [13]. Nowadays there are several chemical techniques for the separation of a racemate into its pure enantiomers, still it remains a challenge in many cases. Often more

¹The curious reader may try to put the left foot into the right shoe to experience the effect.

²The R/S-nomenclature of Cahn, Ingold and Prelog [6] differs from the D/L-nomenclature of Fischer [12], yet both describe the left- and right-handed form of a molecule (see chapter 3).

³Even though Contergan was taken off the market in 1961 the active substance Thalidomid is still used nowadays to treat leprosy. It is also interesting to note that pure (R)-Thalidomid can convert to its (S)-form in the human body.

promising than the separation of the enantiomers in a racemic mixture is the so-called *asymmetric synthesis*. The *stereo-selectivity* of an asymmetric reaction, i.e. a specific stereoisomer (e.g. enantiomer) is selectively produced, is induced by introducing a pure enantiomeric substance to the reaction [14]. A common way of asymmetric induction in a synthesis is by using pure chiral educts often gained from natural resources [15], the so-called chiral pool, or by deploying chiral catalysators to drive the reaction towards the desired enantiomer. Knowles, Noyori and Sharpless received the Nobel prize in 2001 for their contribution to catalyzed asymmetric synthesis [16, 17, 18].

The source of chirality to drive a reaction can also be an external field. Magneto-chiral dichroism give rise to an enantiomeric excess in a photochemical reaction driven by unpolarized light in a magnetic field [19]. The difference in the absorption coefficient of the two enantiomers for circularly polarized light can also induce enantio-selectivity in photochemical reactions [20, 21] and in photolysis [22]. However, the success of asymmetric synthesis by these kinds of external fields has been so far very limited [23].

The scope of this work is to explore the possibility of an alternative way of preparing pure enantiomers from a racemate by means of ultra-short laser pulses, which has not yet been experimentally tested. Quantum dynamical simulations are the tool of these theoretical investigations. The goal is a deeper understanding of the elementary steps of the interaction between ultra-short laser pulses and the two enantiomeric forms of a molecule. For that, the dynamics of chiral quantum mechanical model systems are simulated under the influence of ultra-short electromagnetic fields. Ultimately, the possibility of selective control of the chirality of the molecules in a racemic mixture by means of polarized laser pulses is aspired.

1.2 Controlling chirality with laser pulses

The application of ultra-short laser pulses to investigate and control chemical reactions is the basis of *femtochemistry* [24]. This field was founded only in the middle eighties of the last century by Zewail [25]. He was the first to observe a chemical reaction on a femtosecond timescale by means of *pump-and-probe spectroscopy* [26, 27]. For his pioneering work on femtosecond spectroscopy Zewail was awarded the Nobel Prize in Chemistry in 1999 [28]. Ultra-short laser pulses may not only be applied to analyse chemical reactions but also for controlling its reaction steps. By means of laser pulses it is possible to selectively excite a bond of a molecule and thereby define the path of a chemical reaction. The field of quantum dynamics supplies a theoretical description of femtochemistry [29]. In quantum dynamics the evolution of a quantum mechanical state of a molecule in time

can exactly be described. The goal is usually to find a way to bring the system from its defined initial state to a desired target state. For that, laser pulses may be designed which excite and deexcite population between the quantum states of the system in order to control the molecular dynamics in the desired way.

Several investigations have been made by theoreticians in the last decades with the goal to describe molecular chirality in a quantum model system and eventually to gain control over it by external fields. This research shall be discussed in the following. Most of these investigations are based on a quantum model system as shown in figure 1.3. It consists of symmetric double well potential and an excited single well potential. The minima of the double well potential correspond to the minimum energy configuration of the left- and right-handed forms of a chiral molecule, depicted by a left and a right hand in fig. 1.3. The minimum of the excited potential is exactly above the barrier of the ground state curve. In this excited potential the chirality of the quantum system is not defined, as characterized by the achiral superposition hand in fig. 1.3.

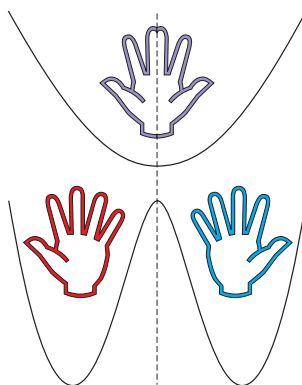


Figure 1.3: A general scheme for the control of chirality in a quantum model system: The ground state is a symmetric double well potential with each minimum corresponding to the left- and right-handed form of the model. The excited state is a single well potential with its minimum centered above the barrier of the ground state potential corresponding to an achiral form of the model.

The origin of the quantum mechanical understanding of the molecular chirality goes back to 1927 when Hund assigned superposition states localized in left and right well of a symmetric double well potential to the left- and right-handed forms of a chiral molecule [30]. Based on Hund's work Harris and Stodolsky examined in 1978 the time dependence of such localized states in a double well potential using a simple two state model [31]. They proposed a change of optical activity with time that should be caused

by the tunneling between the left- and right-handed states and finally the loss of optical activity caused by racemization due to collisions [32]. In the nineties Harris together with Cina extended the model system by adding a harmonic potential (cf. fig. 1.3) serving as electronic excited state and developed a wavepacket theory for the preparation and detection of superpositions of “handed” wavefunctions [33, 34]. Based on these results Maierle and Harris proposed an experimental measurement of a quantum chiral state of a single molecule by transferring the chiral information to the polarization vector of a photon, the so-called method of chiral teleportation [35]. Recently, Duarte-Zamorano and Romero-Rochín have studied the Cina-Harris proposal numerically using ultrashort laser pulses [36].

Quack also investigated theoretically the structure and dynamics of chiral molecules and presented a review of molecular chirality since the days of Hund’s theory, modified due to the discovery of the parity violating weak nuclear interaction [37] (see also [38]). Rather unimportant for the task of this work, but important to mention in this context, are the quantum models proposed by Quack for the experimental determination of the small energetic difference between two enantiomeric forms of a molecule due to the parity-violating weak neutral current perturbation [39, 37, 40] (see also [31]). Predicted by Lee and Yang [41] in 1956, Wu *et. al.* observed the parity violating weak interactions in the β -decay of ^{60}Co shortly after [42]. Lee and Yang were awarded the Nobel Prize in Physics in 1957 for their investigations of the so-called parity laws. Tranter calculated the parity violating energy difference of the enantiomers of some α -amino acids in the order of 10^{-14} J/mol in favor of the natural L-form in 1985 [43]. From high level *ab initio* results by Berger and Quack in 2000 no support for a systematic stabilization of L-alanine at thermally accessible conformations could be found and therefore, it seems that there is at present no direct relation between the parity violating energy difference and the reason for selection of L-amino acids [44, 45]. These results were confirmed independently by calculations of Schwerdtfeger and coworkers [46]. Recently, Berger *et. al.* examined the stereomutation of chiral molecules, as e.g. S_2Cl_2 , where the parity violating perturbation exceeds the ground state tunnel splitting [47]. Berger also proposed a modification to Quack’s approach for the observation of the parity violating energy difference [39] for molecules that are chiral in the electronic excited state, as e.g. carbonyl compounds of the type XYCO [48].

The conversion of a pure enantiomer into its mirror image stereoisomer, the so-called *stereomutation*, using a pump-dump laser scheme was demonstrated by Marquardt and Quack in 1996 using a simple quantum mechanical model system [49]: The electronic ground state is given by a double well potential which describes e.g. the inversion of a chiral substituted amine. For the electronic excited state a harmonic potential is used with its minimum exactly above the barrier of the double well, as introduced by Quack in the eighties [39] (cf. fig. 1.3). A rectangular 1 fs laser pulse excites the pure enantiomer to

the electronic excited state where periodic stereomutation takes place. Within 16 fs the system is transformed into the opposite chiral form in the electronic excited state. Then, a second rectangular 1 fs laser pulse deexcites the system to the electronic ground state producing the opposite pure enantiomer.⁴ Note that since in this pump-dump control scheme no distinction between left- and right-handed molecules is possible, i.e. the laser pulse sequence converts left- in right-handed molecules and *vice versa*, this method cannot be applied for the preparation of pure enantiomers from a racemate. Recently, Marquardt *et. al.* examined stereomutation on a femtosecond time scale, the so-called dynamical chirality, for the extreme limit of a zero barrier as found in the quantum dynamics of bending vibrations in methane isotopomers [51].

Based on similar model considerations but with a different goal Shao and Hänggi theoretically investigated in 1997 the influence of circular polarized (*cw*-) light on the enantio selectivity of a chemical reaction [52]. Two different scenarios based on four level model systems were analyzed, on the one hand the synthesis of a racemic product from achiral educts and, on the other hand the asymmetric synthesis from chiral educts which tend to racemize in the intermediate state of the reaction. In the first case, the circular polarized laser with defined polarization interacted only slightly differently with both enantiomeric transition states; no enantio selectivity of practical usage could be achieved. In the second case, the unstable chiral intermediate produced during the reaction should be stabilized by suppressing racemization until it reacts to the chiral products. The intermediate state was described as quantum mechanical two-level system that represents e.g. a doublet of vibrational eigenstates of a symmetric double well potential. Shao and Hänggi were able to show that the chiral intermediate can be stabilized with circular polarized light and thereby, it should be possible to increase the enantio-selectivity of the reaction [53].

Using a two-level model Salam and Meath demonstrated in the late nineties the possibility for the control of the relative population of left- versus right-handed excited molecular states of enantiomers, $|L_e\rangle$ and $|R_e\rangle$, through the use of circularly polarized pulses of various durations [54, 55, 56]. The control of the relative population in the chiral excited states arises from small difference in coupling of a circularly polarized laser pulses with the left- vs. right-handed forms of the ground states of the enantiomers, $|L_g\rangle$ and $|R_g\rangle$. The pulse duration of circularly polarized laser controls the relative population in the left and right-handed excited states $|L_e\rangle$ and $|R_e\rangle$. For fixed laser-molecule configurations, the populations of the left and right-handed excited state are completely out of phase with each other, one being fully populated, the other unpopulated [54]. For randomly oriented

⁴This method of transforming one enantiomer into the opposite one by means of two UV laser pulses with proper time delay may be considered as special case of the pump-dump laser pulse control, proposed by Tannor and Rice [50].

molecules there is a loss of control of the populations [55], since the couplings between the molecule and the laser depend on the molecular orientation. Salam and Meath also proposed the enantio-selective excitation from a racemate by circularly polarized laser pulses leaving an enantiomeric excess in the ground state after ionization of the excited population [56].

In 1991 Shapiro and Brumer proposed a method for coherent control of the photo-dissociation of a prochiral precursor molecule to yield the preferred chiral fragments using linearly polarized laser pulses [57]. As precursor they considered a BAB' type molecule with C_s symmetry, i.e. a mirror plane through A projects B onto B', making the molecule achiral. Via laser controlled photo-dissociation either the chiral fragment B or B' is selectively split off to yield BA + B' or B + AB' where AB and AB' are also a pair of enantiomers. Nine years later Shapiro *et. al.* applied coherent laser control in a model system consisting of a double well potential with a single well excited state, cf. fig. 1.3, for the preferential production of an enantiomer from a racemic mixture [58]. They used a four level system, with a left- and right-handed state in electronic ground state, called $|L\rangle$ and $|D\rangle$, and two states $|1\rangle$ and $|2\rangle$ in the electronic excited state, where $|1\rangle$ is symmetric with respect to inversion and $|2\rangle$ anti-symmetric. Two linearly polarized pulses, one coupling $|1\rangle$ and $|2\rangle$, and the other coupling $|L\rangle$ and $|D\rangle$ with $|1\rangle$ and $|2\rangle$, excite selectively either the left- and right-handed state to the excited potential. Control arises, as in all coherent control scenarios, through quantum interference effects, i.e. two interfering routes for excitation from the $|L\rangle$ or $|D\rangle$ states to $|1\rangle$ and $|2\rangle$. The racemic mixture is successively excited optically and allowed to relax, enhancing the concentration of either enantiomer by so-called "laser distillation". In 2001 Brumer *et. al.* derived the conditions for a model system and incident light under which enantiomeric control based purely on the electric dipole-electric field interaction is possible, including the effect of orientation of the molecules towards the laser field on the enantiomeric excess achieved by coherent "laser distillation" [59].

Also in 2001, Král *et. al.* demonstrated that cyclic population transfer in a 3-level system, $|1\rangle$, $|2\rangle$ and $|3\rangle$ is possible, using a phase-sensitive adiabatic passage method [60]. This phase sensitive scheme is based on the coexistence of the one and two-photon processes, initiated by three laser pulses in a counter-intuitive order, operating between the same initial ($|1\rangle$) and final states ($|2\rangle$ and $|3\rangle$), leading to interferences between the $|1\rangle \rightarrow |3\rangle \rightarrow |2\rangle$, "clockwise" and the $|1\rangle \rightarrow |2\rangle \rightarrow |3\rangle$ "counter-clockwise" optical processes. The interference, which depends on the overall phase of the three laser fields, results in a selective excitation of one chiral system relative to its mirror image. That is, the phase of the laser fields allows to determine which population transfer process is induced ($|1\rangle \rightarrow |2\rangle$ or $|1\rangle \rightarrow |3\rangle$) in each of the two enantiomers and therefore, each enantiomer can be excited to a different state ($|2\rangle$ or $|3\rangle$). Following such a selective excitation, a number of simple, energetically-dependent, physical separation schemes, such as ionization, followed by ions

extraction by an electric field, can be employed.

All the theoretical results on quantum control of molecular chirality discussed so far are based on simplified model systems. The first molecular model system for which the selective preparation of pure enantiomers by optimal elliptically polarized laser pulses was simulated was presented by Fujimura, Manz and coworkers in 1999 [61]. The quantum dynamical simulations were based on an *ab initio* double well potential and dipole couplings of the model system H₂POSH – the molecular model which is used as basis for the investigations in the work at hand. Note that the initial state of these preliminary simulations was the achiral symmetric ground state of the double well potential which does not correspond to a racemic mixture.

This thesis focusses on the selective preparation of pure enantiomers from a racemate by means of analytical laser pulses. Based on quantum *ab initio* calculations of H₂POSH the possibilities of controlling molecular chirality by means of ultrashort laser pulses are investigated in the first part of this work (chapter 4). The goal is to develop a control mechanism based on laser-dipole interaction that allows chiral discrimination in order to accomplish enhancement of the population of one enantiomer over the other in a racemic mixture. For that, several laser control strategies are designed and tested in quantum dynamical simulations throughout this work. In view of an experimental realization of the proposed laser control a more realistic model system, based on *ab initio* calculations of the molecule (4-methyl-cyclohexylidene)fluoromethane, is introduced and investigated in the second part of this thesis (chapter 5). Finally, the effect of the orientation of the molecules on the selectivity of the laser control is analysed.

While the research of this thesis was in progress Gerbasi *et. al.* applied in 2001 the coherently controlled racemic purification proposed by Shapiro *et. al.* [58, 59] on the chiral model system 1,3-dimethylallene, based on *ab initio* calculations by Derey *et. al.* [62]. Moreover, Brumer *et. al.* have presented *ab initio* studies of the reaction path for achiral methanol-formaldehyde complexation as prototype for a chiral system to be used for coherently controlled racemic purification [63]. Very recently, Král and coworkers demonstrated the laser pulse controlled selective conversion of a racemic mixture of D₂S₂ into pure enantiomers based on a two step scheme consisting of an “enantio-discriminator”, a modification of the cyclic population transfer mechanism [60], and an “enantio-converter” [64].

Yet another molecular model has been recently presented by Koseki, Fujimura and coworkers. They have simulated the laser controlled conversion of a racemate to pure helical enantiomers in difluorobenzo[c]phenanthrene using linearly polarized IR laser pulses [65].

1.3 Outline of the thesis

The rest of this work is organized as follows. Chapter 2 introduces the reader to the theoretical concepts of quantum chemistry and quantum dynamics. Specifically, the numerical methods used to obtain the results presented in this work are explained along with several approaches to molecular control using laser pulses. In chapter 3 an overview on the phenomenon of chirality is given. Molecular stereo-isomerism and the thereby caused chemical and physical properties of chiral molecules are explained. The concepts of chirality are then transferred to the quantum mechanical description of molecules.

The results of the model simulations are presented in chapters 4 and 5, each chapter focussing on a different molecular model system. Chapter 4 deals with the model system H₂POSH, which is optimal for developing different enantio-selective laser control mechanisms; extensions to those and to the model system are also discussed. In chapter 5 an experimentally more realistic model system, (4-methyl-cyclohexylidene)fluoromethane, is presented. The developed laser control is adjusted to this molecular model featuring coupled degrees of freedom and partly unrestricted molecular orientation. The final chapter 6 contains the summary and an outlook.