Dissolution
Dynamic-Nuclear-Polarization and its Combination with Cross Polarization

A dissertation submitted to
ETH ZÜRICH
for the degree of
Doctor of Sciences

presented by
MICHAEL BATEL
Diplom-Physiker
Ruprecht-Karls-Universität Heidelberg
born June 25, 1982
citizen of the Federal Republic of Germany

accepted on the recommendation of
Prof. Dr. Matthias Ernst, examiner
Prof. Dr. Sebastian Kozerke, co-examiner
Prof. Dr. Gunnar Jeschke, co-examiner

2013
meiner Familie
mojoj obitelji
# Contents

Abbreviations and Symbols ......................................................... ix

List of substances ......................................................................... xi

Abstract ......................................................................................... xiii

Zusammenfassung ........................................................................... xv

1. Introduction ................................................................................. 1

2. Theoretical background ............................................................ 5
   2.1. Magnetic Resonance .............................................................. 5
       2.1.1. Hamiltonians in NMR and EPR ........................................ 5
       2.1.2. Spin ensembles and the density operator ............................... 11
       2.1.3. Sensitivity in NMR ............................................................ 13
   2.2. Dynamic Nuclear Polarization ................................................ 15
       2.2.1. The mechanisms of DNP .................................................. 15
       2.2.2. The solid effect ................................................................. 17
       2.2.3. Thermal mixing ................................................................. 23
           2.2.3.1. Concepts of spin-temperature theory ............................ 23
           2.2.3.2. DNP via thermal mixing ............................................ 25
   2.3. Nuclear Cross Polarization .................................................... 35
       2.3.1. CP for the isolated spin pair .............................................. 36
       2.3.2. Thermodynamic description of CP .................................... 38

3. Instrumentation .......................................................................... 41
   3.1. Cryogenic System ............................................................... 43
       3.1.1. Cryogenic performance .................................................. 43
3.2. Microwave source ....................................................... 44
3.3. NMR spectrometer and rf circuit ............................. 45
3.4. Probe 1: Single-sample DNP probe ........................... 47
  3.4.1. Microwave guides ........................................... 47
  3.4.2. NMR circuitry ............................................... 48
  3.4.3. Sensor system ............................................. 49
3.5. Probe 2: Multi-sample dissolution DNP probe .......... 51
  3.5.1. The revolver .................................................. 51
  3.5.2. Microwave cavity .......................................... 53
  3.5.3. Microwave circuit .......................................... 55
  3.5.4. Longitudinal detected EPR ............................... 57
    3.5.4.1. LOD EPR circuit .................................... 57
    3.5.4.2. LOD detection and sensitivity ...................... 58
  3.5.5. NMR circuitry ............................................. 64
  3.5.6. Sensor system ............................................ 65
  3.5.7. Sample cups and grabber ................................ 68
  3.5.8. Dissolution and shuttling components ................ 70
  3.5.9. Performance results and dissolution procedure .... 70
3.6. Thermal heating estimation .................................... 75
3.7. Control software .................................................. 78
  3.7.1. Software sub-units ........................................ 78
3.8. Discussion ........................................................ 83

4. Dissolution DNP-CP .................................................. 85
  4.1. Aspects of combining DNP with CP ......................... 85
    4.1.1. CP in combination with thermal mixing vs. solid effect ... 86
    4.1.2. Timing of dissolution DNP-CP experiments .............. 87
  4.2. B1-field calibration ........................................... 88
  4.3. Adiabatic half-passage pulses .............................. 89
    4.3.1. CP pulse sequences using AHP and hard-90° pulses ... 91
    4.3.2. Efficiency of AHP vs. hard-90° pulses ................. 95
  4.4. Results ........................................................ 98
    4.4.1. DNP-CP using AHP .................................... 98
    4.4.2. Dissolution DNP-CP ................................... 99
4.4.3. Multiple-contact time DNP-CP ........................................ 101
4.5. Discussion ................................................................. 103

5. A spin-thermodynamic model of thermal mixing .......................... 105
  5.1. Model description ...................................................... 105
  5.2. Solution of the differential equations and model fitting .............. 108
  5.3. Results and Discussion .............................................. 109

6. The influence of sample parameters on dissolution DNP ................ 117
  6.1. Pyruvate/trityl-based samples ....................................... 117
    6.1.1. Solid-state DNP and $T_1$ ..................................... 117
    6.1.2. Liquid-state $T_1$ dependence on pH .......................... 118
    6.1.3. Results and discussion ....................................... 118
  6.2. TEMPO-based samples .............................................. 122
    6.2.1. Solid-state DNP enhancement .................................. 122
    6.2.2. CP efficiency .................................................. 123
    6.2.3. Dissolution efficiency ....................................... 123
    6.2.4. Results and discussion ....................................... 123

Conclusion .............................................................................. 129

Outlook .................................................................................... 133

Appendices .............................................................................. 137

A. Cryogenic heat flow ......................................................... 139
   A.1. Heat flow through a succession of materials ....................... 143

B. Cavity dimensions .................................................................. 145

Bibliography ........................................................................... 149

Acknowledgement .................................................................. 161

Curriculum Vitae ................................................................... 163

List of Publications ............................................................... 165
## Abbreviations and Symbols

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>Inverse spin temperature</td>
</tr>
<tr>
<td>$\Delta \omega_e$</td>
<td>EPR line width</td>
</tr>
<tr>
<td>$\epsilon$</td>
<td>Polarization enhancement</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Gyromagnetic ratio</td>
</tr>
<tr>
<td>$k_B$</td>
<td>Boltzmann constant</td>
</tr>
<tr>
<td>$T_1$</td>
<td>Spin-lattice relaxation time, longitudinal relaxation time</td>
</tr>
<tr>
<td>$T_2$</td>
<td>Spin-spin relaxation time, transverse relaxation time</td>
</tr>
<tr>
<td>$T_{1,\rho}$</td>
<td>Rotating-frame relaxation time</td>
</tr>
<tr>
<td>$T_{TM}$</td>
<td>Thermal mixing time</td>
</tr>
<tr>
<td>1D</td>
<td>One dimensional</td>
</tr>
<tr>
<td>$\hat{\mathcal{H}}$</td>
<td>Hamilton operator</td>
</tr>
<tr>
<td>AHP</td>
<td>Adiabatic half-passage</td>
</tr>
<tr>
<td>CE</td>
<td>Cross effect</td>
</tr>
<tr>
<td>CL</td>
<td>Cooling reservoir</td>
</tr>
<tr>
<td>CP</td>
<td>Cross polarization</td>
</tr>
<tr>
<td>cw</td>
<td>Continuous wave</td>
</tr>
<tr>
<td>CZ</td>
<td>Carbon Zeeman reservoir</td>
</tr>
<tr>
<td>DNP</td>
<td>Dynamic nuclear polarization</td>
</tr>
<tr>
<td>DNP-CP</td>
<td>Dynamic nuclear polarization in combination with cross polarization</td>
</tr>
<tr>
<td>DQ</td>
<td>Double quantum</td>
</tr>
<tr>
<td>EPR</td>
<td>Electron paramagnetic resonance</td>
</tr>
<tr>
<td>FWHM</td>
<td>Full width at half maximum</td>
</tr>
<tr>
<td>hfi</td>
<td>Hyperfine interaction</td>
</tr>
<tr>
<td>HZ</td>
<td>Proton Zeeman reservoir</td>
</tr>
<tr>
<td>if</td>
<td>Interaction frame</td>
</tr>
<tr>
<td>L</td>
<td>Lattice</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>LOD</td>
<td>Longitudinal detected (EPR)</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MRS</td>
<td>Magnetic resonance spectroscopy</td>
</tr>
<tr>
<td>mw</td>
<td>Microwave</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>NZ</td>
<td>non-Zeeman reservoir</td>
</tr>
<tr>
<td>OE</td>
<td>Overhauser effect</td>
</tr>
<tr>
<td>PTFE</td>
<td>Polytetrafluorethylene</td>
</tr>
<tr>
<td>rf</td>
<td>Radio frequency</td>
</tr>
<tr>
<td>SE</td>
<td>Solid effect</td>
</tr>
<tr>
<td>SL</td>
<td>Spin lock</td>
</tr>
<tr>
<td>SNR</td>
<td>Signal-to-noise ratio</td>
</tr>
<tr>
<td>TM</td>
<td>Thermal mixing</td>
</tr>
<tr>
<td>VI</td>
<td>Virtual instrument</td>
</tr>
<tr>
<td>ZQ</td>
<td>Zero quantum</td>
</tr>
</tbody>
</table>
List of substances

The substances used and mentioned in this work have been acquired from:

- $[1^{-13}\text{C}]$pyruvic acid ("pyruvate"): ISOTEC/Sigma Aldrich
- $[^{13}\text{C}]$urea: ISOTEC/Sigma Aldrich
- $[1,4^{-13}\text{C}]$fumaric acid: Sigma Aldrich
- TEMPO: 2,2,6,6-tetramethyl-1-piperidinyloxy, Sigma Aldrich
- trityl: tris (8-carboxyl-2,2,6,6-tetra(2-(1-hydroxyethyl))-benzo[1,2-d;4,5-d’]bis (1,3) dithiole-4-yl) methyl sodium salt, donation
- Glycerol-d3: exchangeable protons of glycerol deuterated in LPC, ETH (by Fabienne Arn and Guido Grassi)
- Glycerol-d8: donated by EPR group ETH, Prof. Gunnar Jeschke
- DMSO-d6: Cambridge Isotopes
- D$_2$O: Cambridge Isotopes
- Gd: Gadovist, Bayer HealthCare
Abstract

An important limitation of nuclear magnetic resonance (NMR) applications is the low intrinsic sensitivity that can be overcome by hyperpolarization techniques such as dynamic nuclear polarization (DNP). Ardenkjær-Larsen et al. extended the established solid-state DNP method in 2003 by subsequent dissolution of the hyperpolarized sample (dissolution DNP) making it applicable to in-vivo magnetic resonance imaging (MRI) and spectroscopy (MRS).

The common DNP polarization protocol used in combination with the published single-sample polarizers allows only low dissolution repetition rates, limited to less than one dissolution experiment per hour. Decreasing the minimum repetition time between successive dissolution DNP experiments could not only ease the screening of sample parameters in multi-sample studies, but could allow DNP enhanced MRS experiments that demand a fast succession of injections of hyperpolarized substances.

To increase the repetition rate of dissolution DNP experiments, two approaches are being investigated in this thesis: a) the simultaneous polarization of multiple samples followed by successive dissolutions in a multi-sample dissolution DNP system, and b) the combination of dissolution DNP with Hartmann-Hahn cross polarization (CP) allowing fast polarization of $^1$H followed by polarization transfer from $^1$H to $^{13}$C nuclei.

In the Instrumentation section, the design and performance results of a home-built cryogenic DNP setup are presented with two compatible DNP probes. The first probe is a single-sample probe that allows static heteronuclear solid-state NMR experiments with high sensitivity and radio frequency (rf) field strengths up to 100 kHz. The second probe is a dissolution DNP probe with multi-sample functionality. A revolver-style sample changer accommodating up to six samples allows to exchange the samples between different positions during cryogenic operation. A resonant microwave cavity is used to increase the DNP efficiency at low incident microwave power, and NMR and EPR capabilities are included in the polarizer to monitor and characterize
The multi-sample probe has been found to be highly convenient to conduct series of solid-state DNP experiments with varying sample compositions, since the time-consuming changing of samples in and out of the cold space can be avoided. Although simultaneous polarization of all samples is possible, the multi-sample probe does not allow fast-sequential dissolution DNP experiments in the current setup, since the dissolution of one sample depletes the polarization of the remaining samples.

Using the single-sample probe, the combination of DNP with CP (DNP-CP) was investigated with the aim to reduce the polarization build-up time on $^{13}\text{C}$. This approach is based on the fact that the polarization time on high-$\gamma$ nuclei, such as $^{1}\text{H}$, is usually shorter than that of low-$\gamma$ nuclei, such as $^{13}\text{C}$. A modification of the Hartmann-Hahn CP is presented using adiabatic half-passage pulses. It allows more efficient polarization transfer at low rf-field strengths, which is especially important in the combination with dissolution DNP probes since these usually suffer from a limited rf-field strength. Important aspects for the combination of dissolution DNP with CP are discussed and the DNP-CP experiment is further improved by applying multiple-contact time CP to a suitable sample.

To combine DNP-CP with subsequent dissolution, an additional NMR circuit is incorporated into the dissolution probe allowing heteronuclear NMR experiments with field strengths up to 30 kHz. It is shown, that the polarization transfer gained by the CP in the solid state is retained during the dissolution process. With this technique, the polarization is accelerated by a factor larger than two while enhancing the final polarization level.

To gain further insight into the dynamics during heteronuclear DNP experiments, a spin-thermodynamic model is applied. It models the dynamics of the $^{1}\text{H}$ and $^{13}\text{C}$ polarization levels during heteronuclear DNP experiments for various initial conditions of the nuclear polarizations. Finally, the influences of radical concentration and sample pH on the dissolution DNP-CP efficiency are investigated.

In conclusion, this thesis provides technical, methodological, and experimental contributions to the advancement of the dissolution DNP technique, amongst others, towards faster repetition rates. Along the way, it provides the research field of NMR and MRI at the ETH with a readily available tool for generating hyperpolarized nuclear spins in solution.
Zusammenfassung

Den grössten Nachteil der Kernmagnetresonanz (NMR) stellt deren geringe Sensitivität dar. Diese kann in bestimmten Anwendungen durch Hyperpolarisationsmethoden wie Dynamic Nuclear Polarization (DNP) verbessert werden. Ardenkær-Larsen hat 2003 gezeigt, dass sich DNP in Festkörpern durch schnelles Auflösen der hyperpolarisierten Substanz für die Magnetresonanz Tomographie (MRT) und Spektroskopie (MRS) nutzbar machen lässt (Dissolution DNP).


Um die Repetitionszeit zu verkürzen, werden in dieser Dissertation zwei Ansätze verfolgt: das gleichzeitige Polarisieren mehrerer Proben sowie die Erweiterung des Dissolution-DNP-Experiments durch Hartmann-Hahn-Kreuzpolarisation (CP), die das schnellere Hyperpolarisieren von $^1$H Kernen ausnutzt und anschliessend deren Polarisierung auf die $^{13}$C Kerne überträgt.


Mittels des Probenkopfes für Multikern-NMR-Experimente wurde die Kombination von DNP mit CP (DNP-CP) erprobt, mit dem Ziel, die Polarisationsdauer der $^{13}$C Kerne zu reduzieren. Dieser Ansatz nutzt die meist schnellere Polarisation von Kernen mit hohem gyromagnetischem Verhältnis $\gamma$, etwa $^1$H, im Vergleich zur Polarisation von Kernen mit kleinem $\gamma$, etwa $^{13}$C. Eine Modifikation des klassischen CP durch die Verwendung adiabatischer Pulse wird vorgestellt, durch die die Effizienz des CP bei niedrigen RF-Feldstärken gesteigert werden kann. Dies ist wichtig bei der Anwendung von CP in Dissolution-DNP-Probenköpfen, die meist nur geringe RF-Feldstärken zulassen. Weitere Aspekte des DNP-CP-Experiments mit Hinblick auf die Kombination mit anschliessender Auflösung werden diskutiert und die Effizienz des Experiments wird durch wiederholtes Anwenden des CP gesteigert.

Die Kombination von DNP-CP mit anschliessender Auflösung wird mittels einer Erweiterung des Probenkopfes mit Auflösevorrichtung demonstriert, durch die Multikern-NMR-Experimente bis zu 30 kHz RF Feldstärke möglich sind. Es wird gezeigt, dass der im Festkörper erreichte Polarisationtransfer durch den Auflösevorgang in die flüssigen Phase übertragbar ist. Dadurch wird die effektive Polarisationsrate der $^{13}$C Kerne mehr als verdoppelt bei gleichzeitiger Verstärkung des erreichten Polarisationsgrades.


Zusammenfassend leistet diese Dissertation Beiträge zur technischen und methodologischen Weiterentwicklung der Dissolution-DNP-Methode mit Fokus auf der Beschleunigung der möglichen Wiederholungsrate. Zusätzlich stellt der entwickelte experimentelle Aufbau dem NMR- und MRI-Forschungsfeld der ETH Zürich ein Tool
zur Hyperpolarisation von Kernspins zur Verfügung.
1. Introduction

The inherently low sensitivity is a major drawback of nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) and leads to long measurement times. This is a problem, for example, in spatially-resolved magnetic resonance spectroscopy (MRS), where the distribution of metabolic substances in an organism is of interest. The large background of abundant water protons overwhelms the $^1$H resonances of potentially interesting substrates in low endogenous concentrations. Magnetically active isotopes other than $^1$H, e.g., $^{15}$N or $^{13}$C are difficult to detect with sufficient spatial resolution due to their low natural abundance and lower gyromagnetic ratio $\gamma$.

Besides increasing the static magnetic field or lowering the temperatures (the so-called brute-force method), various methods have been proposed over the years to increase the nuclear spin polarization over the thermal equilibrium. Such hyperpolarization techniques include optical pumping of noble gases [1–3], para-hydrogen induced polarization [4, 5], the Haupt effect in methyl groups [6–8], chemically-induced dynamic nuclear polarization [9], and dynamic nuclear polarization using free radicals (DNP) [10].

In DNP, electron polarization is transferred to the nuclei under microwave irradiation of the electron spins. After the first prediction of the effect in metals by Overhauser in 1953 [11] and the experimental verification of this Overhauser effect by Carver and Slichter shortly after [12], experimental and theoretical research on DNP started prospering: Jeffries proposed a similar DNP effect in non-conducting solids at low temperatures [13], which was first demonstrated and named as the solid effect by Abragam and Proctor in 1958 [14]. The theoretical description of the DNP mechanisms have been extended to systems with abundant radicals with large line widths by the work of Provotorov [15], Borgini [16], and Abragam and Goldman [10] in the 1960s and 1970s leading to the description of DNP via thermal mixing.

In 1967, Hwang and Hill observed the so-called cross effect [17, 18]. Together with the developments by Wind and Griffin in the 1980s and 1990s this effect led DNP to its
second important role in modern NMR besides the Overhauser effect DNP, namely, DNP in low-temperature magic-angle spinning (MAS) NMR [19–21]. It took, however, 50 years until in 2003 Jan H. Ardenkjær-Larsen proposed the combination of solid-state DNP with subsequent rapid dissolution to generate a solution of hyperpolarized nuclei [22] and thus made DNP accessible for MRI. This technique has become known as dissolution DNP and is the third important application of DNP in modern NMR. It has found various applications in the field of solution-state NMR and MRI, a review of which is given in [23].

In dissolution DNP, typically the hyperpolarization is generated at temperatures between 1 – 4.2 K [22, 24, 25] and, often, at a static magnetic field of 3.4 T due to readily available microwave sources at 94 GHz, i.e., the electron Larmor frequency at 3.4 T. The target samples are glass-forming solutions (10 – 500 µl) containing the target molecule and an organic stable free radical like TEMPO or trityl. Typical polarization levels of $^{13}$C as the target nuclei reach up to 50% for trityl-doped samples [22, 26–28] and up to 14% for TEMPO-doped samples [24, 29, 30] by transfer of polarization from the almost fully polarized electron spins. Subsequently, the hyperpolarized sample is rapidly dissolved and transferred to the solution-state spectrometer or MRI. The polarization enhancements in the dissolved samples have been reported to be larger than a factor of 10,000 [22, 31, 32] compared to thermal-equilibrium polarization at ambient temperature.

Several dissolution DNP polarizers based on the same principle structure and functionality have been built in the past 10 years [22, 24, 25, 27, 33]. They consist of a pumped helium-temperature cryostat with a wave guide for microwave irradiation and a mechanical transfer system for moving the sample into and out of the cryostat. The transfer system accommodates a dissolution apparatus that is used to extract the polarized sample from the cryostat. The polarizer is typically equipped with a simple NMR circuit to determine the nuclear polarization levels. A drawback of this design is that only a single sample can be stored in the polarizer, polarized, and dissolved at a time. After this process, the sample tray has to be unloaded and a subsequent target sample has to be loaded into the cryostat. Therefore, the repetition rate for multiple dissolution DNP experiments is limited by the time needed for changing and polarizing the sample.

An important application of dissolution DNP is metabolic MRI [31, 34–36]. Here, a metabolite with hyperpolarized nuclear spins is injected into an organism for in-
tracing of the marker molecule and its metabolic products. This procedure opens unprecedented opportunities in MRI. Like most hyperpolarization techniques, the dissolution DNP method is limited by the fact that the high polarization is available only for a time window on the order of $T_1$. Consequently, the technique is restricted to the detection of hyperpolarized low-$\gamma$ nuclei, which usually have longer relaxation times than high-$\gamma$ nuclei. It is found, that the polarization transfer from electrons to low-$\gamma$ nuclei like $^{13}$C is usually slow and requires polarization times often exceeding 1 hour. Therefore, the repetition time for multiple dissolution DNP experiments using single-sample polarizers is limited to $>1$ hour [22, 30].

Decreasing the minimum repetition time between successive dissolution DNP experiments can be important for, e.g., cardiac experiments of repeated ischemia / reperfusion to study conditioning of the heart. Furthermore, the investigation of the dependence of the DNP efficiency on various sample parameters requires serial experiments, which could be simplified by having multiple samples loaded in the polarizer simultaneously.

It has been shown in the past that the combination of DNP to $^1$H and Hartmann-Hahn cross polarization (CP) [37] to $^{13}$C is a possible way to speed up the DNP process and enhance the polarization of low-$\gamma$ nuclei under MAS DNP conditions [20, 38, 39]. Under conditions similar to the ones in dissolution DNP experiments, however, the combination of DNP with CP has not been presented before this work. The obstacles to overcome when realizing such experiments arise mainly from the NMR circuits of dissolution DNP setups with a single radio-frequency channel and relatively low radio frequency (rf) amplitudes available.

It is the target of this thesis to contribute to technical and methodological developments towards dissolution DNP experiments with an increased repetition rate compared to the rates achievable by the published dissolution DNP systems. This goal is approached from two sites: on the one hand a multi-sample dissolution DNP probe has been developed to investigate the possibility of simultaneous polarization of multiple samples and successive dissolutions. On the other hand, the combination of dissolution DNP with a modification of the Hartmann-Hahn CP method is presented, which exploits the fast polarization build up of $^1$H in combination with subsequent polarization transfer from $^1$H to $^{13}$C to decrease the overall build-up time of the $^{13}$C polarization.

In chapter 2, the theoretical framework used in this work is introduced and a dis-
cussion is given, helping to answer the question which DNP mechanism is dominant in the experimental data presented. The developed instrumentation is presented in chapter 3 and performance results of the dissolution DNP system are given. In chapter 4, the combination of dissolution DNP and CP is introduced. Peculiarities of this experiment are discussed, a modification of the cross polarization technique is presented exploiting adiabatic half-passage rf pulses, and the first solution-state results are presented that have been achieved with this method. In chapter 5, a spin-thermodynamic model is applied to experimental data to gain insight into the dynamics during heteronuclear DNP experiments. Finally, in chapter 6, the influence of selected sample parameters on the efficiency of dissolution DNP experiments is presented.
2. Theoretical background

2.1. Magnetic Resonance

The prerequisite of each DNP mechanism is the interaction of electron spins with nuclear spins in an external magnetic field. The scientific discipline describing nuclear spins and electron spins in magnetic fields is called Magnetic Resonance (MR). Numerous text books offer comprehensive overviews and in-depth theoretical treatments, such as [40–43]. The quantities which are most important for the theoretical treatment of DNP will be introduced in the following.

2.1.1. Hamiltonians in NMR and EPR

In the laboratory frame of reference the Hamiltonian of a system of interacting electron-nuclear spins can be written as

\[ \hat{H}^{\text{lab}} = \hat{H}_{e,Z} + \hat{H}_{n,Z} + \hat{H}_{\text{hfi}} + \hat{H}_{ee} + \hat{H}_{nn} + \hat{H}_{mw} + \hat{H}_{rf} \] (2.1)

precluding electron spin systems forming group spins with \( S > 1/2 \). The interactions are:

- electron Zeeman: \( \hat{H}_{e,Z} \)
- nuclear Zeeman: \( \hat{H}_{n,Z} \)
- electron-nuclear hyperfine: \( \hat{H}_{\text{hfi}} \)
- weak electron-electron: \( \hat{H}_{ee} \)
- nuclear-electron: \( \hat{H}_{nn} \)
- microwave irradiation: \( \hat{H}_{mw} \)
- radio frequency irradiation: \( \hat{H}_{rf} \).

Above, as well as in the following, \( \hat{S} \) and \( \hat{I} \) always stands for the electron and nu-
clear spin operators, respectively. In the product base, their order will be $\hat{S}\hat{I}$. All Hamiltonians will be given in angular frequency units throughout this work. This implies that, e.g. the spin operator $\hat{I}_z$ for a spin-1/2 is written as:

$$\hat{I}_z = \frac{1}{2} \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$$

and that the energy of a spin system in Joules is calculated via:

$$E = \hbar \langle \mathcal{H} \rangle.$$

**Interaction-frame representation**

It is a common tool of MR to describe the state of a spin systems and its evolution in the interaction frame with respect to the interaction $\mathcal{H}_{\text{ef}}$. Any operator $\hat{O}$ is represented in this interaction frame via the transformation:

$$\hat{O} = e^{i\mathcal{H}_{\text{ef}}t} \hat{O} e^{-i\mathcal{H}_{\text{ef}}t}. \quad (2.3)$$

It is common practice to truncate the interaction frame Hamiltonians to their secular (time independent) contributions, while dropping the non-secular (time dependent) contributions. This can be justified by averaging the Hamiltonian over a time larger than the periodicity of the non-secular contributions and should be accounted for by, e.g., an overbar on the Hamiltonian. The latter is usually omitted and in return it is noted that the Hamiltonian is truncated to the secular contributions. This interaction-frame transformation and secular truncation allows a simplification of the Hamiltonians and will be used frequently throughout this work.

**Electron Zeeman interaction**

If electrons are included in the spin system, the electron Zeeman interaction is the leading term, expressed as

$$\mathcal{H}_{\text{e,Z}} = \sum_i \frac{\mu_B}{\hbar} B_0 T^i \hat{S}_i \quad (2.4)$$
or with \( \vec{B}_0^T = (0, 0, B_0) \)

\[
\hat{H}_{e,Z} = \sum_i \frac{\mu_B}{\hbar} B_0 \left( g_{zx}^i \hat{S}_x^i + g_{zy}^i \hat{S}_y^i + g_{zz}^i \hat{S}_z^i \right)
\]

(2.5)

with the Bohr magneton \( \mu_B \), the transposed external magnetic field vector \( \vec{B}_0^T \), and the \( g \)-tensor \( g^i \) of each electron \( i \). For simplicity of subsequent theoretical discussions, the high-field approximation can be applied leaving only the \( z \)-component. Consequently, the Zeeman Hamiltonian of electron \( i \) can be rewritten as:

\[
\hat{H}_{e,Z}^i = \omega_c \hat{S}_z^i + \Delta_i \hat{S}_z^i
\]

(2.6)

with \( \omega_c = \frac{\mu_B}{\hbar} g_{\text{iso}} B_0 \) and \( \Delta_i = \omega_c - \omega_e = \frac{\mu_B}{\hbar} B_0 (g_{zz}^i - g_{\text{iso}}) \). Equation 2.6 implies the restriction that all electrons have the same isotropic \( g \)-value \( g_{\text{iso}} \) and only differ in their relative orientation to the \( z \)-axis. This simplification is reasonable for the systems with only a single free radical species present.

The Zeeman Hamiltonian in equation 2.6 reveals an on-resonance (first term) and off-resonance term. The resonance frequency of an electron will thus depend on its relative orientation of the \( g \)-tensor to the magnetic field (and therefore to the laboratory coordinate system). The relative spread of frequencies arising from this \( g \)-anisotropy strongly depends on the radical chosen and is in the order of \( 2.75 \times 10^{-4} \) for the trityl radical and \( 3.6 \times 10^{-3} \) for the TEMPO radical used in this work.

Finally, in the electron Zeeman interaction frame with \( \hat{H}_{if} = \omega_c \hat{S}_z^i \) equation 2.6 reduces to its off-resonant term:

\[
\hat{H}_{e,Z}^i = \Delta_i \hat{S}_z^i.
\]

(2.7)

**Nuclear Zeeman interaction**

The second important interaction (even though in general not larger than the hyperfine interaction) is the interaction of the nuclear spins with the external magnetic field:

\[
\hat{H}_{n,Z} = -\sum_j \gamma_j \vec{B}_0^T \vec{I} = \sum_j \omega_n^j \hat{I}_z^j
\]

(2.8)
assuming that \( \vec{B}_0 = (0, 0, B_0) \), with the nuclear Larmor frequency \( \omega_n^j = -\gamma^j B_0 \) and the nuclear gyromagnetic ration \( \gamma^j \) of the nuclear spin \( j \). In this work, only chemically equivalent nuclei will be treated, so that chemical shift contributions can be neglected.

Electron-nuclear hyperfine interaction

The most important interaction for DNP is the electron-nuclear hyperfine interaction

\[
\hat{H}_{hfi} = \sum_{j,i} \hat{S}^i A^i_j \hat{I}^j
\]  

(2.9)

where \( A \) is the hyperfine interaction tensor. This tensor contains an isotropic (or Fermi contact) part as well as anisotropic components arising from electron-nuclear dipolar couplings [43, ch. 3.1.3]. The hyperfine Hamiltonian can thus be separated into

\[
\hat{H}_{hfi} = \hat{H}^{iso}_{hfi} + \hat{H}^{aniso}_{hfi}
\]  

(2.10)

with

\[
\hat{H}^{iso}_{hfi} = \sum_{i,j} a_{i,j} \hat{S}^i \hat{I}^j
\]  

(2.11)

\[
\hat{H}^{aniso}_{hfi} = \sum_{i,j} \frac{\mu_0}{4\pi} \frac{\gamma^j \gamma_n \hbar}{r_{i,j}^3} (A_{i,j} + B_{i,j} + C_{i,j} + D_{i,j} + E_{i,j} + F_{i,j})
\]  

(2.12)
with $\gamma_e \equiv \frac{\mu_B}{\hbar} g$ and the Fermi-contact interaction strength $a_{ij}$ (see [43]). The so called dipolar alphabet is given by

$$A_{i,j} = \hat{S}_z^i \hat{I}_z^j \left(1 - 3 \cos^2 \theta_{i,j}\right)$$

$$B_{i,j} = \left(\hat{S}_i^+ \hat{I}_j^- + \hat{S}_i^- \hat{I}_j^+\right) \frac{3 \cos^2 \theta_{i,j} - 1}{4}$$

$$C_{i,j} = \left(\hat{S}_i^+ \hat{I}_j^- + \hat{S}_i^- \hat{I}_j^+\right) \frac{-3 \sin \theta_{i,j} \cos \theta_{i,j} e^{-i\phi_{i,j}}}{2}$$

$$D_{i,j} = \left(\hat{S}_i^- \hat{I}_j^- + \hat{S}_i^+ \hat{I}_j^+\right) \frac{-3 \sin \theta_{i,j} \cos \theta_{i,j} e^{-i\phi_{i,j}}}{2}$$

$$E_{i,j} = \hat{S}_i^+ \hat{I}_j^- \frac{-3 \sin^2 \theta_{i,j} e^{-i2\phi_{i,j}}}{4}$$

$$F_{i,j} = \hat{S}_i^- \hat{I}_j^- \frac{-3 \sin^2 \theta_{i,j} e^{i2\phi_{i,j}}}{4}.$$

(2.13)

Above, $r_{i,j}, \theta_{i,j},$ and $\phi_{i,j}$ are the spherical coordinates of the vector connecting the electron $i$ with the coupled nucleus $j$. The anisotropic hyperfine interaction is caused by dipolar coupling of the electron and nuclear magnetic moments through space. The isotropic part arises from a non-zero overlap of probability density of the electron and the nucleus. It is therefore restricted to intramolecular interactions and to electrons with wave functions (at least partially) in the $s$-orbital.

### Electron-electron and nuclear-nuclear interactions

Both, pairs of close-by electrons and pairs of close-by nuclei interact via the dipolar coupling of their magnetic moments. This coupling has the same formal shape as the anisotropic hyperfine interaction given in equation 2.12 using the dipolar alphabet given in equation 2.13.

In the case of the electron-electron interaction, this holds true only for weakly coupled electron pairs without orbital overlap [43, ch. 3.1.6]. It is justified to make this simplification here since in this work only radical dopants are considered with a single unpaired electron. Otherwise, the zero-field splitting and the exchange coupling would have to be taken into account.

In the high-field approximation, one can transform into the interaction frames of the Zeeman interactions. In this case, both for electron-electron dipolar interactions
and homonuclear dipolar interactions equation 2.12 reduces to its secular term and is truncated after the term $B_{i,j}$. For heteronuclear interactions one can transform into a double rotating frame with both Zeeman interactions. In this case equation 2.12 simplifies even further by truncation after the term $A_{i,j}$ (as will be used in section 2.3.1).

For nuclear-nuclear interactions additionally an isotropic interaction exists called $J$-coupling or scalar coupling. Since it is usually several orders of magnitude smaller than the dipolar coupling it is only observed in liquids or in MAS-NMR where the dipolar couplings are averaged out. Therefore it will be neglected in this work.

### Microwave and radio-frequency irradiations

The manipulation of the spin system is achieved by applying microwave (mw) irradiation with a frequency close to the electron Zeeman resonance or radio-frequency (rf) irradiation close to the nuclear Larmor frequency.

The mw irradiation is usually introduced to the sample via a wave guide while the rf irradiation is generated by a resonating coil surrounding or in the vicinity of the sample. In both cases, the Hamiltonian can be written in analogy to the Zeeman Hamiltonian, e.g. for the case of rf irradiation

$$\hat{H}_{rf} = -\sum_j \gamma_i B_1 \hat{I}_j$$  \hspace{1cm} (2.14)

with the magnetic component $B_1$ of the generated electromagnetic field. The transverse component of the rf-field with field strength $B_1$ can be written as

$$(\vec{B}_1)_\perp = 2B_1 \cos(\omega_{rf} t + \phi) \vec{e}_x$$  \hspace{1cm} (2.15)

arbitrarily aligning it with the $x$-axis of the laboratory frame and allowing for a phase $\phi$.

The longitudinal component $(\vec{B}_1)_\parallel$ is usually several orders of magnitude smaller than $B_0$ and can be neglected. Thus $(\vec{B}_1)_\perp = \vec{B}_1$ and the Hamiltonians for rf and mw
2.1 Magnetic Resonance

irradiation read:

\[ \hat{H}_{rf} = \sum_j -\gamma_n^{j} 2B_{1}^{rf} \cos(\omega_{rf} t + \phi) \hat{I}_x \]  
(2.16)

\[ \hat{H}_{mw} = \sum_i -\gamma_{c}^{i} 2B_{1}^{mw} \cos(\omega_{mw} t + \phi) \hat{S}_x. \]  
(2.17)

In the interaction frames with respect to the Zeeman interactions the rf and mw Hamiltonians become (for single spins)

\[ \hat{H}_{rf} = -\gamma_n B_{1}^{rf} \frac{1}{2} (\cos((\omega_{rf} - \omega_{n,if}) t + \phi) + \cos((\omega_{rf} + \omega_{n,if}) t + \phi)) \hat{I}_x \]
\[ \hat{H}_{mw} = -\gamma_{c} B_{1}^{mw} (\cos((\omega_{mw} - \omega_{c,if}) t + \phi) + \cos((\omega_{mw} + \omega_{c,if}) t + \phi)) \hat{S}_x \]

and if the interaction frame frequencies are chosen equal to the irradiation frequencies \((\omega_{rf} = \omega_{n,if}, \omega_{mw} = \omega_{c,if})\) reduce further to

\[ \hat{H}_{rf} = -\gamma_n B_{1}^{rf} \hat{I}_x -\gamma_n B_{1}^{rf} \cos(2\omega_{rf} t) \hat{I}_x \]
\[ \hat{H}_{mw} = -\gamma_{c} B_{1}^{mw} \hat{S}_x -\gamma_{c} B_{1}^{mw} \cos(2\omega_{mw} t) \hat{S}_x \]

where \(\phi = \frac{\pi}{2}\) can be defined without losing generality.

If the secular truncation is applied to the interaction-frame irradiation Hamiltonians they finally simplify to

\[ \hat{H}_{rf} = \omega_{1,n} \hat{I}_x \]  
(2.18)

\[ \hat{H}_{mw} = \omega_{1,c} \hat{S}_x \]  
(2.19)

with the nutation frequencies \(\omega_{1,n} = -\gamma_n B_{1}^{rf}\) and \(\omega_{1,c} = -\gamma_{c} B_{1}^{mw}\).

2.1.2. Spin ensembles and the density operator

Macroscopic systems with \(N \gg 1\) spins are treated as "ensembles". If the quantum mechanical state of each spin \(i\) is written as function of the eigenbase of the \(\hat{I}_z\) operator \(|\alpha\rangle\) and \(|\beta\rangle\) as

\[ |\psi\rangle = c_1 |\alpha\rangle + c_2 |\beta\rangle \]  
(2.20)
then the expectation value of any spin operator is a function of the product of the coefficients $c_i c_j^*$. For an ensemble of equivalent spins, the expectation value can be derived from the expectation value of the isolated spin by averaging over all $N$ products $c_i c_j^*$, therefore the knowledge of $c_i c_j^*$ for all four combinations of $i, j = 1, 2$ is sufficient to fully characterize the spin system with respect to the spin observables.

This motivates the definition of the density operator

$$\hat{\rho} \equiv |\psi\rangle \langle \psi|$$

which becomes

$$\rho = \begin{pmatrix} c_1 c_1^* & c_1 c_2^* \\ c_2 c_1^* & c_2 c_2^* \end{pmatrix}$$

(2.21)

if written as matrix in the eigenbase of $\hat{I}_z$. The density matrix is composed by the products of coefficients and it can be shown that the density operator fully characterizes the state of a system. The overbar will be dropped from this point on.

The diagonal entries of the spin density operator 2.21 are called populations of state $i$ ($c_i c_i^*$) while the off-diagonal entries are called coherences. If the spin system is at equilibrium with the surrounding lattice the density operator is diagonal (in the eigenbase of the Hamiltonian) with a Boltzmann distribution of populations:

$$\rho = \frac{1}{\text{Tr} \left\{ e^{-\beta \hat{H}} \right\}} e^{-\beta \hat{H}} \rho$$

(2.22)

where

$$\beta = \frac{1}{k_B T}$$

(2.23)

defines the inverse spin temperature $\beta$ using the usual terminology (e.g. [10, p. 401]) and $k_B$ is the Boltzmann constant (for more information see section 2.2.3.1). At thermal equilibrium the spin temperature becomes equal to the lattice temperature $T = T_L$.

To reach equilibrium after a perturbation the coherences decay with the phenomenological time constant $T_2$ (spin-spin relaxation time) while the populations approach there equilibrium distribution with the time constant $T_1$ (spin-lattice relaxation time).
2.1 Magnetic Resonance

2.1.3. Sensitivity in NMR

The detection of nuclear resonances is usually achieved by observing induced voltages in the NMR coil. If the coil axis is assumed to be aligned with the x-axis of the coordinate system, then the induced signal strength \( S \) is proportional to the magnetization along \( x \):

\[
S \propto M_x \equiv \gamma_N N\langle \hat{I}_x \rangle \propto c_1^* c_2^* + c_2 c_1^*
\]

using the relation \( \langle \hat{O} \rangle = \text{Tr} \{ \rho \hat{O} \} \). As shown in the preceding section the coherences are zero in thermal equilibrium. Therefore, before detection rf pulses are used to generate detectable coherences. In the Zeeman interaction frame one can assume the rf-pulse to rotate the density operator around the \( y \)-axis (with \( \hat{H}_{rf} \) analog to equation 2.18 with \( \hat{I}_y \) instead of \( \hat{I}_x \)) such that

\[
\rho(\tau) = e^{-i\hat{H}_{rf} \tau} \rho(0) e^{i\hat{H}_{rf} \tau} = \begin{pmatrix} \cos \frac{\omega_1}{2} \tau & -\sin \frac{\omega_1}{2} \tau \\ \sin \frac{\omega_1}{2} \tau & \cos \frac{\omega_1}{2} \tau \end{pmatrix} \begin{pmatrix} c_1^0 c_1^{0*} & 0 \\ 0 & c_2^0 c_2^{0*} \end{pmatrix} \begin{pmatrix} \cos \frac{\omega_1}{2} \tau & \sin \frac{\omega_1}{2} \tau \\ -\sin \frac{\omega_1}{2} \tau & \cos \frac{\omega_1}{2} \tau \end{pmatrix}
\]

\[
= \begin{pmatrix} c_1^0 c_1^{0*} \cos^2 \frac{\omega_1}{2} \tau + c_2^0 c_2^{0*} \sin^2 \frac{\omega_1}{2} \tau & (c_1^0 c_1^{0*} - c_2^0 c_2^{0*}) \sin \frac{\omega_1}{2} \tau \cos \frac{\omega_1}{2} \tau \\ (c_1^0 c_1^{0*} - c_2^0 c_2^{0*}) \sin \frac{\omega_1}{2} \tau \cos \frac{\omega_1}{2} \tau & c_1^0 c_1^{0*} \sin^2 \frac{\omega_1}{2} \tau + c_2^0 c_2^{0*} \cos^2 \frac{\omega_1}{2} \tau \end{pmatrix}.
\]

The signal strength after the pulse is thus

\[
S \propto 2(c_1^0 c_1^{0*} - c_2^0 c_2^{0*}) \sin \frac{\omega_1}{2} \tau \cos \frac{\omega_1}{2} \tau
\]

and becomes maximum for a 90° pulse \((\omega_1 \tau = 90°)\):

\[
S \propto (c_1^0 c_1^{0*} - c_2^0 c_2^{0*}).
\]

The difference in populations prior to the pulse is therefore determining the signal intensity in NMR experiments. It is called

\[
\text{Polarization} \quad P \equiv (c_1 c_1^* - c_2 c_2^*) \quad (2.24)
\]

and it is the target of DNP to enhance its value above thermal equilibrium.

Corresponding to equation 2.22 the polarization of a spin-1/2 system (with \( \gamma > 0 \))
reads at thermal equilibrium:

\[
P = \frac{e^{\beta_L h \frac{\omega}{2}} - e^{-\beta_L h \frac{\omega}{2}}}{e^{\beta_L h \frac{\omega}{2}} + e^{-\beta_L h \frac{\omega}{2}}} = \tanh \left( \frac{\beta_L h \omega}{2} \right)
\]  

(2.25)

if the Zeeman interaction (equation 2.8) is the dominant contribution to the Hamiltonian. In the high-temperature approximation, where \( \beta_L h \omega \ll 1 \) this can be simplified by truncating after the linear term of the series expansion:

\[
P \approx \beta_L h \frac{\omega}{2}.
\]

(2.26)

In the context of this work, the usage of the high-temperature approximation has to be handled with care since temperatures as low as 1.3 K are reached. For \(^{13}\text{C}\) and \(^{1}\text{H}\) at 1.3 K the exact polarization levels are 0.07% and 0.29%, respectively (at the given field of 3.35 T). Therefore, the relative errors made for the nuclei using the high-temperature approximation is negligible. For electrons, however, the relative error rises above 1% around 13 K and reaches \(\sim 9\%\) at 4.2 K.
2.2 Dynamic Nuclear Polarization

2.2.1. The mechanisms of DNP

Since Overhauser suggested in 1953 [11] to enhance the nuclear polarization of metals by saturating their EPR line several similar mechanisms have been proposed all utilizing microwave irradiation. They are today summarized as DNP methods. The purpose of this section is to introduce the different DNP mechanisms and to emphasize their differences and circumstances under which they occur with a treatment similar to [19].

While the hyperfine term in equation 2.1 is important for all DNP mechanisms, the electron-electron interactions are relevant for the thermal mixing DNP, which will be introduced later. They can be described in analogy to the anisotropic part of the hyperfine interaction (equation 2.12, with $\gamma_e$ and $\hat{S}$ substituted for $\gamma_n$ and $\hat{I}$). An important consequence of these interactions is the electron-electron cross relaxation, mediated by the term $B_{ij}$. Another result of $\hat{H}_{ee}$ is dipolar broadening of the EPR line, referred to as homogenous broadening [43, ch. 3.3.1].

Another reason for EPR line broadening can be a spread of Larmor frequencies $\omega_i^e$ of independent electron spins, called inhomogenous broadening. The reason for this can be, among others [43, ch. 3.3.2], g-anisotropy or hyperfine interactions to nuclei at different relative electron-nuclear positions. The EPR line width due to both homogenous and inhomogenous broadening will be denoted as $\Delta \omega_e$ in the following.

The dominating DNP mechanisms, depending mainly on the time dependence of the contributions to the overall Hamiltonian in equation 2.1, are:

i) The Overhauser effect (OE) relies on cross relaxation between coupled electron-nucleus pairs while saturating the electron Zeeman transition. For the cross relaxation to occur, $\hat{H}_{hfi}$ has to be time-dependent on a scale similar to $\omega_e^{-1}$ [19]. The OE thus is characteristic for metals (such as Li, in which Carver and Slichter initially demonstrated the OE [12]) or liquids doped with paramagnetic compounds, as was first shown by Abragam in 1955 [44]. In solids with fixed paramagnetic centers the OE therefore does not occur. A theoretical treatment of this effect can be found in [45, 46] or in the reviews [47, 48].

ii) The Solid (state) Effect (SE) occurs when the time-average value of $\hat{H}_{aniso}^{hfi}$ is non-
zero, i.e., if there are no modulations averaging the anisotropic hyperfine interactions to zero. Furthermore, the EPR line has to be narrow compared to the nuclear Larmor frequency, i.e., \( \omega_n > \Delta \omega_e \) where \( \Delta \omega_e \) denotes the EPR line width. This restricts the system to non-conducting solids with fixed paramagnetic centers at low concentrations and low \( g \)-anisotropy. The SE was proposed by Jeffries in 1957 [13] and first demonstrated and named by Abragam and Proctor in 1958 [14]. A comprehensive review can be found in [49] and in-depth quantum mechanical treatments are given by the group of Robert Griffin [50] and Shimon Vega [51–53].

iii) The Cross Effect (CE) can occur under the same experimental conditions as the SE. However, it is a three-spin \( \{e-e-n\} \) process in which two electrons with

\[
|\omega_{e,1} - \omega_{e,2}| \approx \omega_n
\]

perform a flip-flop and the nucleus flips by taking up the remaining energy. This restricts the effect to solids with an inhomogenous EPR line width \( \Delta \omega_e > \omega_n \). The CE was first observed by Hwang and Hill [17, 18] and is nowadays the predominant mechanism used in high-field 100 K DNP-MAS experiments. For these, bi-radicals or mixtures of radicals are used rather than mono-radicals so that the chance of finding an electron pair matching the CE condition is larger [54, 55]. A review on the CE with focus on high magnetic fields is given by Hu [56] and a quantum mechanical treatment can be found in [57].

iv) The Thermal Mixing (TM) effect also occurs if the time-average of \( \hat{H}_{hfi}^{aniso} \) is zero and if \( \Delta \omega_e > \omega_n \). In contrast to the CE it can occur even at large electron concentrations so that the inhomogenously broadened EPR line becomes additionally (partly) homogenously broadened. Most important, for the TM the CE condition can be met not only by the irradiated electron spin packet but by any arbitrary electron-electron pair. The TM effect is explained by the spin-temperature theory developed by Redfield, Proctorov, Abragam, and others [10, 15, 16, 58, 59] and is understood to be the major mechanism in dissolution DNP experiments.

The experiments presented later in this work utilize DNP at mainly 1.3 to 4.2 K in amorphous organic solids doped with stable radicals in the range of several tens of mM. For these conditions the above discussion points out that SE, CE, and TM
are possible DNP mechanisms. It will be concluded in this work that the dominant mechanism in all shown TEMPO-based experiments is TM. Note however that at the same time both the SE and the CE might occur with less intensity.

In the subsequent sections the TM mechanism will be introduced. Beforehand, the SE will be introduced since its understanding gives an intuitive insight into the basic principle of DNP.

### 2.2.2. The solid effect

For a basic understanding of the polarization transfer from electron to nuclear spins the case of \( \omega_n > \Delta \omega_e \) will be considered first. In the context of this thesis, the SE is the dominant mechanism only for the case of polarization of \(^1\)H via trityl radicals. Its polarization efficiency was found to be much lower than the polarization efficiency observed in samples undergoing TM and thus no corresponding experiments are presented. For simplicity, only the direct polarization transfer between a single electron-nucleus pair will be treated, mainly following [43, ch. 3.5], [19], and [51]. The distribution of polarization to the bulk nuclei can be treated in a separate step [19]. The following derivation assumes a nucleus with \( \gamma_n > 0 \) (e.g. \(^1\)H or \(^{13}\)C), the derivation for \( \gamma_n < 0 \) can be carried out by analogy.

In the laboratory frame, the Hamiltonian of a coupled electron-nucleus pair is given as:

\[
\hat{H}_{0}^{\text{lab}} = \hat{H}_{e,Z} + \hat{H}_{n,Z} + \hat{H}_{\text{hf}} = \omega_e \hat{S}_z + \omega_n \hat{I}_z + \hat{S} \hat{A} \hat{I} \tag{2.27}
\]

and after transformation into an interaction frame with respect to \( \omega_{mw} \hat{S}_z \)

\[
\hat{H}_0 = \Delta \hat{S}_z + \omega_n \hat{I}_z + \hat{S}' \hat{A} \hat{I} \\
\approx \Delta \hat{S}_z + \omega_n \hat{I}_z + A_{zz} \hat{S}_z \hat{I}_z + A_{zx} \hat{S}_x \hat{I}_x + A_{zy} \hat{S}_y \hat{I}_y \tag{2.28}
\]

with \( \Delta = \omega_e - \omega_{mw} \) and the high-field approximation applied in the second line so that only the secular term (with \( A_{zz} \)) and the pseudo-secular terms (with \( A_{zx} \) and \( A_{zy} \)) remain. To simplify, but without loss of generality, the \( I \)-frame is rotated about \( \hat{I}_z \) by the transformation \( U = \exp(-i\phi \hat{I}_z) \) with \( \phi = \arctan(-A_{zy}/A_{zx}) \), so that the pseudo-secular interaction lies in the new \( xz \)-plane:

\[
\hat{H}_0 = \Delta \hat{S}_z + \omega_n \hat{I}_z + A \hat{S}_z \hat{I}_z + B \hat{S}_z \hat{I}_x \tag{2.29}
\]
with $A = A_{zz}$ and $B = (A_{zx}^2 + A_{zy}^2)^{1/2}$.

Due to the hyperfine interaction, the product basis set $(|\alpha\alpha\rangle = |\alpha_e\rangle \otimes |\alpha_n\rangle, |\alpha\beta\rangle, |\beta\alpha\rangle, |\beta\beta\rangle)$ is not an eigenbase of $\hat{H}_0$ anymore. The diagonalization of $\hat{H}_0$ can be achieved by the unitary transformation:

$$\hat{H}_0^d = U \hat{H}_0 U^{-1}$$

with the transformation matrix

$$U = \begin{pmatrix}
\cos(\eta_{\alpha}/2) & -\sin(\eta_{\alpha}/2) & 0 & 0 \\
\sin(\eta_{\alpha}/2) & \cos(\eta_{\alpha}/2) & 0 & 0 \\
0 & 0 & \cos(\eta_{\beta}/2) & -\sin(\eta_{\beta}/2) \\
0 & 0 & \sin(\eta_{\beta}/2) & \cos(\eta_{\beta}/2)
\end{pmatrix}$$

that holds the eigenvectors of $\hat{H}_0^d$ as rows and with the angles

$$\eta_{\alpha} = \arctan\left(\frac{-B}{A + 2\omega_n}\right), \quad \eta_{\beta} = \arctan\left(\frac{-B}{A - 2\omega_n}\right).$$

In the eigensystem of $\hat{H}_0^d$

$$|1\rangle = \cos(\eta_{\alpha}/2)|\alpha\alpha\rangle - \sin(\eta_{\alpha}/2)|\alpha\beta\rangle \quad \lambda_1 = \frac{\Delta}{2} + \frac{\omega_{12}}{2}$$

$$|2\rangle = \cos(\eta_{\alpha}/2)|\alpha\beta\rangle + \sin(\eta_{\alpha}/2)|\alpha\alpha\rangle \quad \lambda_2 = \frac{\Delta}{2} - \frac{\omega_{12}}{2}$$

$$|3\rangle = \cos(\eta_{\beta}/2)|\beta\alpha\rangle - \sin(\eta_{\beta}/2)|\beta\beta\rangle \quad \lambda_3 = -\frac{\Delta}{2} + \frac{\omega_{34}}{2}$$

$$|4\rangle = \cos(\eta_{\beta}/2)|\beta\beta\rangle + \sin(\eta_{\beta}/2)|\beta\alpha\rangle \quad \lambda_4 = -\frac{\Delta}{2} - \frac{\omega_{34}}{2}$$

the eigenstates are mixtures of the uncoupled product states. The corresponding energy level diagram is sketched in figure 2.1. Since usually $|\eta_{\alpha,\beta}| \ll \pi/2$, the first terms in 2.33 are dominant, while small admixtures of the second terms are added. It is these small admixtures that will make the formerly forbidden transitions $|\alpha\alpha\rangle \leftrightarrow |\beta\beta\rangle$ (double quantum (DQ) transition) and $|\alpha\beta\rangle \leftrightarrow |\beta\alpha\rangle$ (zero quantum (ZQ) transition) allowed using corresponding microwave irradiation or via relaxation processes. In this frame, the nuclear frequencies are
2.2 Dynamic Nuclear Polarization

The transitions in equations 2.35 and 2.36 can be driven by microwave irradiation as introduced in 2.17. If the frequency is chosen equal to the frequency used in the transformation in equation 2.28, one can write the microwave Hamiltonian in the
interaction frame (with arbitrarily chosen phase)

\[
\hat{\mathcal{H}}_{mw} = \omega_{1,e} \hat{S}_x
\]  

(2.37)

with the nutation frequency \( \omega_{1,e} = -\gamma_e B_1 \). Applying the transformation in equation 2.30 one gets the microwave Hamiltonian in the eigenbase of \( \hat{\mathcal{H}}_0 \)

\[
\hat{\mathcal{H}}_{mw} = \frac{\omega_{1,e}}{4} \begin{pmatrix} 0 & 0 & \cos \eta & -\sin \eta \\ 0 & 0 & \sin \eta & \cos \eta \\ \cos \eta & \sin \eta & 0 & 0 \\ -\sin \eta & \cos \eta & 0 & 0 \end{pmatrix}
\]  

(2.38)

with

\[
\eta = \frac{\eta_\alpha - \eta_\beta}{2}.
\]  

(2.39)

The microwave Hamiltonian given in equation 2.38 allows to drive SQ, ZQ, and DQ transitions with transition amplitudes given as its off-diagonal entries. The transitions can be selected if \( \omega_{mw} \) is chosen such that in the interaction frame the corresponding transition energies \( \lambda_i - \lambda_k = 0 \). The ZQ and DQ irradiation frequencies and transition rates are

\[
\text{ZQ: } \Delta = \frac{\omega_{12} + \omega_{34}}{2}, \quad \text{W}_{ZQ} \propto |a_{23}|^2 \propto \omega_1^2 \sin^2 \eta
\]

\[
\text{DQ: } \Delta = \frac{-\omega_{12} + \omega_{34}}{2}, \quad \text{W}_{DQ} \propto |a_{14}|^2 \propto \omega_1^2 \sin^2 \eta,
\]  

(2.40)

with the entries \( a_{ij} \) of the Hamiltonian in equation 2.38.

The generation of nuclear hyperpolarization via the SE relies on the interplay of microwave induced ZQ or DQ transitions and electron and nuclear spin lattice relaxation. In the following, both \( T_1 \) relaxation rates are included as well as the microwave induced DQ and ZQ transitions to retain generality. The nuclear and electron polarization can be expressed as

\[
P_n = \frac{N_1 - N_2 + N_3 - N_4}{\sum_i N_i} = N_1 - N_2 + N_3 - N_4
\]  

(2.41)

\[
P_e = N_3 - N_1 + N_4 - N_2
\]  

(2.42)

with the population \( N_i \) of the \( i \)-th state and \( \sum_i N_i = 1 \). Furthermore the thermal
equilibrium populations and polarization will be denoted $N_i^0$ and $P_{e,n}^0$, respectively. For the derivative of the populations one gets:

$$\frac{d}{dt}N_1 = T_{1,e}^{-1}(N_3 - N_1 - (N_3^0 - N_1^0)) + T_{1,n}^{-1}(N_2 - N_1 - (N_2^0 - N_1^0)) + W_{DQ}(N_4 - N_1)$$

$$\frac{d}{dt}N_2 = T_{1,e}^{-1}(N_4 - N_2 - (N_4^0 - N_2^0)) + T_{1,n}^{-1}(N_1 - N_2 - (N_1^0 - N_2^0)) + W_{ZQ}(N_3 - N_2)$$

$$\frac{d}{dt}N_3 = T_{1,e}^{-1}(N_1 - N_3 - (N_1^0 - N_3^0)) + T_{1,n}^{-1}(N_4 - N_3 - (N_4^0 - N_3^0)) + W_{ZQ}(N_2 - N_3)$$

$$\frac{d}{dt}N_4 = T_{1,e}^{-1}(N_2 - N_4 - (N_2^0 - N_4^0)) + T_{1,n}^{-1}(N_3 - N_4 - (N_3^0 - N_4^0)) + W_{DQ}(N_1 - N_4)$$

(2.43)

and after some algebra the derivative of the nuclear polarization reads

$$\frac{d}{dt}P_n = -2T_{1,n}^{-1}(P_n - P_n^0) + W_{DQ}(P_e - P_n) - W_{ZQ}(P_n + P_e).$$

(2.44)

In the steady state equation 2.44 becomes static and one obtains

$$P_{n}^{\text{DNP}} = P_n^{\text{ss}} = \frac{2T_{1,n}^{-1}P_n^0 + P_e^{\text{ss}}(W_{DQ} - W_{ZQ})}{2T_{1,n}^{-1} + W_{DQ} + W_{ZQ}}.$$ 

(2.45)

To find the upper limit for $P_n^{\text{ss}}$ one can introduce the assumptions:

i) *fast electron relaxation*: $T_{1,e}^{-1} \gg W_{DQ}, W_{ZQ}, T_{1,n}^{-1}$,

ii) *slow nuclear relaxation*: $T_{1,n}^{-1} \ll W_{DQ}, W_{ZQ}, T_{1,e}^{-1}$.

Assumption i) leads to a steady-state electron polarization unchanged from equilibrium: $P_e^{\text{ss}} \approx P_e^0 = \frac{-\gamma_e}{\gamma_n} P_n^0$. With this the

$$\text{DNP enhancement} \quad \varepsilon \equiv \frac{P_{n}^{\text{DNP}}}{P_n^0}$$

becomes

$$\varepsilon = \frac{2T_{1,n}^{-1}}{2T_{1,n}^{-1} + W_{DQ} + W_{ZQ}} - \frac{\gamma_e}{\gamma_n} \frac{W_{DQ} - W_{ZQ}}{2T_{1,n}^{-1} + W_{DQ} + W_{ZQ}}.$$ 

(2.47)

Finally, one can choose one of the transitions $W_{DQ}$ or $W_{ZQ}$ by selective microwave irradiation given in equations 2.40 so that $W_{ZQ} = 0$ or $W_{DQ} = 0$, respectively, and
apply assumption ii) to get

\[ \epsilon_{DQ} \approx -\frac{\gamma_e}{\gamma_n} > 0 \quad \epsilon_{ZQ} \approx \frac{\gamma_e}{\gamma_n} < 0 \] (2.48)

since \( \gamma_e < 0 \).

Three important conclusions can be drawn from the derivation above:

i) Equation 2.47 shows the importance to be able to selectively irradiate either one of the ZQ or DQ transition. This results in the restriction of the SE to systems with narrow EPR line widths, i.e. the SE condition:

\[ \Delta \omega_e < \omega_n. \] (2.49)

ii) The transition rates given in equation 2.40 can be approximated for small hyperfine couplings where \( A, B \ll \omega_n \). In this case

\[ \eta_a = \arctan \left( \frac{-B}{A + 2\omega_n} \right) \approx -\frac{B}{2\omega_n}, \quad \eta_\beta = \arctan \left( \frac{-B}{A - 2\omega_n} \right) \approx \frac{B}{2\omega_n} \] (2.50)

and

\[ \eta = \frac{\eta_a - \eta_\beta}{2} \approx -\frac{B}{2\omega_n}. \] (2.51)

With this the DQ and ZQ transition rates can be approximated to

\[ W_{DQ,ZQ} \propto \sin^2 \left( \frac{-B}{2\omega_n} \right) \approx \left( \frac{B}{2\omega_n} \right)^2. \] (2.52)

Since \( B \) is solely composed of off-diagonal elements of the hyperfine coupling it reflects the dipolar coupling between the electrons and the nucleus. With this one gets

\[ B \propto \gamma_n \quad \Rightarrow \quad W_{DQ,ZQ} \propto \frac{\gamma_e^2}{\omega_n^2}. \] (2.53)

This result shows that the DQ and ZQ transition rates are independent of the type of nucleus if all other parameters remain equal. Furthermore, it shows that the rate of the SE will decrease with increasing magnetic field if \( \omega_{1,e} \) in equation 2.38 remains constant. This decrease in polarization rate translates to a lower
steady-state polarization enhancement in equation 2.47 if the nuclear relaxation rate remains constant.

iii) Together with the independence of the DQ and ZQ transition rates on the type of nucleus, equation 2.48 shows that the enhancement via the SE is inverse proportional to $\gamma_n$.

### 2.2.3. Thermal mixing

The conditions in dissolution DNP experiments usually do not fulfill the restriction necessary for the SE. By far most dissolution DNP experiments are done with a trityl radical polarizing $^{13}$C nuclei [22, 47] or with derivatives of the TEMPO radical polarizing $^1$H and $^{13}$C nuclei [29]. In both cases, the condition 2.49 is not met. Similarly, in the early years of DNP the polarization of solid doped alcohols [60] could not be explained by the SE anymore. It was the spin temperature theory that allowed to describe DNP in these conditions within a spin-thermodynamic framework.

In the following, an introduction will be given to the concept of spin temperature theory as reviewed by Abragam and Goldman [10, 61] and the resulting DNP mechanism will be introduced for both the high-temperature and the low-temperature case. A comprehensive qualitative review can be found in [62] and more recent theoretical discussions are given in [63, 64].

#### 2.2.3.1. Concepts of spin-temperature theory

The spin-temperature theory is essentially based on the *spin-temperature hypothesis* first introduced by Redfield in 1955. It was used to describe the population of nuclear spin states of solids in the rotating frame [58]:

> A spin system isolated from the lattice and subjected to spin-spin interactions proceeds toward a state of internal equilibrium such that the probabilities of finding the system in any of its energy levels are given by a Boltzmann distribution $\exp(-E_i/k_BT_S)$. This distribution defines the spin temperature $T_S$ of the system.

[61, p. 12]

In other words, an isolated spin system (number of particles and total energy are constants of motion) with time-independent interactions that allow transitions between
its eigenstates can be described as a canonical ensemble with equilibrium temperature $T_S$. The density operator therefore has the form given in equation 2.22.

The term *canonical* in this sense does not relate to the spin system being isolated (a statistical canonical ensemble is defined as being only closed, i.e., with a temperature defined by a large bath with which it is in thermal contact allowing energy to be exchanged [65]) but to the nature of its Boltzmann distributed level population. The spin system is understood to be in *internal equilibrium* whenever its energy levels are populated corresponding to a Boltzmann distribution. The corresponding spin temperature in this case depends solely on the preparation of the spin system.

The time scale on which the spin-temperature theory can be applied is restricted. Spin-temperature theory aims on describing the state of a spin system only by considering populations of eigenstates while neglecting any coherences. This simplification is reasonable if any off-diagonal elements (coherences) of the density operator are zero. Since this condition is not met for most non-equilibrium situations, the coherences have to decay before it makes sense to apply spin-temperature theory. Hence, the useful time scale is restricted to times $t > T_2$ (compare section 2.1.2).

Furthermore, realistic spin systems are not strictly isolated but tend to equilibrate their temperature with the surrounding lattice with the phenomenological spin-lattice relaxation rate $T_1$. A spin temperature exists hence after a time $t > T_2$ and is unique only on a timescale intermediate between $T_2$ and $T_1$. This implies the restriction of $T_1 \gg T_2$, a condition usually met in solids. On a time scale similar to $T_1$ it is still possible to apply spin-temperature theory, however one has to include the thermal coupling to the lattice.

Similarly, spin systems might be loosely coupled to other spin systems with which they can exchange polarization on a time scale of the cross-relaxation rate [66, 67]. In this case the systems are not isolated and will eventually reach a common spin temperature. If however the cross-relaxation rate is smaller than the $T_2$ relaxation rates the baths will reach internal equilibria with unique spin temperatures which in a second step will equilibrate on a larger time scale [61, ch. 1.F].

The existence of spin-spin interactions enables two important phenomena necessary for the spin-temperature theory: a) The coupling among neighboring spins leads to a quasi-continuous spread (broadening) of the energy levels. A result of this is that any initial coherence does not simply oscillate with a discrete frequency but with a distribution of frequencies, hence leading to the necessary dephasing, that is, $T_2$ relax-
2.2 Dynamic Nuclear Polarization

b) The coupling between closest neighbors allows energy-conserving flip-flop transitions. These processes establish the spin temperature.

For the following derivation of the thermal mixing DNP mechanism it is important that the spin-temperature hypothesis can be applied to any situation or frame with a static Hamiltonian (and the fulfilled condition of a closed system and existing internal interaction allowing energy-conserving processes). Furthermore, for cases in which different parts of the Hamiltonian of a system commute (at least in good approximation), each corresponding energy contribution is a separate constant of motion and can thus be assigned a unique spin temperature. If additionally small non-secular interactions are present, these interactions lead to a slow mixing of the different spin-temperatures [61, ch. 1.F].

2.2.3.2. DNP via thermal mixing

Qualitatively, the TM mechanism for DNP can be understood as a two-step process:

i) Dynamic cooling/heating is the process in which the spin temperature of a non-Zeeman (NZ) electron reservoir is being altered from thermal equilibrium by microwave irradiation. This non-Zeeman reservoir can be understood to arise from any interaction leading to EPR line broadening.

ii) Thermal mixing is the process in which the spin temperature of the nuclear Zeeman reservoir equilibrates with the one of the electron non-Zeeman reservoir. This process is mediated via $\hat{H}_{\text{hfi}}^{\text{aniso}}$ and is essentially a three-spin process analogue to the CE process. The difference, however, is that not necessarily the irradiated spin packet has to take part in the flip-flop-flip process. Since in the dynamic cooling step the entire electron non-Zeeman reservoir is cooled, any electron-electron pair fulfilling the condition $|\omega_{e,1} - \omega_{e,2}| \approx \omega_n$ can perform the three-spin process and mediate the thermal mixing.

Different spin-thermodynamic models for DNP based on this two-step process have been proposed, differing in the approximations they make and thus differing in the situations they are applicable to [15, 16, 64, 68]. They have the following in common:

i) They are restricted to steady-state situations (hence, are not able to explain dynamic effects like the cooling process).
ii) They assume strong coupling between the electron non-Zeeman and nuclear
Zeeman reservoir such that both together can be described by a common spin
temperature. The result is that the second step, e.g., thermal mixing itself is
assumed to occur infinitely fast such that its physical mechanism is neglected in
the theoretical treatment.

iii) They apply the spin-temperature hypothesis separately to the Zeeman and non-
Zeeman baths of all spin species. This implies the high-field case, since otherwise
Zeeman and non-Zeeman energies might start to overlap leading to equalization
of their spin temperatures.

The second point thereby reduces the theoretical discussion to the description of the
spin temperature of the electron non-Zeeman reservoir and its modification upon
(off-) resonant irradiation, as Abragam and Goldman state in [10, ch. 5.1.2]:

The root of the problem is the lack of a theory capable to predict the temperature
of the non-Zeeman electronic Hamiltonian upon off-centre saturation of the EPR
resonance line.

The naming thermal mixing of the overall DNP mechanism is still reasonable. This
is because the polarization transfer onto the nuclear Zeeman reservoir, even though
not explicitly described, is realized via thermal mixing with the electron non-Zeeman
reservoir.

High-temperature case

One considers a spin system containing fixed radicals with Larmor frequency \( \omega_e \) and
a single nuclear species with electronic and nuclear Zeeman interactions as well as
electronic dipolar spin-spin interactions. Hyperfine interactions are assumed to be
negligible compared to the other interactions, however, large enough to enable ther-
mal mixing between the nuclear Zeeman and electron non-Zeeman reservoir. The
resulting Hamiltonian in the interaction frame similar to the electron Zeeman inter-
action but off-resonant about \( \Delta = \omega - \omega_e \) can be written as:

\[
\mathcal{H} = \mathcal{H}_{e,Z} + \mathcal{H}_{e,D} + \mathcal{H}_{n,Z}. \tag{2.54}
\]
In the high-temperature limit, given if

\[ E_k \ll k_B T \] (2.55)

where \( E_k \) stands for the \( k \)-th eigenvalue of \( \hat{\mathcal{H}} \), the density operator given in 2.22 can be truncated after the linear term of its expansion series:

\[ \rho \approx \frac{1}{\text{Tr}\left\{ \hat{\mathbb{1}} - \beta \hbar \hat{\mathcal{H}} \right\}} \left( \hat{\mathbb{1}} - \beta \hbar \hat{\mathcal{H}} \right) \approx \frac{1}{Z} \left( \hat{\mathbb{1}} - \beta \hbar \hat{\mathcal{H}} \right) \] (2.56)

where one defines \( Z = \text{Tr}\left\{ \hat{\mathbb{1}} \right\} \) as the dimension of the Hilbert space and the second approximation being valid because \( Z > 1 \gg \text{Tr}\{\beta \hbar \hat{\mathcal{H}}\} \). With the assumptions (ii) and (iii) from the beginning of this section one can write:

\[ \rho = \frac{1}{Z} \left[ \hat{\mathbb{1}} - \alpha \hbar \hat{\mathcal{H}}_{e,Z} - \beta \hbar \left( \hat{\mathcal{H}}_{e,D} + \hat{\mathcal{H}}_{n,Z} \right) \right] \] (2.57)

with the separately secular parts of the Hamiltonian, i.e., mutually isolated energies, \( \hat{\mathcal{H}}_{e,Z} \) and \( \hat{\mathcal{H}}_{e,D} + \hat{\mathcal{H}}_{n,Z} \) and their spin temperatures \( \alpha \) and \( \beta \), respectively. The expectation values of both energy baths read:

\[ \langle \hat{\mathcal{H}}_{e,Z} \rangle = -\frac{\alpha \hbar}{Z} \text{Tr}\left\{ \hat{\mathcal{H}}_{e,Z}^2 \right\} \] (2.58)

\[ = -\frac{\alpha \hbar \Delta^2}{Z} \text{Tr}\left\{ S_z^2 \right\} \] (2.59)

\[ \langle \hat{\mathcal{H}}_{e,D} + \hat{\mathcal{H}}_{n,Z} \rangle = -\frac{\beta \hbar}{Z} \text{Tr}\left\{ \hat{\mathcal{H}}_{e,D}^2 + \hat{\mathcal{H}}_{n,Z}^2 \right\} \] (2.60)

To transform equation 2.60 to a similar form as the one of equation 2.59, one can define a local field in the rotating frame [10, p. 404]

\[ B_L^2 \equiv \frac{\text{Tr}\left\{ \hat{\mathcal{H}}_{e,D}^2 + \hat{\mathcal{H}}_{n,Z}^2 \right\}}{\gamma_e^2 \text{Tr}\left\{ S_z^2 \right\}} \] (2.61)

and correspondingly a local frequency

\[ L^2 = \gamma_e^2 B_L^2 = \frac{\text{Tr}\left\{ \hat{\mathcal{H}}_{e,D}^2 + \hat{\mathcal{H}}_{n,Z}^2 \right\}}{\text{Tr}\left\{ S_z^2 \right\}} \] (2.62)
This allows to rewrite equation 2.60 to:

$$\langle \mathcal{H}_{e,D} + \mathcal{H}_{n,Z} \rangle = -\frac{\beta \hbar}{Z} \text{Tr} \left\{ \mathcal{H}_{e,D}^2 + \mathcal{H}_{n,Z}^2 \right\} = -\frac{\beta \hbar L_Z^2}{Z} \text{Tr} \left\{ S_z^2 \right\}. \quad (2.63)$$

Provotorov derived in his theory of saturation [15, 61] the effect of weak rf irradiation off-resonant about $\Delta$. For the rates of change of $\alpha$ and $\beta$ he derived the expressions today known as Provotorov equations:

$$\frac{d\alpha}{dt} = -W(\Delta)(\alpha - \beta) \quad (2.64)$$
$$\frac{d\beta}{dt} = W(\Delta) \left( \frac{\Delta^2}{L^2} \right) (\alpha - \beta) \quad (2.65)$$

where, translated to the case of microwave irradiation off-resonant about $\Delta$, $W(\Delta) = \pi \omega_1 g(\Delta)$ defines the mw-driven Zeeman transition rate and $g(\Delta)$ the absorptive EPR line shape.

The equations above neglect the relaxation to the lattice. For the electron Zeeman term the usual spin-lattice relaxation rate $T_1,e$ can be assumed. The relaxation of the combined electron dipolar and nuclear Zeeman term is assumed to be governed by the electron dipolar relaxation $T_{1,D}$. The combined rate $T_{1,n}$, however, is scaled by the large common heat capacity such that it can be expressed as:

$$T_{1,n} = T_{1,D} \frac{\langle \mathcal{H}_{e,D} \rangle + \langle \mathcal{H}_{n,Z} \rangle}{\langle \mathcal{H}_{e,D} \rangle} (1 + f)^{-1} \quad (2.66)$$

where the leakage factor $f$ accounts for all nuclear spin-lattice relaxation pathways other than the electron dipolar bath. With this, one can extend equations 2.64 and 2.65 to:

$$\frac{d\alpha}{dt} = -W(\Delta)(\alpha - \beta) - \frac{1}{T_{1,e}} (\alpha - \alpha_L) \quad (2.67)$$
$$\frac{d\beta}{dt} = W(\Delta) \left( \frac{\Delta^2}{L^2} \right) (\alpha - \beta) - \frac{1}{T_{1,n}} (\beta - \beta_L). \quad (2.68)$$

Considering the fact that the derivation given above is done in the (off-resonant) Zeeman interaction frame, where the dipolar and nuclear Zeeman interactions are unchanged, the relaxation term in equation 2.68 would be equal in a treatment in the
laboratory frame, hence
\[ \beta_L = \frac{1}{k_B T_L} \] (2.69)
is simply the inverse lattice temperature. For the same reason however, the equilibrium spin temperature in equation 2.67 has to be scaled by the interaction frame energy:
\[ \alpha_L = \beta_L \frac{\omega_e}{\Delta} \gg \beta_L. \] (2.70)
Note that it is precisely this scaling of the equilibrium spin temperature of the electron Zeeman bath in the rotating frame and its mixing with the electron dipolar bath described by Provotorov’s equations 2.67 and 2.68 that leads to the hyperpolarization of the dipolar bath.

For the steady-state case, equations 2.67 and 2.68 have to become static ($\frac{d\alpha}{dt} = \frac{d\beta}{dt} = 0$) and one can solve them for the static spin temperatures (neglecting $\beta_L$ in equation 2.68):
\[ \alpha_{st} = \alpha_L \frac{1 + W(\Delta) T_{1,n} \left( \frac{\Delta^2}{L^2} \right)}{1 + W(\Delta) T_{1,e} + W(\Delta) T_{1,n} \left( \frac{\Delta^2}{L^2} \right)} \] (2.71)
\[ \beta_{st} = \beta_L \frac{W(\Delta) T_{1,n} \left( \frac{\omega_e}{L^2} \right)}{1 + W(\Delta) T_{1,e} + W(\Delta) T_{1,n} \left( \frac{\Delta^2}{L^2} \right)}. \] (2.72)
If one defines an electron dipolar frequency $D$ in analogy to equation 2.62 as:
\[ D^2 = \frac{\text{Tr} \left\{ \hat{H}_{e,D}^2 \right\}}{\text{Tr} \left\{ \hat{S}^2 \right\}} \] (2.73)
and uses the expression 2.66 for $T_{1,n}$ one gets:
\[ T_{1,n} = T_{1,D} \left( \frac{L^2}{D^2} \right) (1 + f)^{-1} \] (2.74)
and can finally rewrite equation 2.72 to:

$$
\beta_{st} = \beta_L \frac{\omega_c}{\Delta} \frac{W(\Delta)T_{1,D} \left( \frac{\Delta^2}{D^2} \right) (1 + f)^{-1}}{1 + W(\Delta)T_{1,e} + W(\Delta)T_{1,D} \left( \frac{\Delta^2}{D^2} \right) (1 + f)^{-1}}. \quad (2.75)
$$

One can simplify equation 2.75 by assuming:

- **complete saturation**: In this case $W(\Delta)T_{1,e}$ and $W(\Delta)T_{1,D} \gg 1$ and equation 2.75 simplifies to:

$$
\epsilon = \frac{\beta_{st}}{\beta_L} = \frac{\omega_c \Delta}{\Delta^2 + \left( \frac{T_{1,e}}{T_{1,D}} \right) D^2 (1 + f)} \quad (2.76)
$$

- **complete saturation without leakage**: Here even $f = 0$ and the enhancement reads

$$
\epsilon = \frac{\omega_c \Delta}{\Delta^2 + \left( \frac{T_{1,e}}{T_{1,D}} \right) D^2} \quad (2.77)
$$

For this case one can calculate the upper limit of the maximum achievable polarization to be

$$
\epsilon_{max} = \pm \frac{\omega_c}{2D} \sqrt{\frac{T_{1,D}}{T_{1,e}}} \quad (2.78)
$$

at the off-center irradiation frequencies:

$$
\Delta_\pm = \pm D \sqrt{\frac{T_{1,e}}{T_{1,D}}} \quad (2.79)
$$

**Low-temperature case**

The Provotorov equations 2.64 and 2.65 cannot be applied for arbitrary cold temperatures since the truncation of the expansion series of the density operator becomes invalid. Borghini [16] derived an expression for the nuclear spin temperature valid at arbitrary temperatures under the restriction of a mainly inhomogeneously broadened EPR line and full saturation of on-resonant spins. The following theory is therefore known as the **Borghini model** [10, 16].

The condition of inhomogeneous broadening restricts the EPR line to be broadened either by an anisotropic $g$-tensor or because of hyperfine interactions with neighbor-
ing nuclei. For the spin-temperature hypothesis to be applicable there have to be internal interactions allowing a Boltzmann distribution of populations to be established. These interactions are assumed to be dipolar spin-spin couplings and it is the electron-electron cross relaxation that establishes a unique spin temperature within the bath of the EPR broadened line, the electron non-Zeeman reservoir. Hence, the EPR line has to be dominantly broadened by $g$-anisotropy or hyperfine interactions, however, additionally has to contain a smaller dipolar broadening \[10, 16\]. The dipolar broadening is assumed large enough to allow efficient cross relaxation while being small enough to be neglected in the overall Hamiltonian.

In the following, the terminology of Abragam and Goldman \[10\] is used and their derivation is followed for the case of EPR broadening by $g$-anisotropy in which the EPR line is composed of individual spin packets. For the ease of discussion, the electron Hamiltonian is separated in the (on-resonant) Zeeman term $\hat{H}_{e,Z}$ and the (off-resonant) term $\hat{H}_{NZ}$ referring to the non-Zeeman contribution which is broadening the EPR line. The system is described in the laboratory frame with the Hamiltonian:

$$\hat{H} = \hat{H}_{e,Z} + \hat{H}_{NZ} + \hat{H}_{n,Z} = \omega_e \hat{S}_z - \sum_i \Delta_i \hat{S}_i^z + \omega_n \hat{I}_z$$

(2.80)

where $\hat{S}_z$ and $\hat{I}_z$ are the total spin operators of all electron and nuclear spins, respectively. The operators $\hat{S}_i^z$ are sums over all electron spins with a common frequency offset within $\Delta_i \pm \delta$.

For this system, the density operator reads

$$\rho = \frac{1}{\text{Tr} \left\{ e^{-a \hbar \omega_e \hat{S}_z - \beta \hbar \left( \sum_i \Delta_i \hat{S}_i^z + \omega_n \hat{I}_z \right) } \right\} e^{-a \hbar \omega_e \hat{S}_z - \beta \hbar \left( \sum_i \Delta_i \hat{S}_i^z + \omega_n \hat{I}_z \right) }}$$

(2.81)

if again a close coupling of the electron non-Zeeman reservoir with the nuclear Zeeman reservoir is assumed. One can calculate the expectation values of the separate
Hamiltonians to be:

\[
\langle \hat{H}_{e,Z} \rangle = \frac{1}{2} N_e \omega_e \sum_i f_i P_{e,i} \tag{2.82}
\]

\[
\langle \hat{H}_{NZ} \rangle = -\frac{1}{2} N_e \sum_i f_i \Delta_i P_{e,i} \tag{2.83}
\]

\[
\langle \hat{H}_{n,Z} \rangle = \frac{1}{2} N_n \omega_n P_n \tag{2.84}
\]

where

\[ f_i = \frac{\text{# of electrons with } \Delta \in (\Delta_i \pm \delta)}{N_e} \]

with

\[
\sum_i f_i = 1 \quad \sum_i f_i \Delta_i = 0 \tag{2.85}
\]

is the relative weight of the spin packet \( i \) and its polarization:

\[
P_{e,i} = -\tanh \left[ \frac{\hbar}{2} \left( \alpha \omega_e - \beta \Delta_i \right) \right]. \tag{2.86}
\]

Taking into account spin-lattice relaxation and electron Zeeman transitions induced by microwave irradiation one finds for the rate equation of the electron Zeeman bath:

\[
\frac{d}{dt} \langle \hat{H}_{e,Z} \rangle = \frac{1}{2} N_e \omega_e \sum_i f_i \frac{dP_{e,i}}{dt} = -\frac{1}{2} N_e \omega_e \left( \frac{1}{T_{1,e}} \sum_i f_i (P_{e,i} - P_0) + U f_{mw} P_{e,mw} \right) \tag{2.87}
\]

where \( P_0 = -\tanh \left[ \frac{\hbar}{2} \alpha L \omega_e \right] \) is the electron thermal equilibrium polarization and \( U \) the microwave-induced transition rate while irradiating spin packet \( i = mw \). For the coupled electron non-Zeeman and nuclear Zeeman bath one finds:

\[
\frac{d}{dt} (\hat{H}_{n,Z} + \hat{H}_{NZ}) = -\frac{N_n}{2} \omega_n \frac{P_n - P_{n,0}}{T_{1,n}} + \frac{N_e}{2} \left( \frac{1}{T_{1,e}} \sum_i f_i \Delta_i (P_{e,i} - P_0) + U f_{mw} \Delta_{mw} P_{e,mw} \right) = -\frac{N_n}{2C} \omega_n \frac{P_n}{T_{1,n}} + \frac{N_e}{2} \left( \frac{1}{T_{1,e}} \sum_i f_i \Delta_i P_{e,i} + U f_{mw} \Delta_{mw} P_{e,mw} \right) \tag{2.88}
\]
where equation 2.85 was used in the second line. Furthermore, the relative concentration of free electrons \( C = \frac{N_e}{N_n} \) was introduced as well as the approximation \( |P_n| = \tanh \left( \frac{\hbar}{2} \beta \omega_n \right) \gg |P_{n,0}| \) for high nuclear polarization levels.

In the steady state both equations 2.87 and 2.88 have to become static. In this case one finds (by multiplying 2.87 with \( \Delta_{mw}/\omega_e \) and adding to 2.88):

\[
\sum_i f_i (\Delta_i - \Delta_{mw}) P_{e,i} + \Delta_{mw} P_0 - \frac{1}{C} \omega_n \frac{T_{1,e} T_{1,n}}{T_{1,n}} P_n = 0. \tag{2.89}
\]

The relation derived above still has two independent unknown, \( \alpha \) and \( \beta \) and, once again, for the low temperature case no general theory is known that connects both upon irradiation. However, for the case of saturating irradiation (saturating the irradiated spin packed \( i = mw \)) one knows that \( P_{e,mw} = 0 \) in equation 2.86 and hence

\[ \alpha \omega_e = \beta \Delta_{mw}, \tag{2.90} \]

a relation already found by Redfield in the rotating frame [58]. This relation essentially defines the inverse spin temperature of the electron non-Zeeman reservoir and with this the inverse spin temperature of the nuclear Zeeman reservoir. Hence, the polarization of packet \( i \) becomes \( P_{e,i} = -\tanh \left[ \frac{\hbar}{2} \beta (\Delta_{mw} - \Delta_i) \right] \) and one finally gets Borghini’s relation:

\[
\sum_i f_i (\Delta_{mw} - \Delta_i) \tanh \left[ \frac{\hbar}{2} \beta (\Delta_{mw} - \Delta_i) \right] = -\Delta_{mw} P_0 + \frac{1}{C} \omega_n \frac{T_{1,e} T_{1,n}}{T_{1,n}} P_n. \tag{2.91}
\]

The key assumption of the Borghini model is the saturation condition in equation 2.90. This assumption is questionable for many dissolution DNP setups where non-sophisticated oversized microwave containers are used, or at higher temperatures where the fast electron \( T_{1,e} \) hampers strong saturation. The largest drawback of this assumption however, is the fact that it neglects the EPR absorption line dependence of the saturation condition. In particular, it still allows full saturation at large offset frequencies \( \omega_{mw} \) where there is no EPR absorptive signal existent anymore. This leads to strongly overestimated wings in the DNP profile, as shown by, e.g., Ardenkjæer-Larsen [69].

Jannin et al. suggested in [68] to use the steady-state condition 2.87 together with
Borghini’s equation 2.91 as a set of two equations that one can solve numerically. This way, one obtains a frequency and microwave-strength dependent saturation and DNP profile. He showed that, with "rather arbitrarily" [68, p. 65] chosen parameters one can fit experimental data obtained under thermal mixing conditions much better than with the initial Borghini model.
2.3. Nuclear Cross Polarization

The technique of nuclear cross polarization (CP) was introduced by Hartmann and Hahn in 1962 [37] and has become a routine tool for solid-state NMR applications. Its general purpose is to transfer polarization from high-$\gamma$ to low-$\gamma$ nuclei in spin systems with strong homonuclear dipolar couplings as is the usual case for solid-state NMR. The basic pulse sequence is shown in figure 2.2 a). It consists of an excitation pulse generating transverse magnetization of the high-$\gamma$ spins followed by a simultaneous spin lock (SL) on both spin species. If the spin-lock amplitudes are chosen such that the nutation frequencies of both spin species are equal the transverse magnetization of the high-$\gamma$ nuclei can (partly) be transferred to the low-$\gamma$ nuclei.

A comprehensive theoretical treatment is given in [70] or can be found in [42]. A brief quantum mechanical description shall be given below for the situation of an isolated spin pair as well as the thermodynamic description of a static powder. The symbol "$I$" will be used for the high-$\gamma$ nucleus and "$Q$" for the low-$\gamma$ nucleus. This notation deviates from the common convention using $S$ for the low-$\gamma$ nucleus and is chosen here to allow the symbol $S$ to be used unambiguously for the electron spin.

![Figure 2.2.](image_url) Hartmann-Hahn cross polarization pulse sequence. The conventional pulse sequence for immediate detection of low-$\gamma$ magnetization (a) and the modified sequence to store generated low-$\gamma$ polarization as Zeeman polarization (b).
2.3.1. CP for the isolated spin pair

The spin Hamiltonian of a coupled heteronuclear spin pair under simultaneous on-resonant rf-irradiation (during the mixing period $t_m$) on both spins can be written in the laboratory frame as

$$\hat{H}_{\text{lab}} = \omega_{0,I} \hat{I}_z + \omega_{0,Q} \hat{Q}_z + \hat{H}_{I}\hat{Q} + 2\omega_{1,I} \cos(\omega_{0,I} t) \hat{I}_x + 2\omega_{1,Q} \cos(\omega_{0,Q} t) \hat{Q}_x$$

(2.92)

with the Larmor frequencies $\omega_{0,I}$ and $\omega_{0,Q}$ and the rf-nutation frequencies $\omega_{1,I} = -\gamma_I B_{1,I}$, and $\omega_{1,Q} = -\gamma_Q B_{1,Q}$ and the dipolar coupling term $\hat{H}_{I}\hat{Q}$. Note that the $J$-coupling is neglected in favor of the dominating dipolar coupling Hamiltonian.

One can apply the usual transformation into the Zeeman interaction frame for both nuclei (double-rotating frame) such that equation 2.92 simplifies to:

$$\hat{H} = \omega_D 2 \hat{I}_z \hat{Q}_z + \omega_{1,I} \hat{I}_x + \omega_{1,Q} \hat{Q}_x$$

(2.93)

where all non-secular contributions of the dipolar coupling have been neglected (compare section 2.1.1). The dipolar coupling strength is given as

$$\omega_D = \frac{\mu_0}{4\pi} \frac{\gamma_I \gamma_Q \hbar}{r_{i,j}^3} \left(1 - \frac{3}{2} \cos^2 \theta_{i,j} \right).$$

(2.94)

One can now transform further into a double-interaction frame of both rf-irradiation Hamiltonians $\omega_{1,I} \hat{I}_x$ and $\omega_{1,Q} \hat{Q}_x$ and obtain:

$$\hat{H}' = \omega_D 2 \hat{I}_z' \hat{Q}_z'$$

$$= \omega D 2 \left( \hat{I}_z \cos(\omega_{1,I} t) - \hat{I}_y \sin(\omega_{1,I} t) \right) \cdot \left( \hat{Q}_z \cos(\omega_{1,Q} t) - \hat{Q}_y \sin(\omega_{1,Q} t) \right)$$

$$= \omega D 2 (\hat{I}_z' \hat{Q}_z \cos(\omega_{1,I} t) \cos(\omega_{1,Q} t)$$

$$- \hat{I}_y \hat{Q}_y \cos(\omega_{1,I} t) \sin(\omega_{1,Q} t)$$

$$- \hat{I}_x' \hat{Q}_z \sin(\omega_{1,I} t) \cos(\omega_{1,Q} t)$$

$$+ \hat{I}_y' \hat{Q}_y \sin(\omega_{1,I} t) \sin(\omega_{1,Q} t))$$

(2.95)

Finally, in the case of the Hartmann-Hahn match:

$$\omega_{1,I} = \omega_{1,Q}$$

(2.96)
the Hamiltonian during the mixing period can be given as:

\[ \mathcal{H}' = \omega_D 2(\hat{I}_z \hat{Q}_z (\frac{1}{2} + \frac{1}{2} \cos(2\omega_1 t)) ) - \hat{I}_z \hat{Q}_y \frac{1}{2} \sin(2\omega_1 t) - \hat{I}_y \hat{Q}_z \frac{1}{2} \sin(2\omega_1 t) + \hat{I}_y \hat{Q}_y (\frac{1}{2} - \frac{1}{2} \cos(2\omega_1 t))) \]

\[ \approx \frac{\omega_D}{2} 2\hat{I}_z \hat{Q}_z + \frac{\omega_D}{2} 2\hat{I}_y \hat{Q}_y \] (2.97)

with the truncation to the secular part applied in the last line.

Without loss of generality one can describe the transverse magnetization of the $I$-spins generated by the first pulse in the CP-pulse scheme (figure 2.2) as $\hat{I}_x$. Note that both in the double-rotating frame of the Zeeman interactions as well as in the frame of the Zeeman plus rf-interactions $\hat{I}_x$ (as well as $\hat{I}_y, \hat{Q}_x, \hat{Q}_y$) has the same form. The evolution under the Hamiltonian in equation 2.97 during the mixing period can be written using the product operator formalism (see [40, 71]) as:

\[ \hat{I}_x \left( \frac{1}{2} \omega_D t \right) 2\hat{I}_z \hat{Q}_z \rightarrow \hat{I}_x \cos \left( \frac{1}{2} \omega_D t \right) + 2\hat{I}_y \hat{Q}_z \sin \left( \frac{1}{2} \omega_D t \right) \]

\[ \left( \frac{1}{2} \omega_D t \right) 2\hat{I}_y \hat{Q}_y \rightarrow \hat{I}_x \cos^2 \left( \frac{1}{2} \omega_D t \right) - 2\hat{I}_z \hat{Q}_y \cos \left( \frac{1}{2} \omega_D t \right) \sin \left( \frac{1}{2} \omega_D t \right) 
+ 2\hat{I}_y \hat{Q}_y \sin \left( \frac{1}{2} \omega_D t \right) \cos \left( \frac{1}{2} \omega_D t \right) + \hat{Q}_x \sin^2 \left( \frac{1}{2} \omega_D t \right) \]

\[ = \hat{I}_x \frac{1 + \cos(\omega_D t)}{2} + \hat{Q}_x \frac{1 - \cos(\omega_D t)}{2} \]

\[ - 2\hat{I}_z \hat{Q}_y \frac{1}{2} \sin(\omega_D t) + 2\hat{I}_y \hat{Q}_z \frac{1}{2} \sin(\omega_D t) \] (2.98)

For the discussed ideal case, equation 2.98 shows that during the mixing period the initial $\hat{I}_x$ is periodically interconverted between $\hat{I}_x$ and $\hat{Q}_x$.

Simultaneously, anti phase coherences are generated (last line of equation 2.98). Considering $\sin(-x) = -\sin x$ and the fact that in a powder there will be a symmetric distribution of $\omega_D$ values around $\omega_D = 0$ due to its orientation dependence, these
terms can be neglected for powder systems and one gets the evolution of $\hat{I}_x$

$$\hat{I}_x \xrightarrow{\mathcal{H}_I} \hat{I}_x \frac{1 + \cos(\omega_D t)}{2} + \hat{Q}_x \frac{1 - \cos(\omega_D t)}{2}. \quad (2.99)$$

### 2.3.2. Thermodynamic description of CP

In multi-spin systems with a random distribution of dipolar coupling tensor orientations it can be convenient to describe the Hartmann-Hahn CP in terms of spin thermodynamics. Its concepts have been introduced in section 2.2.3.1 and will be applied here. The derivation follows mainly the discussion given in [72].

The ensemble of $I$ and $Q$ spins of abundance $N_I$ and $N_Q$ will be described using canonical density operators as given in equation 2.22 with unique inverse spin temperatures $\beta_I$ and $\beta_Q$. Additionally, the following thermodynamic quantities have to be defined for the spin ensembles (restricting the discussion to the high-field approximation and spin-1/2 nuclei):

- **Curie constant**: 
  \[ C_i = \frac{N_i}{3} I_i (I_i + 1) \gamma_i^2 \hbar = \frac{1}{2} \frac{N_i}{4} \gamma_i^2 \hbar \quad (2.100) \]

- **Energy**: 
  \[ E_i = -\frac{N_i}{4} \gamma_i^2 \hbar^2 \beta_i B_0 = -\hbar \beta_i C_i B_0^2 \quad (2.101) \]

- **Polarization**: 
  \[ P_i = c_{\alpha} c_{\alpha}^* - c_{\beta} c_{\beta}^* = \frac{1}{2} \beta_i \hbar \gamma_i B_0 \quad (2.102) \]

- **Magnetization**: 
  \[ M_i = \frac{1}{2} \hbar \gamma_i N_i P_i = \hbar \beta_i C_i B_0 \quad (2.103) \]

where $c_{\alpha,\beta} c_{\alpha,\beta}^*$ stands for the diagonal entries of the density operator at internal equilibrium.

To allow the combination of DNP with CP, the derivation is started with the $I$ and $Q$ spins being at internal equilibrium but possibly at different, non-thermal equilibrium spin temperature $\beta_i^0 \neq \beta_Q^0 \neq \beta_L$. Furthermore, a $90^\circ$ pulse is applied on the $Q$ spins in analogy to the $I$ spins at the beginning of the sequence and for both spins $-90^\circ$ pulses at the end of the sequence (figure 2.2 b). This allows the transferred magnetization on $Q$ and the remaining $I$ magnetization to be stored as Zeeman polarization.

(i) $90^\circ$ pulses are assumed to preserve the magnetization of both nuclear species. Hence, after the excitation pulses the magnetization vectors lie in the transverse
plane with magnitude:

\[ M_1^i = hC_i\beta_i^0 B_0 \quad \text{for } i = I, Q. \]  

(ii) The rf term in the rotating frame can be assumed to be dominant if the spin-locking field strength on both nuclei is larger than the internal interactions (mainly the homo and heteronuclear dipolar couplings). In this case it is possible to describe both spin systems with canonical density operators with rotating-frame Zeeman spin temperatures. Since both magnetizations are defined by the first 90°-pulses one can calculate the rotating-frame spin temperatures to be:

\[ M_1^i = hC_i\beta_i^0 B_0 = hC_i\beta_i^1 B_{1,i} \]
\[ \beta_i^1 = \frac{\beta_i^0 B_0}{B_{1,i}} \]  

such that \( \beta_i^1 \gg \beta_i^0 \) since usually \( B_0 \gg B_1 \).

(iii) During the spin lock the heteronuclear dipolar couplings lead to a mixing and finally equilibration of both rotating-frame spin temperatures. During this period, the total spin energy has to be preserved, such that:

\[ E^I_1 + E^Q_1 = E^\text{final} \]
\[ \hbar \beta^1_I C_i B^2_{1,i} + \hbar \beta^1_Q C_i B^2_{1,Q} = \hbar \beta^1_F \left( C_i B^2_{1,i} + C_i B^2_{1,Q} \right). \]  

One can define the constant

\[ \mu = \frac{C_i B^2_{1,Q}}{C_i B^2_{1,i}} = \frac{N_Q}{N_I} \]  

where the right-hand side holds if the Hartmann-Hahn match (\( |\gamma_I B_{1,i}| = |\gamma_Q B_{1,Q}| \)) is met. With this, the final common rotating frame spin temperature reads:

\[ \beta_F^1 = \frac{\beta^1_I C_i B^2_{1,i} + \beta^1_Q C_i B^2_{1,Q}}{C_i B^2_{1,i} + C_i B^2_{1,Q}} \]
\[ \beta_F^1 = \frac{1}{1 + \mu} \left( \beta_F^1 + \mu \beta_Q^1 \right). \]
(iv) In analogy to equation 2.105, the $-90^\circ$-pulses at the end of the sequence regenerates Zeeman inverse spin temperature:

$$\beta_i = \beta_i^1 \frac{B_{1,i}}{B_0}. \quad (2.109)$$

Using equation 2.105 for $i = I, Q$ in equation 2.108 and plugging 2.108 into equation 2.109 the final reached inverse spin temperature on the low-$\gamma$ nuclei reads:

$$\beta_Q = \left[ \frac{1}{1 + \mu} \left( \beta_i^0 \frac{B_0}{B_{1,i}} + \mu \beta_Q^0 \frac{B_0}{B_{1,Q}} \right) \right] \frac{B_{1,Q}}{B_0} \beta_Q = \frac{1}{1 + \mu} \left( \beta_i^0 \frac{\gamma I}{\gamma_Q} + \mu \beta_Q^0 \right). \quad (2.110)$$

Equation 2.110 shows the dependence of the final inverse spin temperature in the laboratory frame as function of the relative concentrations of $I$ and $Q$ spins and their initial inverse spin temperature prior to the CP pulse.

For the case of sparse $^{13}$C compared to $^1$H nuclei $\mu \ll 1$ and if the CP is conducted after the spin systems has reached thermal equilibrium, the CP enhancement reads

$$\epsilon_{CP} \equiv \frac{\beta_Q}{\beta_Q^0} = \frac{\gamma I}{\gamma_Q} \approx 4.$$

Further implications of this equation will be discussed in section 4.1.
3. Instrumentation

In this chapter a general description will be given of the cryogenic setup assembled in this work before introducing all components needed for low-temperature DNP experiments, optionally including dissolution capability. A single-sample DNP probe as well as a multi-sample dissolution DNP probe realized in this work will be introduced.

Part of this work has been published in [73] and has been realized together with Dr. Marcin Krajewski. Andreas Hunkeler did the majority of the mechanical realization of the in-house built components. Alexander Däpp and Oliver With designed and realized the rf tuning and matching circuits. They were also responsible for the implementation of various electronic parts. Martin Gimmersky optimized the microwave cavity using numerical simulations.

The system is based on a helium-temperature cryostat that is mounted in a 7 T Bruker wide-bore (89 mm) magnet charged to 3.35 T. The system is shown schematically in figure 3.1.
Figure 3.1. Schematic drawing of the complete DNP system including dissolution capability. The flow-type cryo system consists of an external liquid-helium supply dewar (1) connected to the variable-temperature cryostat (2) via a vacuum shielded transfer line. Helium is dragged into the sample space by evacuating the cryostat with two vacuum pumps (3) connected in series. The DNP probe (4) is mounted and sealed to the cryostat within the bore of the magnet. A microwave source (5) is connected to the waveguide leading to the sample space. For the dissolution probe the dissolution system (6) is attached to the tubing of the dissolution stick (7) for dissolution and shuttling to the nearby NMR/MRI spectrometer. An OPENCORE NMR console (8) is used to monitor the nuclear polarization while the entire system is controlled by LabVIEW software (9). Dotted lines indicate data communication pathways.
3.1 Cryogenic System

The DNP probes are inserted in a cryo system that consists of a variable-temperature insert (VTI), a liquid-helium transfer line, and vacuum pumps. An ITC-503 controller (Oxford Instruments) is used for temperature regulation.

The VTI is a SpectrostatNMR cryostat (Oxford Instruments) working with a continuous liquid-helium flow drawn through the transfer line from a liquid-helium supply dewar. A needle valve controlled by a stepper motor regulates the flow of liquid helium. Through a capillary, the helium is guided to the bottom of the cryostat and enters the sample space.

For initial cool-down and for operation at temperatures above 3 K, the cryostat is pumped by an oil-free piston pump (GF4, Oxford Instruments). In this mode, the exhaust gas is pumped through a tube surrounding the helium-supply capillary within the transfer line. Thereby, the transfer line is precooled by the exhaust helium gas reducing the overall consumption of liquid helium.

For temperatures below 3 K, the evaporated helium is pumped directly through an exhaust port on the cryostat. Large diameter tubing (ISO-KF 40) minimizes the pressure drop along the exhaust line. For this purpose two pump stands have been assembled both consisting of one roots pump backed by a rotary vane pump:

1. roots pump: Okta 250 A, Pfeiffer Vacuum; rotary vane pump: SV40B, Oerlikon Leybold Vacuum

3.1.1 Cryogenic performance

The following data has been measured on the multi-sample dissolution DNP probe. This probe exhibits a larger overall heat conductivity compared to the single-sample DNP probe if both are equipped with equal NMR transmission lines (section 3.6). Therefore, the performance results given below can be understood as a lower limit for both probes.

The initial cool-down of the system to below liquid-helium temperature is conducted by pumping on the cryostat through the transfer line exhaust tube with a
fully opened needle valve of the liquid-helium supply. This takes approximately 50 min and uses 3-6 l of liquid helium. The system can be operated in three cryogenic modes:

1. For inter-experimental periods, e.g., over-night parking, the system is kept at 20 – 80 K by weakly pumping on the transfer line exhaust tube with the helium-supply needle valve opened 8 – 15%. In this mode the cryogenic consumption is below 0.4 l of liquid helium per hour.

2. In continuous mode, the helium needle valve is kept partially open while the system is pumped to low vacuum using one of the pump stands. This allows experimental periods of constant low temperatures limited in time only by the liquid-helium supply dewar. The system reaches temperatures down to 1.9 K with 4 l of liquid helium per hour.

3. Lowest temperatures are reached in single-shot mode. For this mode the cryostat is first filled with liquid helium. Subsequently, the helium-supply needle valve is closed and the cryostat pumped to < 2 mbar. For microwave irradiation below 30 mW on the dissolution probe, the system reaches a single-shot temperature of ~ 1.3 K for a maximum duration of < 3 h with a liquid-helium consumption of 0.13 l per hour.

The helium-supply dewar can be changed at probe temperatures of 4.2 K or higher after pressurizing the cryostat to atmospheric pressure. Samples can also be loaded at temperatures of 4.2 K or higher for both probes. On the multi-sample dissolution probe the revolver mechanism was found to work at all achievable temperatures and pressures. The samples could be interchanged reliably between cavity and dissolution port at any time during the DNP experiments. If working with the multi-sample probe, the system is heated to 80 K and evacuated for 5 min after sample loading. This is done to prevent traces of contamination gases from freezing and blocking the revolver mechanism.

### 3.2. Microwave source

Two similar microwave sources are available: a model VCOM-10/94/200-DD (ELVA-1) ("DD model") that can provide up to 180 mW of continuous wave (cw) power at
frequencies between 93.75 and 94.25 GHz and a model VCOM-10/94/200-DP (ELVA-1) ("DP model") providing up to > 170 mW over an extended frequency range of 93.5 to 94.5 GHz. Both sources supply microwaves in the TE$_{1,0}$ mode in a WR10 waveguide.

Both sources feature a voltage-controlled power attenuator (0 – 40 dB). For amplitude-modulated LOD experiments (see section 3.5.4), the microwave source is operated in cw mode with an analog amplitude modulation signal fed to its power attenuator. For this operation a fast switching time of the microwave source is important. The response time was measured on the DD model at the center frequency (94 GHz) at different cw power levels. The attenuation signal was a 1 kHz rectangular signal of 0 and 40 dB attenuation amplitude. The response time for the attenuation was measured to $\tau_{\text{fall}} = (100 \pm 2) \mu$s and the relaxation time to $\tau_{\text{rise}} = (112 \pm 2) \mu$s (figure 3.2).

![Power response of the DD model microwave source to a 1 kHz rectangular power modulation signal.](image)

**Figure 3.2.** Power response of the DD model microwave source to a 1 kHz rectangular power modulation signal.

### 3.3. NMR spectrometer and rf circuit

Both probes allow $^{13}$C and $^1$H NMR experiments at cryogenic temperature. This is achieved with an OPENCORE NMR spectrometer [74] of which major components
have been donated by Dr. Kazuyuki Takeda. The spectrometer is controlled via the Opencore NMR software by Takeda or a LabVIEW implementation by Marcin Krajewski (section 3.7). The rf circuitry between the spectrometer and the probes tuning/matching circuits consists of:

- corresponding to the demands: a BLAX1000 (1 kW), a AMT 1 kW, and a BLAX300 (300 W) broadband amplifier used for $^1\text{H}$ and $^{13}\text{C}$,

- a high-power bandpass filter on the $^1\text{H}$ transmit channel to allow $^1\text{H}$ decoupling using the broadband amplifiers,

- a passive $\lambda/4$-switch on the circuit of the nucleus to be detected [75],

- a 26 dB preamplifier (build by Marcin Krajewski),

- and low-power bandpass filters on both receiving channels.
3.4. Probe 1: Single-sample DNP probe

The DNP probe described is home built for the use of static solid-state DNP experiments at temperatures down to 1.3 K without dissolution capabilities. Its skeleton is a single glass-fiber tube (18 mm inner diameter, 1 mm wall thickness) to reduce thermal conductivity to the cryo space. An overview of the probe is given in figure 3.3 and a close up of the sample-space area of the probe in figure 3.4 a).

3.4.1. Microwave guides

The microwaves are guided into the cryostat through a WR28 copper waveguide. The last 60 cm of waveguide to the sample space are made from stainless steel (non-plated) to reduce thermal conduction. Immediately above the sample, the WR28-waveguide is converted to a circular 4 mm Cu waveguide.

At the magnetic field of 3.35 T, the EPR wavelength is 3.2 mm and the dominant mode in the circular waveguide is TE_{1,1} with its electric field oriented radially with the magnet symmetry. In this mode the 90° elbow guides the microwaves to the sample with less than 1 dB losses as shown in figure 3.4 b). The axis of the waveguide-elbow ending and the direction of microwave propagation equals the NMR solenoid axis. The microwaves are therefore irradiated into the sample with the magnetic field aligned in the \( x - y \) plane of the magnet.

Figure 3.3. Overview of the single-sample DNP probe.
3.4. Instrumentation

3.4.2. NMR circuitry

The losses on the entire setup were measured by comparing the power (detected with a zero-bias microwave diode, ZBDA-10/94/20, Elva-1) reaching the probe to the power reaching the end of the 90° elbow. The transmission losses are −7.6 dB averaged over incident power settings of 10, 40, 80, 120, and 180 mW.

The NMR circuit is based on the McKay design [76] for cryogenic NMR probes. Besides the simplicity of this setup, the reason for this choice was the absence of capacitors in the cold space minimizing the tuning and matching sensitivity to temperature changes. The NMR transmission line (inner and outer conductor: Cu) with the NMR coil and sample container (that has 4 mm outer diameter and is inserted directly into the coil) is inserted into the system through the central glass-fiber tube. This allows changing of samples without warming of the entire probe and can be done at any
temperature above 4.2 K and ambient pressure.

The NMR circuit is double-tuned to 142 MHz \(^1\text{H}\) and 35 MHz \(^{13}\text{C}\) by tuning and matching components located outside the probe at ambient temperature \((Q(\text{H}) = 84, Q(\text{C}) = 36)\). The probe allows rf-field amplitudes corresponding to a nutation frequency of 100 kHz using 280 W on the proton and 270 W on the carbon channel.

### 3.4.3. Sensor system

**Helium-level sensor**

The sample space of the cryostat can be filled with liquid helium. It is essential to be able to monitor the level of liquid helium during cryogenic operation. For this purpose a capacitive helium-level sensor has been incorporated into the probe. It consists of two 220 mm long coaxial cylindrical electrodes with a radius of 1.5 mm (outer radius of inner electrode) and 4.25 mm (inner radius of outer electrode). Holes are drilled into the top and bottom end of the outer cylinder to allow helium to enter the space in-between the electrodes. Figure 3.5 shows a schematic cross section of the sensor.

The capacity of the coaxial cylinder capacitor can be calculated using the formula

\[
C = 2\pi \varepsilon_0 \varepsilon_r \frac{L}{\ln \left( \frac{R_2}{R_1} \right)}
\]

with the vacuum permittivity \(\varepsilon_0 = 8.854 \times 10^{-12} \text{ Fm}^{-1}\), the relative permittivity \(\varepsilon_r\) of the material filling the space in-between the electrodes, the length of the cylinder \(L = 220 \text{ mm}\), and the radii \(R_2\) (outer electrode) and \(R_1\) (inner electrode). For vacuum \((\varepsilon_r = 1)\) one can calculate a capacitance of

\[
C_{\text{air}} = 11.75 \text{ pF}.
\]

**Figure 3.5.** Cross section of the helium-level sensor used in the single-sample probe (lengths in mm).
If liquid helium ($\varepsilon_r \approx 1.05$ [77]) fills the sensor the capacity changes by 0.59 pF, or

$$\Delta C = 0.59 \frac{h}{220} \text{ pF}$$

with the helium level $h$ in mm.

The capacity is read out by a capacitance-to-digital converter (AD7746, Analog Devices). This device has a sensitive dynamic range of $\pm 4$ pF on top of additionally up to 17 pF common mode (offset) capacitance and is therefore able to cover the full range of the He-sensor. Calibration of the sensor and conversion from capacitance to helium level in % is done in the LabVIEW control software (section 3.7).

**Temperature sensor**

To be able to determine the temperature of the sample a Cernox resistor (Lake Shore Cryotronics Inc.) has been positioned on the height of the NMR coil. The sensor is rated from 1.4 to 325 K. Since it was calibrated down to 1.202 K (by Lake Shore) it is used in this setup down to this temperature.
3.5. Probe 2: Multi-sample dissolution DNP probe

A multi-sample dissolution DNP probe was built for dissolution DNP purposes (figure 3.6). It exhibits the following features:

- Multi-sample functionality using a revolver-style sample changer: The probe was built for sequential polarization of up to six samples. It is intended for the pre-polarization of multiple samples for repetitive in-vivo dissolution DNP experiments.

- A resonant microwave cavity: It is used to increase the DNP efficiency at low incident microwave power, reducing heating of the sample during microwave irradiation.

- EPR detection: A solenoid with vertical axis is wound around the microwave cavity allowing amplitude-modulated longitudinal EPR detection.

- Two NMR circuits: A simple saddle coil with a single-tuned NMR circuit is included in the cavity to follow the polarization degree during DNP. A second saddle coil can be used for multinucleus NMR experiments.

3.5.1. The revolver

The key feature of the multi-sample probe is the "revolver", allowing up to six samples to

![Figure 3.6. The multi-sample dissolution DNP probe. The top end holds the vertical (1) and rotational (2) pneumatics for the revolver mechanism, the dissolution-port tube (3) and microwave guide (4) run from there to the cryo space (figure 3.7).](image)
be loaded, polarized, and dissolved separately. The system allows exchanging the samples at cryogenic temperature. Polarization, NMR, and EPR measurement can be carried out at the location of the cavity, while sample loading, unloading, and dissolution are performed at a second location. The principal design is shown in figure 3.7.

Figure 3.7. The revolver-style lower end of the DNP probe. The rotationally and vertically movable axis (1) connects the room-temperature space to the sample holder platform (2). Six bottom-closed cylinders (3) can be combined with the top part of the cavity (4) to form the resonant microwave structure. The dissolution port (5) runs from room-temperature to the sample space guiding the grabber (6) to reach the sample cups (7). A pin-in-channel system (8) guides the revolver mechanism to open, rotate, and close to the correct positions.

A central shaft is mounted such that it can be rotated and moved up and down, thereby connecting the room-temperature high-pressure top section of the DNP probe with the sample area. At the lower end, a platform is attached featuring six equivalent sample holders. Each holder is a bottom-closed cylinder forming the lower half of the microwave cavity. The design exhibits a rotational symmetry that is broken by three unique sites that are at fixed positions within the probe: the top part of the microwave cavity and the dissolution port located opposite one another with respect to a rotation of the revolver and the position of the CP coil (section 3.5.5). This leads to six distinct revolver positions in which one of the six samples is in the cavity and another sample
in the dissolution-port position.

### 3.5.2. Microwave cavity

The microwave cavity is designed with two goals in mind: First, to effectively use the microwave power, allowing for cost-effective sources, the quality factor (Q) of the resonant cavity should be high, and second, to reduce heating, the excited microwave magnetic field should be concentrated within the sample volume and - at the same time - the electric field at the location should be minimized to avoid direct sample heating. While the latter cannot be fully achieved for sample sizes larger than the microwave wavelength, oversized (multi-mode) cavities allow the available microwave power to be concentrated at the sample location.

![Diagram of the microwave cavity](image)

**Figure 3.8.** (a) The microwave cavity. Top (1) and bottom (2) part of the oversized resonant microwave structure, NMR coil (3), EPR coil (4), microwave guide inlet being the wave guide cross section (5), sample cup (6) with closing lid (7), and brass rods (8) for optimizing the microwave field and stabilizing of the sample cups. (b) Cross section through the microwave cavity. Overlaid is the simulated normal component of the microwave B-field, plotted in dB units with respect to the maximum B-field found at the entrance of the microwave guide into the cavity (simulation by Alexander Däpp, ETH). The metallic rods (8) promote the homogenization and concentration of the microwaves in the sample space (9).

The cavity is shown in figure 3.8 a. It has been optimized by Martin Gimmersky, using numerical simulations (CST Microwave Studio), to maximize and homogenize the fields within the sample volume (figure 3.8 b). For this purpose, eight metallic
rods are placed inside the cavity. The four located in the lower part of the cavity additionally facilitate accurate positioning of the sample cup. For the exact dimensions of the cavity used in the simulations see appendix B.

The cavity shown in figure 3.8 is built from non-magnetic brass and composed of an upper and lower part such that it can be opened for changing the samples. To ensure correct closing of the cavity, the six lower halves are mounted on sapphire beads acting as spherical bearings (<100 µm play). Correct functioning of the closing mechanism is checked using a vertical lift monitor (section 3.5.6).

**Cavity efficiency**

An additional NMR probe was built that can be inserted into the dissolution port to conduct NMR experiments on the sample cup in the dissolution-port position. This "NMR stick" is a 6 mm outer diameter semi-rigid rf-transmission line (both conductors Cu) with a vacuum-tight sealing to the top end of the dissolution port. An NMR saddle coil allows free movement of the sample revolver system. With the NMR stick, DNP experiments were conducted on samples outside the cavity to compare the DNP efficiency inside and outside the cavity (Note that this experiment was conducted before the CP-coil (section 3.5.5) has been incorporated into the probe. Otherwise the CP-coil would have been sufficient for the described experiment). For a sample containing 16.2 mM trityl, 1 mM Gd in [1-13C]pyruvic acid the dependence of the polarization levels on the microwave power was measured at 1.4 K inside the closed cavity and outside the opened cavity.

Figure 3.9 shows the DNP efficiencies for both experiments. The polarization inside the cavity decreases with power levels above 20 mW. At 180 mW of microwave power the temperature of the sensor on the cavity shows an increase of 0.23 K (17%) compared to the temperature at a microwave power of 20 mW. The polarization profile for the sample outside the opened cavity shows that the saturation condition is not yet reached at a microwave power of 180 mW where the polarization reaches 25%. This polarization level could be, however, accepted as sufficient if complemented with fast-successive dissolution experiments.

It has been observed that even with closed cavity there is sufficient microwave power exiting the cavity so that the remaining samples experience DNP. The source for this leakage has not been identified but is assumed to be due to either the helium
Figure 3.9. Dependence of the steady-state solid-state $^{13}$C DNP polarization inside the cavity (circles) and in the dissolution-port position with opened cavity (crosses) as a function of the microwave power (1.4K).

exchange hole in the lower parts of the cavity or imperfect closing of the cavity leading to a slit of <50 $\mu$m (where 50 $\mu$m is the estimated accuracy of the lift monitor, section 3.5.6). Due to strong variations in reproducibility the extent of DNP experienced outside the closed cavity has not been quantified.

3.5.3. Microwave circuit

The microwaves are guided to the cavity from the microwave source via a multi-stage microwave guide. The source supplies microwaves in a WR10 waveguide (section 3.2). After an isolator (ELVA-1, IS-10/94/2) and a circulator (ELVA-1, CR-10/94/2), the microwaves are converted into the oversized WR28 to reduce losses during transmission to the sample area. After this conversion to WR28 outside the probe the wave guide consists of:

1. a 90° WR28 bend (Cu) to redirect the initially horizontal transmission axis to point vertically down the probe;

2. a vacuum seal (70 $\mu$m thick Mylar foil). This is necessary to allow cryogenic operations that include generation of low vacuum in the cryostat;

3. two successive ~ 40 cm WR28 silver-plated stainless steel waveguides;
4. a 60° axial twist for geometrical reasons;

5. a downconversion to WR10 for coupling to the microwave cavity.

6. (the final redirection of the transmission axis to the horizontal plane is achieved within the cavity structure as shown in figure 3.8 (5). This is not considered as part of the waveguide structure anymore.)

The losses with and without the Mylar foil were determined in a similar manner as described in section 3.4.1. The overall transmission loss of the waveguide was determined to $-1.16 \, \text{dB}$ of which $-0.16 \, \text{dB}$ trace back to the Mylar foil, $-0.6 \, \text{dB}$ to the combination of 90°-bend and 60°-twist, and the remaining $-0.4 \, \text{dB}$ to the silver-plated straight wave guides.

![Figure 3.10. Cavity reflection measurements. At an incident power of 180 mW, the transmission losses through the 90°-bend and 60°-twist combination was determined (“Transmission through 90-60”) as well as the reflection on the cavity (including the 90-60 combination) with different loads. The data is plotted as power dB compared to the mean of the reference measurement of the incident microwave power (“Transmission reference”). The coupling to the microwave cavity was quantified by reflection measurements. Figure 3.10 shows power reflections of the cavity with different loads, given in dB.](image-url)
The data is normalized to the incident microwave power ("Transmission reference") and yields an average of $-19.4 \, \text{dB}$ reflection of the three measurements with an $\text{H}_2\text{O}$ load. Since for the reflection measurements the $90^\circ$-bend and $60^\circ$-twist combination had to be included, their common attenuation has to be added twice to the reflection data. Therefore, the cavity reflection with load was found to be $-18.2 \, \text{dB}$.

3.5.4. Longitudinal detected EPR

For monitoring of the EPR spectrum under DNP conditions, a solenoid EPR coil was wound on the outer surface of the cavity to enable longitudinal detection (LOD) of EPR [78]. In the implementation chosen here, amplitude modulation of cw microwave irradiation is used to periodically saturate the electron magnetization. The resulting time-dependent longitudinal magnetization then induces an alternating voltage in the EPR coil with an axis parallel to $B_0$.

3.5.4.1. LOD EPR circuit

In LOD EPR modulation frequencies in the range of 1 kHz are used. In the area of the EPR coil, the brass wall of the cavity was chosen to be only 400 $\mu\text{m}$ thin, below 10% of the skin depth of brass at the frequency of 1 kHz. Therefore, changes in the longitudinal electronic magnetization are able to penetrate through the cavity wall.

The general EPR setup is shown schematically in figure 3.11 and consists of four subunits. A computer for signal controlling and detection, a data acquisition and signal generation device, the microwave source with variable power, and the detection circuit. On the controlling computer, a periodic signal is generated for amplitude modulation and homodyne detection of the LOD signal is performed using a NI data acquisition (DAQ) device (NI USB-6229 DAQ). The amplitude modulation signal is supplied by the DAQ digital to analog converter, amplified and fed to the microwave power attenuator.

The EPR detection circuit consists of a copper coil (380 turn and 100 $\mu\text{m}$ diameter wire) aligned parallel to the $B_0$ field. The circuit is non-resonant and well isolated from ground to minimize cross talk with the power-modulation signal. The coil is connected in differential mode to an audio preamplifier (SSM2019) followed by an active 50 kHz low-pass filter preventing high-frequency noise to be aliased during
data sampling.

3.5.4.2. LOD detection and sensitivity

The modulation of the microwave power is chosen using a rectangular periodic signal. The frequency of the signal is optimized considering the longitudinal relaxation time of the electrons (ranging from $T_{1,e} \gtrsim 1$ s to $\ll 1$ ms depending mainly on the radical and temperature [69, 79]) and the reaction time of the microwaves power modulation. Latter was measured to $\tau_{\text{fall}} = (100 \pm 2) \mu$s and $\tau_{\text{rise}} = (112 \pm 2) \mu$s (section 3.2). If full attenuation and recovery of the microwave power is desired, $\approx 5\tau_i$ should be used as minimum duration of the attenuation/recovery period. The signal frequency is therefore limited to $< 1$ kHz. Figure 3.12 shows the dependence of the steady-state microwave power over one period of 1 ms for different attenuation strengths. Figure 3.12 b) shows that $2 - 3$ V attenuation is sufficient for the 1 kHz operation, where the actual power difference between high and low-power periods is maximum. An optimum modulation frequency of 675 Hz was found in an effort to minimize cross talk and interfering signals from the surrounding.
The homodyne detection of the response of the electron magnetization to the modulation signal is realized digitally in the controlling PC. The signal is continuously digitized with 135 kHz sampling rate by the DAQ. On the fly, blocks of 200 sampled points (each block corresponding to a full modulation period) are added in a point-by-point manner. This summation corresponds to a digital down-mixing with the modulation frequency and a lock-in integration at the same time. An example of the resulting averaged signal of one modulation period is shown in figure 3.13 for the microwave frequency set to the maximum of the EPR absorption line ("on-resonant") and to a point in the wing of the EPR line ("off-resonant"). The intensity in the EPR spectrum at the corresponding microwave frequency is calculated by summation over the absolute values (after subtracting the bias) of the LOD signal.
The LOD signal intensity is proportional to the first time derivative of the electron magnetization, i.e., the electron longitudinal relaxation rate and the saturation efficiency. To investigate the temperature dependence, LOD EPR measurements were conducted on a sample containing 50 mM TEMPO in (1/1)\textsubscript{vol} D\textsubscript{2}O/ Glycerol at temperatures between 1.3 K and 71 K (figure 3.14). Figure 3.15 summarizes the extracted signal-to-noise ratios (SNR) for equal acquisition parameters as a function of the sample temperature (675 Hz saturation frequency, 51 points per spectrum, 377 s of acquisition time per spectrum). The SNR per 377 s of acquisition time at 2 K equals one, making LOD measurements during exact DNP conditions below 2 K impractical. The reason for this decrease in SNR is the dependence of the LOD signal on the longitudinal relaxation-rate of the electron. Below liquid-helium temperatures, the relaxation time increases to an extent such that the change in magnetization becomes too slow to induce a detectable voltage in the EPR coil.
Since the shape of the EPR resonance is not expected to change considerably below 10 K, the chosen setup has proven to suffice for EPR measurements close to the DNP conditions. Figure 3.16 shows an example of two EPR spectra of a (1/1)\textsubscript{vol} D\textsubscript{2}O/Glycerol sample containing 50 mM TEMPO (dotted line) and additional 16 mM trityl (solid line).

The LOD signal intensity was further monitored for different radical concentrations. LOD spectra of samples containing [\textsuperscript{1-13}C]pyruvic acid doped with 5, 13, 15, 17, and 25 mM of the trityl radical were acquired at different temperatures. Figure 3.17 shows LOD spectra of all samples at temperatures ranging from 3.7 K to 133 K. For the series of spectra acquired at 20 K, figure 3.18 shows the LOD signal intensities (as peak integrals) revealing a mainly quadratic increase with the radical concentration. The quadratic dependence is assumed to arise from the product of the linear increase in radical concentration (and thus participating spins) with a linear increase of the homogenously broadened line width with increasing radical molarity. The latter translates into a linear increase of LOD signal since at each saturation frequency the amount of spins saturated (and hence contributing to the signal) is proportional to the homogeneous line width.

Further discussions considering dependencies on electron spin-lattice relaxation times, microwave power, and modulation amplitude and frequency can be found in literature [80–82].

**Figure 3.16.** LOD EPR spectra of 50 mM TEMPO (dotted line) and a mixture 50 mM TEMPO and 16 mM trityl (solid line) both in (1/1)\textsubscript{vol} D\textsubscript{2}O/Glycerol.
Figure 3.17. LOD spectra of $[1^{13}C]$pyruvic acid doped with 5, 13, 15, 17, and 25 mM of the trityl radical at temperatures ranging from 3.7 K to 133 K.
Figure 3.18. Signal intensities (peak integrals) of the LOD spectra of [1\(^{13}\)C]pyruvic acid doped with 5, 13, 15, 17, 18, 20 and 25 mM of the trityl radical at 20 K. The data is fitted with a cubic polynomial: 
\[ f = 0.2 \times x^2 + 0.05 \times x^3. \]
3.5.5. NMR circuitry

Two independent NMR circuits have been incorporated into the multi-sample probe: 

i) a low-sensitivity single-tuned circuit for DNP progress monitoring with the NMR coil inside the cavity and ii) a dual-tuned circuit with the NMR coil outside the cavity used for heteronuclear experiments. In order to allow free rotation of the revolver to exchange the samples in the coils, a saddle-coil geometry was chosen for both of them. Both circuits allow NMR experiments at all operating temperatures.

![Diagram of dissolution DNP probe](image_url)

**Figure 3.19.** Lower end of the modified dissolution DNP probe for double-resonance experiments. For dissolution DNP-CP experiments the revolver-style sample changer allows a sample to be rotated from the position for microwave irradiation (1) via the position where the CP pulse can be applied (2) to the dissolution port (3).

i) For monitoring the nuclear polarization levels during DNP experiments, an NMR saddle coil with two effective windings is mounted inside the upper part of the microwave cavity (3.8 a). The circuit is single-tuned (although it can potentially be double-tuned) and has a two-stage tuning and matching design. A first fixed pretuning in the cold space is achieved above the cavity by a series capacitor generating a series LC circuit with the NMR coil. A second fine-tuning and matching unit is located at the top of the probe at room temperature. A semi-rigid rf transmission line (4.6 mm shield diameter, stainless steel) connects the two tuning
stages. Due to the close vicinity of the NMR coil to the brass wall of the cavity, considerable amount of generated rf field concentrates between the coil wires and the cavity wall. Taking into account the principle of reciprocity of electrodynamics, the sensitivity of the coil in the sample space is reduced. Therefore, this circuit is not suited to detect thermal equilibrium NMR signals and thus cannot be used to quantify the polarization level. It is however used to track the course and progress of the DNP experiment.

ii) For experiments requiring higher sensitivity and double-resonance experiments (such as CP experiments, hence the name "CP coil") an additional saddle coil (5 effective windings, 0.8 mm diameter Ag wire) has been installed in the dissolution DNP probe (see figure 3.19). Since the motivation for this coil was to be used for dissolution DNP-CP experiments the coil was placed in the position before the dissolution-port position of the revolver-style sample changer. This minimizes the delay between the CP experiment and dissolution. The rf circuit is double tuned to 142 MHz ($^1$H) and 35 MHz ($^{13}$C) by tuning and matching components located outside the probe at ambient temperature ($Q(^1\text{H})=112$, $Q(^{13}\text{C})=69$) and allows rf-field amplitudes corresponding to a nutation frequency of 30 kHz on both channels. To reduce losses on the transmission line, a Cu semi-rigid transmission line (4.6 mm shield diameter) was used. Only the lower 10 cm of the outer conductor were replaced by non-plated stainless steel to reduce thermal heating of the sample space. Submerging the saddle coil and the non-isolated part of the inner conductor of the transmission line in liquid helium proved effective in preventing rf arcing. For all conducting components of this circuit being in helium-gas atmosphere, pedantic care has to be taken to isolate them to prevent arcing. The connection to the vacuum feed through was isolated using epoxy adhesive.

3.5.6. Sensor system

The dissolution DNP probe is equipped with several sensors to control its performance and to monitor the status of the DNP experiments. All sensor readings are fed to the LabVIEW control software described in section 3.7.

Two temperature sensors (Cernox resistors, Lake Shore Cryotronics Inc.) are moun-
ted inside the polarizer. One is located on the bottom of the cryostat. The other is mounted on the outside of the microwave cavity at the height of the sample location. Both sensors are read out by the ITC temperature controller.

**Helium-level sensor**

To monitor the level of liquid helium in the cryostat, a cylindrical capacitor is mounted at the lower end of the DNP probe. It is a smaller version of the sensor described in section 3.4.3 (two 80 mm long coaxial cylindrical electrodes with a diameter of 2.88 and 2 mm, respectively).

The exact temperature of the sample cannot be measured. It is therefore not obvious at which helium level the sample temperature starts rising and the dissolution should be conducted latest. Therefore, the polarization course was monitored and compared to the helium level. Figure 3.20 shows the temperature, helium level, and $^{13}$C NMR signal intensity during a DNP experiment at single shot. The polarization slowly starts decreasing once the helium level falls below 18% which is about the height of the sample compared to the helium sensor.

**Pressure sensor**

A pressure sensor is mounted at the vacuum port of the cryostat to estimate the system pressure (Series P3301, tecsis GmbH). This sensor cannot be utilized for temperature calibration of the sample during cryogenic operation since a pressure drop of unknown magnitude builds up between the lower part and the vacuum port of the cryostat. The analog voltage signal is digitized using the voltage input channel of the capacitance-to-digital converter (section 3.4.3).

**Revolver sensors**

The correct operation of the revolver-style sample changer is monitored by a sensor subsystem. It consists of three phototransistors for digital decoding of the actual revolver position into TTL signals, two switches (TTL) for assuring correct functionality of the revolver pneumatics, and an in-house-built vertical lift monitor. The analog voltage output of the lift monitor allows measurement of the vertical movement of
Figure 3.20. Temperature, helium level, and $^{13}$C NMR signal course during a DNP experiment in single shot. Once the helium level drops below 18% the nuclear polarization starts decreasing, showing that a dissolution should be conducted before this point in time. Note that the experiment was not a typical single shot experiment since the initial helium level was not sufficiently high here.
the revolver axis with a resolution of \( \sim 50 \mu m \). All revolver sensors are mounted at the top end of the probe, avoiding further heating of the sample space.

### 3.5.7. Sample cups and grabber

The frozen samples sit in sample cups shown in 3.7 and 3.8. The geometry of the cups is defined by following characteristics: The sample area is a semi-spherical shape with a volume of 150 \( \mu l \) giving an effective load volume of 100 \( \mu l \), assuming a packing factor of approximately 70\%. The cup is closed by a perforated lid permitting the dissolution medium to penetrate during dissolution. The lid prevents frozen sample beads from being jolted out of the cup during movement of the revolver or due to boiling helium. The lower sections of the cups are hollow and clasp around the lower four metallic rods of the microwave cavity. The upper outer shape of the cup is cone-like with a decreasing diameter towards the top. This geometry enables the dissolution stick, with fitting shape, to seal the cup when being pressed on it. Finally, the grabber locks into a circular channel in the side of the cup for loading and dissolution purposes.

The grabber, shown in 3.21, is used to grab and steady the sample cups. It consists of a hollow tube with double-layer structure. The outer layer ends in six fingers, each having hooks pointing inwards to lock into the circular channel of the sample cups. The inner tube can be moved in and out to open and close the fingers of the grabber. The grabber is utilized for fixing and lifting of the cups during dissolution and for loading sample cups through the dissolution port. This can be done during system temperatures as low as 4.2 K at ambient pressure.

A modified version of the grabber has been realized allowing the grabber to be mounted in the dissolution port during single shot mode (see section 3.1.1), called cold grabber. It was found to increase the dissolution efficiency since with its use the samples experience less heating during the grabbing and lifting preceding each dissolution. To allow vacuum sealing o-rings have been included on the top end of the grabber sealing to the dissolution port tube. The grabber consists of only a single tube (without the opening tube) and is sealed with a simple rubber plug. Lacking the opening tube, the grabber cannot release a cup once it is locked to its fingers. Therefore, the cold grabber is only utilized for dissolution experiments while the initial grabber is used for loading the samples into the cold system. After a dissolution
Figure 3.21. (a) The grabber. The outer tube (1a) of the 2-layer structure ends in six fingers with hooks (2a) for "grabbing" the cups. The inner layer (3a) can be longitudinally slid to open the fingers by pushing against their spreader (4a). (b) The dissolution stick sealed to a sample cup. A PTFE tube (1b) guides the dissolution medium to the dissolution inlet (2b) at the sample space (3b). Through the outlet (4b) the dissolved medium is guided to the room-temperature space by a second PTFE tube (5b).
using the cold grabber it is removed from the probe and the cup is manually released.

### 3.5.8. Dissolution and shuttling components

The dissolution apparatus is based on a design described previously [27]. The main hardware components are: (i) a 10 ml stainless-steel vessel that can be pressurized and heats the dissolution medium (usually a buffered solution) to 160 °C, (ii) a system of valves for pre-pressurizing, starting the dissolution, and shuttling of the dissolved sample to the MRI/NMR system, (iii) a dissolution stick (figure 3.21 b) to guide the hot dissolution medium to the sample space through a PTFE tube connected to the cooker. The dissolution stick has to be sealed tightly to the sample cup. This seal prevents the hot liquid from entering the cryo-temperature space. The dissolved sample is guided out of the polarizer through a second PTFE tube in the dissolution stick. The usage of (iv) a collecting device next to the DNP magnet or at the MRI/NMR system will not be discussed here. The type of device used depends on the application the polarized sample is used for. (v) Temperature and pressure sensors monitor the functionality of the dissolution system. All valves and sensors are controlled by the LabVIEW software.

### 3.5.9. Performance results and dissolution procedure

DNP experiments were conducted on a sample with 16.2 mM trityl radical, 1 mM Gd dissolved in [1-\(^{13}\)C]pyruvic acid. Before switching to the single-shot mode, the system was kept at constant 3.45 K for 60 min to measure a thermal-equilibrium reference spectrum. The relaxation time of the \(^{13}\)C signal at this temperature was about 400 s. After reaching the single-shot temperature of 1.4 K, the sample was irradiated for 60 min until reaching the polarization plateau. The microwave frequency and power were previously optimized and set to 93.875 GHz and 20 mW, respectively (figures 3.22a and 3.9). Low-flip angle (\(\sim 4^\circ\)) one-dimensional \(^{13}\)C NMR spectra were acquired over the entire course of experiment to determine the degree of \(^{13}\)C polarization. The integrated NMR intensities were compared to the measured average thermal-equilibrium signal and translated into polarization using the measured thermal-equilibrium \(^{13}\)C polarization at 3.45 K as a reference. The polarization build-up curve was fitted with a mono-exponential curve yielding a polarization at
Figure 3.22. a) $^{13}$C DNP enhancement (dashed line) as a function of the microwave irradiation frequency overlaid with the LOD EPR spectrum (solid line) of 16 mM trityl in [1-$^{13}$C]pyruvic acid. The LOD spectrum was acquired at 10 K, the DNP enhancement curve at 3.47K. The positive DNP maximum was found at 93.875 GHz, which is unchanged at 1.3 K. b) Solid-state $^{13}$C polarization as a function of the microwave irradiation time. The sample contained 16.2 mM trityl and 1 mM Gd in [1-$^{13}$C]pyruvic acid at a temperature of 1.4 K. At time $t = 500$ s, the microwaves were switched on with a power setting of 20 mW.
the plateau of $45 \pm 5\%$ with a build-up constant of $670 \pm 20$ s (figure 3.22b).

For dissolution of a hyperpolarized sample, the target sample cup has to be rotated to the dissolution-port position of the revolver. Dissolution and ejection of the sample involves pressurizing the system to ambient pressure. Then the grabber is employed to hold the target sample cup and lift it above the liquid-helium bath. The dissolution stick is slid into the hollow sample grabber and sealed against the sample cup with a locking mechanism. The dissolution medium with the dissolved sample can be shuttled to the liquid-state MRI/NMR system by blowing room-temperature helium gas after dissolution through the entire dissolution line or collected immediately next to the DNP magnet.

For performance tests, the DNP system was installed next to a 7 T NMR spectrometer. A 140 $\mu$l sample of [1-$^{13}{C}$]pyruvic acid doped with 15 mM trityl was polarized at optimum positive DNP microwave frequency with 20 mW for 60 min at 1.3 K. After reaching the DNP enhancement plateau as monitored by $^{13}{C}$ NMR spectroscopy, the dissolution sequence was started following the procedure described above. With a delay of 30 s between sample rotation and dissolution due to initial leak tightness tests, the sample was dissolved in 8 ml D2O.

The solution was shuttled over a distance of 4 m through PTFE tubing (3 mm inner diameter) into an NMR tube mounted in a standard solution-state probe in the 7 T spectrometer. The shuttling time until arrival of the main bolus is estimated to be less than 5 s. Low-flip angle 1D $^{13}{C}$ spectra were acquired in the NMR spectrometer with a repetition time of 6.65 s. The integral over the pyruvate resonance, normalized by the thermal equilibrium signal yields an enhancement factor of 15,000 (or 9.3% $^{13}{C}$ polarization at 295 K and a magnetic field of 7 T).

In combination with a 9.4 T MRI system (Bruker BioSpec) dissolution experiments were performed on samples containing 25 $\mu$l [1-$^{13}{C}$]pyruvic acid doped with 13.5 mM trityl and 1.5 mM Gd yielding a solid-state polarization of $\sim 45\%$. The dissolution workflow was optimized to reduce the exposure of the polarized sample to high-temperature dissolution components. The time between sample rotation and dissolution was minimized, the routine dissolution sequence is shown in figure 3.24.

The sample was dissolved in 4 ml Tris-buffer and collected in a syringe where it was mixed with 250 $\mu$l of a 1 M NaOH solution to yield pH = 8. The dissolved solution was carried manually to the MRI system and injected into a phantom. The sample entered the phantom 27 s after dissolution and was measured with low-flip
Figure 3.23. DNP enhanced $^{13}$C polarization in the liquid state at room temperature in a 9.4 T MRI. The inlay shows the time series of low-flip angle 1D $^{13}$C spectra of the hyperpolarized [1-$^{13}$C]pyruvic acid dissolved in 4 ml Tris-buffer with a final pH = 8.

Figure 3.24. Standard dissolution DNP protocol as used if the sample is collected next to the DNP magnet and carried manually to the NMR/MRI.
angle (<10°) one-dimensional $^{13}$C spectra. The inset in figure 3.23 shows the interesting part of the spectra. The highest measured liquid-state $^{13}$C DNP enhancement was calculated to be greater than 16,000 (13% polarization at 295 K and 9.4 T). Assuming the measured $T_1$ of the dissolved sample (42.3 s) to be constant between the time of dissolution and the arrival in the MRI system, the liquid-state polarization can be extrapolated to be greater than 25% (enhancement factor >30,000) immediately after dissolution, as is plotted in 3.23. This corresponds to a loss of polarization during the dissolution of 44%. Reasons for the polarization loss during dissolution other than relaxation due to exposure of the frozen solid to warm components are not known. The few reported values in the literature range from 20% to 45% loss during dissolution [22, 24]. Over the years 2011-2013 numerous dissolution experiments have been repeated with the same protocol reaching up to 33% solution-state polarization (mean polarization level: (25 ± 6)%).
3.6. Thermal heating estimation

The probes introduced in section 3.4 and 3.5 unavoidably heat the sample area. With this in mind the used materials and geometries were chosen with the attempt to minimize the introduced heating power under the mechanical restraints given by the demands on the probes capabilities. An estimation of the introduced heating power of both (neglecting the cryostat efficiency) shall be given here. Note that the heat flows calculated here are from room temperature to the cryo space. It is essential where these components end in relation to the sample or to the liquid helium level. In thermally conducting structures composed of different successive materials the effective heating can be reduced considerably if only short pieces are made of thermally insulating material.

The heat flow through probe structures reaching vertically from room temperature to the cryo space is calculated using equation A.8 derived in the appendix A:

\[ \dot{Q} = -\frac{A}{L} \Sigma(300K) \]  

(3.1)

with the cross section \( A \), the length \( L \), and the integrated thermal conductivity \( \Sigma(300K) \) from 0 to 300 K. All \( \Sigma \) values of the utilized materials are given in appendix A. For both probes a length of \( L = 1 \) m is approximated.

Radiation shields are incorporated in all hollow structures besides the microwave guides and the dissolution-port tube in the probe 2. For those components, the transmitted radiation is additionally calculated using the Stefan-Boltzmann law for the power irradiated from the area \( A \):

\[ P = A \sigma_{SB} T^4. \]  

(3.2)

with the Stefan-Boltzmann constant \( \sigma_{SB} = 5.67 \times 10^{-8} \text{Wm}^{-1}\text{K}^{-4} \) [83].

Heat flows: Probe 1

The heating power of the skeleton of probe 1 adds up to \( \sim 61 \) mW neglecting the exchangeable NMR line in table 3.1. The large heat flow of the Cu-Cu transmission line emphasizes that, for experiments with critical lowest achievable temperature or maximum single-shot duration, an NMR transmission line should be used based on
silver-plated stainless steel or similar with heat flows of $\sim 200$ mW. The Cu-Cu transmission line used in the setup described here maximizes the NMR sensitivity with a brute-force approach. It was chosen for reasons of simplicity and because optimal cryogenic performance is not needed for the conducted experiments in this work.

**Heat flows: Probe 2**

The heating power of the skeleton of probe 2 adds up to $\sim 500$ mW if including only the fix NMR transmission line for the NMR coil in the cavity (table 3.1). Part of this heat arises from the silver plating of the mw guide. This plating ends above the liquid-helium level, however, from this point the wave guide is made of Be-Cu and Cu components efficiently forwarding the heat transferred by the silver plating. The NMR transmission line ends above the liquid helium bath were it connects to stainless-steel parts. Therefore the heat introduced by the inner conductor (Cu, 157 mW) is not fully applied to the liquid helium. The overall heating power of the skeleton is estimated to $\sim 420$ mW.

The additional NMR transmission line for CP experiments is a 4.6 mm Cu-Cu transmission line. The last $\sim 10$ cm of the outer conductor is replaced by stainless steel. The inner conductor hence guides 157 mW to the liquid helium bath. For the combination of the outer conductors, the temperature of the junction can be estimated to $\sim 200 - 250$ K (using equation A.11 in the appendix A) yielding a heat flow of $\sim 90$ mW. This drastically reduces the heat transfer of the CP transmission line from $\sim 970$ mW (plain Cu) to $\sim 250$ mW (with modified outer conductor).

<table>
<thead>
<tr>
<th>Component</th>
<th>Cross section [m²]</th>
<th>Material</th>
<th>Conducted heat [mW]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber glas tube</td>
<td>$5.97 \times 10^{-5}$</td>
<td>fiber glas</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\Sigma(300K) = 900 \frac{W}{m}$</td>
<td></td>
</tr>
<tr>
<td>MW guide: heat flow</td>
<td>$6.45 \times 10^{-6}$</td>
<td>stainless steel lower 60 cm</td>
<td>33</td>
</tr>
<tr>
<td>MW guide: radiation</td>
<td>$2.56 \times 10^{-5}$</td>
<td>constantan</td>
<td>12</td>
</tr>
<tr>
<td>Sensor cables</td>
<td></td>
<td>copper</td>
<td>$\lesssim 1$</td>
</tr>
<tr>
<td>NMR transmission line</td>
<td>$(5.4 + 0.8) \times 10^{-6}$</td>
<td>copper 1232</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3.1.** Calculated heating power introduced by the probe 1.
### 3.6 Thermal heating estimation

<table>
<thead>
<tr>
<th>Component</th>
<th>Cross section $[m^2]$</th>
<th>Material</th>
<th>Conducted heat $[mW]$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central tube</td>
<td>$1.48 \times 10^{-5}$</td>
<td>stainless steel</td>
<td>44</td>
</tr>
<tr>
<td>Revolver axle</td>
<td>$6.1 \times 10^{-6}$</td>
<td>stainless steel</td>
<td>18</td>
</tr>
<tr>
<td>Dissolution-port tube heat flow</td>
<td>$2.4 \times 10^{-5}$</td>
<td>stainless steel</td>
<td>73</td>
</tr>
<tr>
<td>Dissolution-port tube radiation</td>
<td>$1.77 \times 10^{-4}$</td>
<td></td>
<td>81</td>
</tr>
<tr>
<td>MW guide: heat flow</td>
<td>$6.45 \times 10^{-6}$</td>
<td>stainless steel</td>
<td>20</td>
</tr>
<tr>
<td>MW guide plating</td>
<td>$1.1 \times 10^{-7}$</td>
<td>silver</td>
<td>39</td>
</tr>
<tr>
<td>MW guide: radiation</td>
<td>$2.56 \times 10^{-5}$</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>Sensor cables</td>
<td></td>
<td>various</td>
<td>$\sim 1$</td>
</tr>
<tr>
<td>NMR transmission line shield</td>
<td>$4.1 \times 10^{-6}$</td>
<td>stainless steel</td>
<td>12</td>
</tr>
<tr>
<td>NMR transmission line inner conductor</td>
<td>$0.8 \times 10^{-6}$</td>
<td>copper</td>
<td>157</td>
</tr>
<tr>
<td>NMR transmission line inner conductor plating</td>
<td>$0.03 \times 10^{-6}$</td>
<td>silver</td>
<td>14</td>
</tr>
</tbody>
</table>

*Table 3.2. Calculated heating power introduced by the probe 2.*
3.7. Control software

All components of the experimental setup are controlled via LabVIEW (National Instruments). An overview of the software, its structural composition, and the purposes of the subunits will be given here.

For ease of description, the following terminology common in the LabVIEW environment will be used:

- **VI** stands for *virtual instrument* and is the name for a LabVIEW program. A VI is composed of two levels: the *front panel* and the *block diagram*. A **sub-VI** refers to a VI that is incorporated into a parent VI.

- The **Front panel** is the user interface of each VI.

- The **Block diagram** holds the source code of the VI in a graphical rather than script-like representation.

- The interaction with the user (in the front panel) is done via **controls** (excepting input) and **indicators** (displaying output of the VI).

3.7.1. Software sub-units

The system block diagram of the software package is shown in figure 3.25. The communication with each hardware component is realized with a separate VI (with the exception of the helium-level and pressure monitors). All VIs can be operated independently or from a Master VI. The latter combines all VIs as sub-VIs into one user interface. The main VIs are:

- The **DNP Master** (*DNPMaster.vi*) provides a combined user interface for the entire software package. It gives access to all controls and indicators and allows execution control for all sub-VIs. It continuously checks the alarm-notification status of critical sub-VIs and reacts in case of occurring problems. Upon start, the user can define the paths and names for all log files using the file handler vi.

- The **File handler** (*Manage_Paths.vi*) allows to define the paths and names for the log files of all VIs that log/store data. A sub-VI (*Read_Path.vi*) can be called by other VIs to read out the specific logging path and file name.
• The **Temperature control** (ITCControl.vi) allows monitoring and controlling of the cryostat temperature. It communicates with the ITC (section 3.1) that drives the helium inlet needle valve, a heater incorporated in the cryostat and reads out the temperature sensors.

• The **Logbook** (logbook.vi) is an implementation of a digital lab journal. It logs entries consecutively numbered to a global lab journal file. Additionally, the entries made during a given experiment are stored in a separate lab journal file (with file name and directory defined by the file handler). If running, the VI can print all new entries done during a day at midnight or upon closing for storage of the lab journal in printed version.

• **Back up** (Backup.vi) simplifies back up from the used solution-state NMR/MRI machine to the DNP computer.

• The **He usage tracker** (HeliumUsage.vi) simplifies logging of the usage of liquid helium as coolant. It calculates the used volume of liquid and the recovered fraction from the values supplied by the experimenter. It logs all entries consecutively to a global file and additionally adds all made entries to the logbook.

• **Messaging** (Messaging.vi) tracks specific experimental parameters chosen by the experimenter (temperature, He level, etc.) and can send messages to one or more recipients if chosen boundary values are passed. The recipients can be chosen and messages can be sent as text messages on mobile network and/or via email.

• The **NMR Console** (OpenConsole_Master.vi) was implemented by Marcin Krajewski and is a LabVIEW implementation of the console used to operate the Opencore spectrometer [74]. As an alternative, the program “Opencore NMR” by Takeda can be used. The LabVIEW implementation allows pulse-program compilation, definition of the digital filter parameters, transfer to the spectrometer and reading of the acquired data from the spectrometer buffer. It allows automated periodic repetition of experiments that are stored in consecutively numbered directories (as subdirectories of a directory defined by the file handler). Basic processing (phasing, filtering, fft, peak integration, and similar) can be done in the VI.
• The **He-level and pressure monitor** (*He_Level_Readout.vi*) monitors and displays the level of liquid helium and the pressure in the cryostat. It communicates with the capacitance-to-digital converter (section 3.4.3) and calculates He-level values in % of the He-level sensor length and the pressure as fraction of the atmospheric pressure (\(\approx \) bar). The experimenter has to choose between probe 1 and 2 for correct calculation of the values.

• The **Microwave control** (*ELVA Monitor.vi*) allows to set the frequency and cw-power level of the microwave source.

• The **EPR console** (*EPR.vi*) is used to conduct LOD EPR experiments (section 3.5.4). In the EPR console, the shape, amplitude, and frequency of the mw power modulation signal can be chosen. A list of mw frequencies to be scanned can be chosen alongside with the number of averages for each frequency step. The processing and storing of the spectra is done at the end of each EPR experiment.

• The **Revolver control** (*RevolverControl.vi*) monitors and displays the actual position of the sample revolver and allows revolver rotation, either by choosing a target position or by manual control of the pneumatics.

• The **Revolver lift monitor** (*Lift_Monitor.vi*) reads, calculates and displays the vertical position of the revolver axis (section 3.5.6).

The VIs needed for dissolution are grouped together in the Master VI:

• **Dissolution sequence** (*Dissolution_givingTrigger.vi*) defines the exact temporal sequence of the actions of the valves when starting the dissolution. The dissolution can be started by a button in the VI or, if the corresponding option is chosen, by a hardware buzzer mounted on the DNP magnet. The Dissolution sequence VI also allows the experimenter to dry the dissolution hardware components using an automated drying sequence.

• **Dissolution valves** (*DissValves_manual.vi*) allows manual control of the dissolution valves. This can be used for cleaning of the dissolution components.
• The **Dissolution cooker control** (*CookerControl.vi*) displays and allows setting of the target cooker temperature. It communicates with an external cooker controller (bang-bang controller) that excepts the target temperature and controlling parameters.

• **Dissolution pressure sensor** (*pressure_sensors.vi*) displays the pressure in the dissolution cooker.
Figure 3.25. System block diagram of the DNP control software realized using LabVIEW.

3 Instrumentation
3.8. Discussion

The cryogenic setup chosen in this work has been shown to achieve the desired temperature of \( T < 1.4 \) K. It is designed to fit into wide-bore NMR magnets and is therefore without large efforts transferrable, even to magnets charged to different magnetic fields and hence field independent. At the same time, since the cryostat can be removed from the magnet, the latter could be used for conventional NMR experiments at the magnetic field chosen for the DNP probes.

The liquid helium usage depends on the operation chosen and is acceptably low. The design realized here does not rely on a closed-cycle cryogen path, like presented by [84]. Therefore, the cryogenic system is connected to a helium recovery system of the institute. Furthermore, the cryogenic system is independent of the magnet’s cryogenic space. A combination of both, as is realized in [25, 84], might reduce the overall usage of liquid helium during DNP operation while increasing the usage during stand-by periods in which the polarizer is not used.

The large heating introduced by the NMR transmission line of the probe 1 (table 3.1) is subject of possible cryogenic improvements. Especially for DNP experiments with low demands on the maximum \( B_1 \)-field strengths a stainless-steel based transmission line could reduce the consumption of liquid helium.

The probe 1 proved efficient for experiments with high demands on the \( B_1 \)-field strength at temperatures down to 1.3 K. It allows heteronuclear experiments at up to 100 kHz on both \(^{13}\text{C}\) and \(^1\text{H}\) channels. The absence of electrical components in the cryo space allows the transmission line to end close above the sample. This minimizes the region in which the inner conductor is not isolated and therefore prohibits arcing already at low liquid helium levels in the sample space. The microwave guides in probe 1 reveal moderate attenuation of \(-7.6\) dB allowing sufficient microwave power to reach the sample. If necessary, this could be improved by \(~5\) dB by silver plating of the stainless-steel parts of the microwave guides.

The performance tests of the microwave circuit in the probe 2 have demonstrated that the microwave magnetic field is effectively concentrated at the sample location requiring only \(~10\) mW of microwave power (measured at the microwave source) for reaching maximum DNP enhancements. The multi-sample revolver system has been tested successfully at the operating temperature and pressure ranges of the system. The dissolution procedure with the actual design involves pressurizing of the DNP
probe to ambient pressure, leading to heating of the sample space to 4.2 K. Further heating is introduced by the dissolution components. The latter has been minimized by using the cold grabber shown in section 3.5.7.

Simultaneous polarization of all 6 samples was shown to be possible with a compromised polarization level by lowering the revolver mechanism. However, pressurizing the sample space during dissolution of one sample means heating and therefore losses in DNP enhanced polarization of the remaining samples and makes dissolution DNP experiments with a high repetition rate unfeasible. This problem could be addressed by making the dissolution conductible under vacuum conditions and correspondingly lower temperature. For this, the remaining sample space would need to be sealed from the combined grabber/dissolution stick assembly as was presented by Marcin Krajewski [85].
4. Dissolution DNP-CP

In this chapter, practical aspects are discussed which are important for the combination of CP with dissolution DNP. Methodological techniques are introduced that have been developed (partial saturation method for $B_1$ calibration, section 4.2) or optimized (CP using adiabatic half-passage pulses, section 4.3) in this work to allow the combination of CP with dissolution DNP. Finally, the first successful realization of the dissolution DNP-CP experiment is presented.

Parts of this chapter have been published in [86]. The CP experiments conducted in this work always transfer polarization from $^1H$ to $^{13}C$, other heteronuclei are not considered. All methodological work has been conducted on probe 1 whereas the dissolution DNP-CP experiments were conducted on probe 2.

4.1. Aspects of combining DNP with CP

For equal spin concentrations $\mu = 1$ of carbons ($Q$) and protons ($I$) equation 2.110 in section 2.3 reads:

$$\beta_Q = \frac{1}{1+\mu} \left( \beta_0^{0} \frac{\gamma I}{\gamma Q} + \mu \beta_0^{0} \right).$$

This shows that the relative contribution of both initial inverse spin temperatures $\frac{C(\beta_Q^0)}{C(\beta_I^0)}$ to the final $^{13}C$ inverse spin temperature is 1/4, if the Zeeman polarization of both spin species is transferred to the transverse plane before the CP mixing. This motivates the usage of the initial $90^\circ$ pulse on $^{13}C$ at the beginning of the CP sequence (fig. 2.2 (b)). For situations where both $^{13}C$ and $^1H$ are fully polarized ($\beta_Q^0 = \beta_I^0$) prior to the CP pulse this leads to an increase of the polarization transfer of 20%.

To store the transferred polarization for, e.g., multiple-contact time CP or for the combination with subsequent dissolution the generated transverse $^{13}C$ magnetization has to be converted into longitudinal magnetization. For this, additional $-90^\circ$ pulses are added to the conventional CP pulse scheme shown in figure 2.2 b). The $-90^\circ$
pulse on $^1\text{H}$ is necessary for two reasons: i) if used for multiple-contact time CP, the $^1\text{H}$ Zeeman polarization has to rebuild after each CP pulse. The $-90^\circ$ pulse uses the remaining magnetization after the CP to speed up this process. ii) If used in combination with systems undergoing TM the generated $^{13}\text{C}$ Zeeman polarization will mix with the $^1\text{H}$ polarization. Without the $-90^\circ$ pulse on $^1\text{H}$ the $^{13}\text{C}$ polarization would be even stronger depleted after CP.

### 4.1.1. CP in combination with thermal mixing vs. solid effect

For the case of sparse $^{13}\text{C}$ compared to $^1\text{H}$ nuclei $\mu \ll 1$ and if the CP is conducted after the spin system has reached thermal equilibrium, the CP enhancement reads

$$\epsilon_{CP} = \frac{\beta_Q}{\beta_{Q,0}} = \frac{\gamma_A}{\gamma_Q} \approx 4.$$  

Note that the enhancement of 4, as calculated above, is the upper limit for all situations (with $\mu \ll 1$) in which $\beta_Q = \beta_I$ prior to the CP, hence not only for a thermal equilibrium situation. As was shown in section 2.2.3.2, the thermal mixing step in thermal mixing (TM) DNP equilibrates the modified electron non-Zeeman spin temperature with the Zeeman spin temperature of any participating nuclear species. Hence, after DNP enhancement using the TM mechanism, the maximum CP enhancement equals 4.

For the solid-effect (SE) mechanism of DNP, it was shown in section 2.2.2, equation 2.48 that the enhancement is anti-proportional to the nuclear $\gamma$. Therefore, after SE DNP one expects $\beta_{Q,SE}^I \approx \frac{\gamma_A}{\gamma_Q} \beta_I^SE \approx 4 \cdot \beta_I^SE$. If CP is conducted after this, the upper limit for the CP enhancement reads:

$$\epsilon_{CP} = \frac{\beta_Q}{\beta_{Q,0}^SE} = \frac{\beta_I^SE}{\beta_Q} \frac{\gamma_A}{\gamma_Q} = 1.$$  

(4.1)

The given discussion motivates the combination of CP with the TM DNP whereas the combination with SE DNP does not seem to be promising in terms of further polarization enhancement due to CP. However, since the combination of DNP with CP usually accelerates the effective build up of the low-$\gamma$ nuclei an increase in repetition rate can be achieved with both mechanisms.
4.1.2. Timing of dissolution DNP-CP experiments

As discussed above in section 4.1.1, TM is the desired DNP mechanism for the combination of dissolution DNP with CP and is thus used in this work by choosing TEMPO as radical. In section 2.2.3, it is discussed that in TM both nuclear Zeeman baths mix with the electron non-Zeeman reservoir. This implies that they also mix with each other (via the electron bath). In general this process is occurring independently of the presence or absence of microwave irradiation as was shown by Cox et al in 1973 [66]. However, at temperatures $< 1.5$ K microwave irradiation is able to enhance the mixing strength.

Even if the reconversion of the remaining $^1$H transverse magnetization into Zeeman magnetization is included as discussed above, the $^1$H inverse spin temperature will be lower by a factor $> \epsilon_{CP}$ after the CP. Depending on the effective thermal-mixing strength between both Zeeman baths, the $^1$H bath will therefore deplete the CP-enhanced $^{13}$C polarization. Figure 4.1 shows an example of the depletion after the CP pulse.

![Figure 4.1](image_url)

**Figure 4.1.** Relaxation of $^{13}$C polarization after a CP pulse at 1.35 K given in enhancements $\epsilon$ and $^{13}$C polarization levels. After the CP pulse at $t = 1800$ s, the polarization is monitored with low-flip angle acquisitions with a repetition time of 60 s (dotted line and o). Additionally, the direct $^{13}$C DNP build up of the sample is included for comparison (solid line).

An important requirement to be met in dissolution DNP-CP experiments is thus a strict and tight timing of the CP - dissolution succession. It is for this reason, why in
4 Dissolution DNP-CP

probe 2 the CP coil shown in figure 3.19 in section 3.5.5 was positioned in the revolver position before the dissolution port. With this setup, the delay between the CP pulse and dissolution can be reduced to below 20 s.

4.2. $B_1$-field calibration

A necessity for performing advanced NMR techniques such as nuclear cross polarization is the accurate calibration of the rf-field strength ($B_1$) often referred to as $90^\circ$-pulse width calibration. Using the conventional nutation method this requires several $T_1$ cycles [87] making it troublesome at temperatures below 4 K where $T_1$ can be as long as 200 s and even up to $>10000$ s. Here, a fast method for $B_1$-field calibration is introduced achieving $B_1$ calibration within $\ll 1 \times T_1$ for slow relaxing spin systems. The method is based on partial saturation of the nuclear spins and therefore referred to as partial saturation method and presented in [88].

The nuclear magnetization is partly saturated by a train of more than ten 1-pulse-acquire experiments. For a given power setting a pulse length is chosen such that an estimated flip angle between $\sim 10^\circ$ to $40^\circ$ is reached. The repetition rate is set to the minimal possible value but larger than the nuclear $T_2$ to avoid detection of spin echoes. The acquired data has to be processed depending on the ratio of the pulse train duration to $T_1$:

a) **Pulse train duration $\ll T_1$:**

This is the usual case for DNP applications below 4 K. There, the relaxation of the spin system can be neglected on the time scale of the saturation pulse train. One can fit the $n$-th signal with the actual used flip angle $\alpha$ as fit parameter to:

$$S_n = S_0 \cos^{n-1} \alpha \cdot \sin \alpha$$

(4.2)

with the initial magnetization $S_0$ and without knowledge of the exact pulse repetition rate. From $\alpha$ and the chosen pulse duration, $B_1$ can be calculated for the used rf power.

b) **Pulse train duration $\sim T_1$:**

In this case the relaxation cannot be neglected anymore and the system will approach a steady state during saturation. For a fit, the $T_1$, the pulse repetition rate
Adiabatic half-passage pulses

$T_R$, and the thermal equilibrium signal have to be known. If the pulse train is started at thermal equilibrium ($S_0 = S_{\text{equ}}$), one can fit the $n$-th signal recursively with

$$S_n = \left[ S_{n-1} \cos \alpha \cdot e^{-\frac{T_R}{T_1}} + S_0 \left( 1 - e^{-\frac{T_R}{T_1}} \right) \right] \cdot \sin \alpha. \tag{4.3}$$

The method was tested on a sample of [1-13C]pyruvic acid doped with 15 mM trityl at 3.5 K on the probe head 1. The $^{13}$C $B_1$ was calibrated at 50 W with the conventional nutation experiment as well as the partial-saturation method. In the nutation experiment, each data point was acquired after a saturation pulse followed by 200 s ($\sim 1 \times T_1$) relaxation delay. The entire experiment took 50 minutes and could be shortened to several $T_1$ if the approximate $B_1$-field strength is known and only few data points are acquired around 360° pulse length to minimize the necessary relaxation delay as suggested by Keifer et al. [87]. For the partial saturation method, 20 data points were acquired within 14 s. 1-pulse-acquire pulse lengths of 1 µs and 2 µs were chosen for two separate experiments. The results of both calibration methods are shown in figure 4.2 which demonstrate that in the context of low-temperature DNP, the introduced method gives a possibility for fast determination of the $B_1$-field strength.

### 4.3. Adiabatic half-passage pulses

The dissolution DNP-CP experiment creates additional demands on the cryogenic probe design. The primary obstacle to overcome is the need for high rf power for the CP transfer to be efficient while being rf-power limited due to strong arcing affinity of the helium atmosphere found in typical flow-type cryogenic probes. It will be shown in this section that using adiabatic half-passage pulses (AHP) [89, 90] instead of conventional hard 90° excitation pulses improves the efficiency of the CP transfer specifically at low rf-power levels. For this, the efficiency of both pulse schemes will be compared.

All experiments on AHP optimization and characterization were performed on a sample containing 4.5 M [$^{13}$C]urea in (1/1)$_{\text{vol}}$ glycerol/D$_2$O doped with 50 mM TEMPO. The experiments were conducted on the probe head 1 (section 3.4) with the sample covered by liquid helium, at 4.2 K and ambient pressure. The choice of 4.2 K for the experiments instead of the more typical 1.3 K for dissolution experiments was
Figure 4.2. Conventional vs. partial-saturation method for $B_1$ calibration. a) Conventional nutation experiment. b) Partial-saturation method using 1 µs (left) and 2 µs (right) saturation pulses. The partially saturated data was fitted with the fit given in equation 4.2.
motivated by the high temperature stability under these conditions and by the lower helium consumption during the large number of experiments needed to optimize and characterize the CP conditions.

4.3.1. CP pulse sequences using AHP and hard-90° pulses

For adiabatic conversion of longitudinal to transverse magnetization (sweep-in) hyperbolic-secant pulses [89, 90] were chosen with an amplitude shape of

$$|\omega_1(t)| = \omega_1^0 \text{sech}(\alpha t)$$ (4.4)

and an irradiation frequency modulation of

$$\Delta\omega(t) = A \frac{\tanh(\alpha t)}{\tanh(\alpha)}$$ (4.5)

where $A$ describes the frequency sweep amplitude and $\alpha$ the truncation. The effective 90° rotation of the magnetization is achieved by limiting the hyperbolic-secant function to the first half of the pulse. For regenerating Zeeman polarization (sweep-out) after the CP mixing period in order to store the gained polarization, the same hyperbolic-secant pulse was used, however, reversed in time.

To achieve adiabatic conversions the adiabaticity condition

$$|\omega_{\text{eff}}(t)| > \left| \frac{d\theta}{dt} \right|$$ (4.6)

has to be fulfilled for all spins with effective nutation frequency $\omega_{\text{eff}}$ where

$$\theta = \arctan\left(\frac{\omega_1(t)}{\Delta\omega(t)}\right)$$

is the angle between the effective rf field and the z-axis. In static powders the range of chemical shifts is large, such that offset effects have to be taken into account. As introduced in [91] a possible approach to this is the restriction to offset-independent adiabaticity as is the case for the chosen hyperbolic-secant in this work. It assumes
that the adiabaticity factor

$$K(\omega^0_I, \Omega, t) = \left| \frac{\omega_{\text{eff}}(\omega^0_I, \Omega, t)}{\frac{\partial}{\partial t}} \right| > 1$$  \hspace{1cm} (4.7)

is equally large for all chemical shifts at the time of their on-resonance. Spins with chemical shift $\Omega$ are on-resonant in equation 4.5 if

$$\Delta \omega(t_\Omega) = \Omega$$  \hspace{1cm} (4.8)

at the time $t_\Omega$. Plugging equation 4.8 into equation 4.7 gives the offset-independent adiabaticity at on-resonance conditions:

$$K(t_\Omega) = \frac{\omega^1_1(t_\Omega)^2}{\left| \frac{d\Delta \omega(t_\Omega)}{dt} \right|}. \hspace{1cm} (4.9)$$

The AHP pulse parameters were optimized by restricting to $K(t_\Omega) > 1$ and by finding the maximum recovered magnetization after a block of sweep-in pulse, 500 $\mu$s spin lock, and sweep-out pulse. An example for the AHP sweep-in and sweep-out with peak rf field strength $\omega^0_1 = 100$ kHz is given in figure 4.3 (optimum AHP parameters see figure caption).
Figure 4.3. Amplitude and frequency modulation functions for the hyperbolic secant AHP sweep-in and sweep-out pulses for $\omega_0 = 100$ kHz. The experimentally optimized pulse parameters were $\alpha_{1H} = 10$, $\omega_{13C} = 20$, $A_{1H} = 150$ kHz, $A_{13C} = 50$ kHz, pulse length $\tau = 2 \cdot 350 \mu s$, resolution $= 1 \mu s$. 
The CP sequences for optimizing purposes using hard 90° pulses and AHP pulses are shown in figure 4.4. Both start with the saturation of both nuclei preceding a variable DNP build-up period $t_{DNP}$ which is followed by the CP sequence block and the readout (figure 4.4a). The CP-sequence blocks are $[90° - SL - -90°]$ and [sweep-in – SL – sweep-out] for hard 90° and AHP pulses, respectively (figure 4.4b). For $T_1p$ measurements, the DNP-CP sequences are modified by omitting the CP block from the channel not used.

![Diagram](image)

**Figure 4.4.** DNP-CP sequence. (a) The DNP-CP sequence starts with a saturation pulse train on both nuclei, followed by the DNP build-up period with variable duration $t_{DNP}$. The CP block is followed by the read out, consisting of four phase-cycled acquisitions. The microwaves are tuned to the optimum positive DNP condition and kept on during the entire experiment. (b) The CP blocks use hard 90° pulses and AHP for rotation of the magnetization.
4.3.2. Efficiency of AHP vs. hard-90° pulses

The following experiments for characterization and comparison of both CP blocks were conducted on probe 1. The Hartmann-Hahn match was optimized for each of the two DNP-CP implementations (figure 4.4b) separately using a mixing time of $t_{\text{mix}} = 1$ ms and $t_{\text{DNP}} = 10$ s (figure 4.5). Microwaves were irradiated on the optimum DNP condition throughout the entire experiment. The CP mixing time $t_{\text{mix}}$ was optimized independently for both implementations of the DNP-CP sequence based on the experimentally determined Hartmann-Hahn conditions for a 30 s DNP build-up time.

To characterize the rotating-frame relaxation times and the magnetization losses due to the projection of the magnetization onto the spin-lock field given by imperfect 90° rotations, time-dependent spin-lock measurements for the sequence with hard 90° pulses and for the sequence with AHP pulses were carried out. A maximum rf-field strength of 100 kHz was chosen for the AHP pulses with the AHP parameters given in the caption of figure 4.3 and $t_{\text{DNP}} = 30$ s. For both nuclei, the measured $T_{1\rho}$ values are comparable in both excitation schemes and plotted in figure 4.6 as fraction of a reference signal without the CP block.

For both nuclei the $T_{1\rho}$ measurement using 90° pulses shows losses of about 10% compared to the reference signal (figure 4.6). Using the adiabatic-pulse scheme the losses are reduced to 5% and 0% for $^1$H and $^{13}$C, respectively. The losses on $^1$H could not be eliminated entirely under the 100 kHz limit of the peak rf-field amplitude of the hyperbolic-secant pulse. The reason for this are the strong homonuclear dipolar couplings of the $^1$H spin system (FWHM 70 kHz) which reduces the adiabaticity during the hyperbolic-secant pulse. The higher losses in the sequence using hard pulses...
The described DNP-CP sequences (figure 4.4) were used with $t_{\text{DNP}} = 30$ s and omitting the CP block on the channel not used. Data is given as ratio to a reference spectrum after 30 s DNP build up without CP block and equal read-out parameters. All decays were approximated with a bi-exponential function with the parameters for $^1$H: $T_{1p,a} = 9.9 \pm 0.7$ ms, $T_{1p,b} = 0.7 \pm 1.4$ ms (hard 90° pulses), and $T_{1p,a} = 10.0 \pm 0.8$ ms, $T_{1p,b} = 0.7 \pm 1.4$ ms (AHP pulses); for $^{13}$C: $T_{1p,a} = 156.9 \pm 20.8$ ms, $T_{1p,b} = 11.9 \pm 2.4$ ms (hard 90° pulses), and $T_{1p,a} = 141.1 \pm 13.2$ ms, $T_{1p,b} = 9.2 \pm 1.4$ ms (AHP pulses).

are attributed to imperfect 90° rotations due to significant resonance-offset effects and subsequent losses due to a projection of the magnetization onto the spin-lock field.

To compare the CP transfer efficiencies of both sequences the build up of the polarization transfer was measured as a function of the CP mixing time at 100 kHz field strength. Figure 4.7 shows both CP mixing-time curves after 30 s microwave irradiation. At the optimum mixing time of $\tau_{\text{mix}} = 1$ ms, the CP sequence with AHP pulses gives a signal which is about 15% higher than the signal of the sequence using hard 90° pulses. Note that the CP factor of $>10$ arises from the fact that for this experiment $t_{\text{DNP}} = 30$ s was chosen. Since in this sample the $^1$H DNP build up is faster than the build up of the $^{13}$C nuclei (this is the usual case) the high CP enhancement is due much higher inverse spin temperature of $^1$H compared to $^{13}$C prior to the CP pulse.

The dependence of the CP efficiency of both sequences on the available mixing field strength was analyzed by measuring the CP mixing-time curves after 30 s DNP
4.3 Adiabatic half-passage pulses

Figure 4.7. CP transfer efficiency dependence on the mixing time for both CP implementations. The DNP-CP sequence was used with $t_{\text{DNP}} = 30$ s. Data is given as ratio relative to the same reference spectrum as used in figure 4.6, i.e. the data plotted corresponds to the polarization enhancement gained by the CP blocks. The experiment is used to quantify the polarization transfer efficiency of the two CP implementations.

Figure 4.8. The CP factor as a function of maximum available rf-field strength for both CP sequences. In each experiment the CP condition was optimized separately. The bars show the relative increase of the CP factor between the hard-90° sequence and the AHP sequence at each field strength.
build up for 20, 50, and 100 kHz mixing and AHP peak field strength. Both sequences were optimized at each field strength. In all optimization and characterization measurements the NMR spectra were acquired with four phase-cycled averaged FIDs, each with a 45° excitation pulse. Figure 4.8 shows the CP factors of both CP sequences as function of the peak rf-field strength. The data shows a decrease in the CP factor for both sequences. However, the relative difference between the CP factors increases up to 40% at 20 kHz. These results demonstrate the advantage of using AHP pulse sequences compared to hard-pulse sequences specifically at low available rf-field strength.

4.4. Results

4.4.1. DNP-CP using AHP

The performance of the implementation for the combined dissolution DNP-CP experiments was tested on a sample of 4.5 M [13C]urea in a solution of (1/1) _vol_ glycerol-d3/D2O doped with 30 mM TEMPO in the probe head 2.

To characterize the plain DNP process of 13C and 1H nuclei, time series of low flip-angle spectra were acquired with a repetition time of 60 s. 1H DNP enhancements were calculated by comparing the NMR signal intensities with a set of thermal equilibrium spectra. The 13C thermal equilibrium signal intensities could not be quantified satisfactorily in these experiments due to the high amount of background signal arising from the electrical isolation of the used rf coil and transmission line. Therefore, the 13C signal intensities are scaled such that in the steady-state DNP plateau the spin temperature of the 13C spins equals the spin tem-

![Figure 4.9. DNP and DNP-CP polarization build-up curves at 1.35 K. The plain DNP 1H (+) and 13C (o) polarizations are monitored in time series of low-flip angle acquisitions with a repetition time of 60s. The DNP-CP enhanced 13C polarization (- o -) is acquired in separate DNP-CP experiments with varying microwave irradiation times.](image-url)
temperature of the $^1$H spins. This assumption holds true for systems undergoing thermal mixing as is the case for the given sample. The solid-state polarization values are given with a relative accuracy of about 10% arising from the observed variation of the DNP enhanced signals from experiment to experiment. The build up of the $^{13}$C and $^1$H polarization at 1.35 K under microwave irradiation is shown in figure 4.9. The polarization build-up curves were approximated by mono-exponential functions with time constants of $\tau_{^1H} = 580 \pm 10$ s and $\tau_{^{13}C} = 1014 \pm 48$ s and plateau values of $P_{\text{max}} = 7.4\%$ and 30% for $^{13}$C and $^1$H, respectively.

Also shown in figure 4.9 is the $^{13}$C polarization using the DNP-CP sequence as a function of the microwave irradiation times. All CP experiments were conducted with optimized Hartmann-Hahn match at 30 kHz mixing field strength. The DNP-CP build up is characterized by applying CP pulses after a variable polarization time and immediate signal acquisition. This curve builds up roughly with the same time constant as the $^1$H enhancement representing a reduction of the build-up time by about a factor of two compared to the direct $^{13}$C DNP build up. The final polarization is enhanced by the CP transfer by about a factor of two to a final polarization in the solid state of 14%.

After the CP period, the enhanced $^{13}$C polarization will decay, under continued microwave irradiation, towards the DNP equilibrium value. Figure 4.1 shows for this sample the apparent experimental DNP-CP build up during the first 1800 s and for later times the decay of the CP enhanced polarization under microwave irradiation towards the DNP equilibrium value. This initial decay can be fitted by a mono-exponential function with the decay-time constant $\tau_{\text{TM}} = 249$ s. For a $20 – 30$ s delay between the CP process and the start of the dissolution this leads to about 10% polarization loss until dissolution.

### 4.4.2. Dissolution DNP-CP

For the combination with dissolution the sample (again 4.5 M $^{13}$C]urea in a solution of (1/1)$_{\text{vol}}$ glycerol-d3/D$_2$O doped with 30 mM TEMPO) was polarized at optimum DNP conditions for 35 min positioned in the microwave cavity. Remaining at 1.35 K, the sample was then rotated into the CP coil where a single CP experiment was conducted. Immediately after the CP pulse, the sample was rotated into the dissolution-port position while the polarizer was pressurized. From the CP pulse to the time of
dissolution this process takes \( \sim 20 \text{ – } 30 \) s while the temperature reaches \( \sim 3 \) K at the time of dissolution.

The sample was dissolved in 4 ml Tris buffer that was pressurized and heated to 150 °C. The solution was shuttled to a 300 MHz NMR spectrometer, rested for 10 s in a container to separate the liquid from the chasing He gas, and drained directly into an empty 5 mm NMR tube preloaded into the solution-state probe. One-dimensional \(^{13}\text{C}\) spectra were acquired with a flip angle of 3° every 4 s.

For comparison, a conventional dissolution DNP experiment with 60 min polarization time was conducted on the same sample without applying a CP pulse and dissolved and acquired with the same protocol. For quantification of the liquid-state Boltzmann polarization in both cases 400 spectra were acquired after full relaxation of the hyperpolarized samples to thermal equilibrium and averaged to a single thermal reference.

![Figure 4.10](image.png)

**Figure 4.10.** Liquid-state \(^{13}\text{C}\) polarization after dissolution of a DNP-enhanced sample without (a) and with (b) CP prior to dissolution.

Figure 4.10 a and b show the time series of solution-state \(^{13}\text{C}\) polarization levels following dissolution at time \( t = 0 \) s of a direct \(^{13}\text{C}\) DNP and a DNP-CP enhanced sample, respectively. If the curves are extrapolated back to \( t = 0 \) s with constant \( T_1 \) (39 and 40 s for case a and b), the polarizations reached are 4.6% and 8.8% without
and with CP, respectively. Both dissolution efficiencies (63% and 72%) are similar to previously observed values [22, 24, 73] and their difference is assumed to be an experimental variation independent of the solid-state pulse scheme. The additional polarization enhancement gained by the CP pulse in the solid state was thus shown to be transferable to the solution state.

### 4.4.3. Multiple-contact time DNP-CP

As mentioned in section 4.1.2 in this chapter and later discussed in section 5.3 the DNP-CP enhanced $^{13}\text{C}$ polarization relaxes back to the DNP steady-state level after the CP pulse with a time constant $T_{TM}$ (thermal mixing time). This effect can be seen in figure 4.1 in this chapter and in figure 5.6 in chapter 5. At the same time the $^1\text{H}$ polarization builds up back to the steady-state DNP level. If the rate of $^1\text{H}$ buildup $\tau_{1H}^{-1}$ is faster than $T_{TM}^{-1}$, then multiple-contact time CP experiments can be utilized to further enhance the $^{13}\text{C}$ polarization (multi DNP-CP). This was implemented by repetitive applications of the entire AHP-CP block shown in figure 4.4b.

A sample of 3.6 M [1,4-$^{13}\text{C}$]fumaric acid doped with 50 mM TEMPO and 16 mM trityl (in DMSO-d6, 2 mM Gd) was found to fulfill this condition with a ratio $\frac{T_{TM}}{\tau_{1H}} \approx 10$ at 4.2 K. Figure 4.11 shows the comparison of the $^{13}\text{C}$ polarization build up using plain DNP, single DNP-CP, and multi DNP-CP at 4.2 K. Using multi DNP-CP an enhancement of $\epsilon_{CP} = 3.5$ could be achieved over the plain DNP while accelerating the build up by $\sim 5$. With the single DNP-CP technique an enhancement of $\epsilon_{CP} = 2$ and acceleration of the build up of $\sim 12$ could be achieved.

The reduced build-up of the multi DNP-CP compared to the single DNP-CP technique arises from the repetitive saturation of $^1\text{H}$ polarization. Its effect increases with increasing CP repetition rate. Figure 4.12 shows the dependency of the achieved CP factor and the multi DNP-CP build-up rate as a function of the CP repetition rate for the given sample. It shows that in this case the optimum results could be obtained with repetition rates between 10 – 20 s.
Figure 4.11. Comparison of plain DNP, DNP-CP, and multi DNP-CP on a sample of 3.6 M [1,4-13C]fumaric acid doped with 50 mM TEMPO and 16 mM trityl (in DMSO-d6, 2 mM Gd) at 4.2 K.

Figure 4.12. CP factor and multi DNP-CP build-up rate as a function of the CP repetition rate at 4.2 K (sample as in figure 4.11).
4.5. Discussion

The discussion given in section 4.1 and in the theory (section 2.2.2) lead to the conclusion that, for the combination of CP with DNP, the TM mechanism should be preferred over the SE. Two drawbacks of this mechanism become important when used for DNP-CP:

i) Equation 2.76 indicates an inverse dependency of $\varepsilon$ on the electron dipolar frequency $D$. It was shown by Heckmann et al. [92] that this quantity can be interpreted as the EPR line width $\Delta \omega_e$. They show that equation 2.76 can be fitted to the correlation between measured deuteron enhancements and $\Delta \omega_e$ of various radicals. If using a radical with $\Delta \omega_e > \omega_{1H}$ to allow TM on $^1H$ this line width is larger by a factor of $> 4$ compared to the needed line width for direct $^{13}C$ DNP via TM and, therefore, will yield a smaller DNP enhancement. This finding is in agreement to achieved enhancements published in literature that vary from 25% to 45% $^{13}C$ polarization using trityl radicals [22, 28, 69, 84] and 6% to 14% for TEMPO [24, 29, 30, 33]. Thus, optimizing DNP-CP with respect to the used radical could be promising, e.g., investigating the usage of galvinoxyl as suggested by Lumata et al. [93].

ii) The shown thermal mixing between both $^1H$ and $^{13}C$ Zeeman reservoirs (fig 4.1) makes the timing of the CP - dissolution succession critical such that the delay between CP and dissolution should be minimized to $\ll T_{TM}$. At temperatures below 2 K the thermal mixing rate can be reduced by avoiding mw irradiation. Therefore, for dissolution DNP-CP experiments the microwave source should be turned off at the time of CP.

The partial saturation method for $B_1$ calibration introduced in section 4.2 has been shown to allow fast estimation of the $B_1$ field strength for slow relaxing spin systems. Possible artifacts due to spin echoes could be avoided with a repetition rate smaller than the nuclear line width. As a prerequisite to this method, the order of magnitude of the calibrated $B_1$ field has to be known.

The optimization of the Hartmann-Hahn CP by using AHP has improved the CP efficiency. In the context of dissolution DNP-CP, the often encountered restriction in rf-field strength directs the focus to low-rf CP techniques. The data presented in fig-
Figure 4.8 shows a much lower decrease in the CP factor for the AHP CP sequences compared to the hard-90° sequence when lowering the rf-field strength and demonstrates the advantage of using AHP sequences compared to hard-pulse sequences especially at low rf-field amplitudes. Further adiabatic CP techniques should be investigated with the aim of maximizing the achievable transfer efficiency at rf-field strengths of < 20 kHz, which should be readily achievable in dissolution DNP probes.

The polarization enhancement gained by the CP was shown to be transferrable to the solution state. It is noteworthy that the polarization gain by DNP-CP in the liquid might differ from the gain detected in the solid state because the nuclei in the vicinity of the polarizing agent, which polarize particularly well, are not detectable in the solid due to strong paramagnetic frequency shifts. In the solution state, however, all nuclei are detected. On the other hand, the CP efficiency will most likely be low for nuclei with strong paramagnetic frequency shifts. It is difficult to predict how the combination of these two effects will influence the observed polarization enhancement in solid and solution state for different samples and further investigations on this topic should be conducted.

The acceleration of the build up and enhancement of the final $^{13}$C polarization achievable with the dissolution DNP-CP method strongly depends on the mutual ratios of $\tau_{1H}$, $\tau_{13C}$, and $T_{TM}$ as well as on the achievable $^1$H steady-state DNP level. These quantities vary with sample parameters such as radical concentration and degree of deuteration and need to be optimized for each compound and sample condition. In section 4.4.3 it is shown that for a [1,4-$^{13}$C] fumaric acid sample the acceleration of the build up can reach $\sim 12$. Furthermore, for this sample the ratio $\frac{T_{TM}}{\tau_{1H}} \approx 10$ is favorable for the application of multiple-contact time CP allowing CP enhancements of up to $\sim 3.5$. Multiple-contact time CP is also applied by the group of Bodenhausen to enhance the $^{13}$C sodium acetate polarization in their DNP-CP experiments [94, 95].
5. A spin-thermodynamic model of thermal mixing

The TM mechanism as introduced in section 2.2.3 assumes that any participating nuclear species mixes its inverse spin temperature instantly with the electron non-Zeeman bath. However, with $^1$H and $^{13}$C nuclei participating simultaneously in the DNP process and furthermore applying polarization transfer from one to the other, the assumption of instant coupling between the nuclear Zeeman and electronic non-Zeeman reservoir is not correct anymore.

To get a qualitative insight into the dynamics of a spin system with multiple coupled spin reservoirs a thermodynamic model is applied similar to the one suggested by Goldman [96]. It is not the intention of this model to describe the physical process of polarization transfer from electrons to nuclei but to describe the interdependence of the spin temperatures of two different nuclear spin species experiencing TM. This chapter was partly presented in [97].

5.1. Model description

Figure 5.1 shows the considered reservoirs: the lattice L (with inverse spin temperature $\beta_L$), the proton and carbon Zeeman reservoirs HZ and CZ ($\beta_H$ and $\beta_C$, respectively), the electronic non-Zeeman reservoir NZ ($\beta_e$), and an imaginary cooling reservoir CL ($\beta_{CL}$). The latter is a virtual reservoir, however, the process of dynamic cooling via microwave irradiation is assumed to be equivalent to the coupling to such a virtual cooling reservoir and the substitution is hence considered as reasonable. The coupling rates shown in figure 5.1 are the thermal coupling rate constants between NZ and both nuclear reservoirs ($k_C$ and $k_H$), the spin-lattice relaxation rates of HZ and CZ ($R_H$ and $R_C$) and NZ ($R_e$), and the cooling rate ($R_{CL}$). CL is assumed to be
always cooler than L (\(T_{CL} < T_L\)) and L is assumed to have infinite heat capacity. Note that the arrows in the chosen picture indicate the flow of the inverse spin temperature \(\beta\) rather than the spin-temperatures \(T_S\). Finally, the ability to turn microwave irradiation on and off is included by the possibility to decouple NZ from CL.

**Figure 5.1.** Spin-thermodynamic model with flow of inverse spin temperatures \(\beta\). The \(^{13}\text{C}\) Zeeman reservoir (CZ), \(^1\text{H}\) Zeeman reservoir (HZ), and the electronic non-Zeeman reservoir (NZ) relax to the Lattice (L) with relaxation rates \(R_C\), \(R_H\), and \(R_e\), respectively. NZ is coupled to both CZ and HZ with the thermal coupling rate constants \(k_C\) and \(k_H\) and gets cooled via the microwave-induced cooling rate \(R_{CL}\) from the cooling reservoir (CL). All inverse spin temperatures \(\beta\) can be substituted by the DNP enhancements \(e\) if normalizing all by the lattice inverse spin temperature \(\beta_L\).

The inverse spin temperatures of CZ, HZ, and NZ in the drawn model are described by a set of three coupled differential equations

\[
\dot{\beta}_C(t) = -\frac{\kappa_C}{C_C} \beta_C(t) + \frac{\kappa_C}{C_C} \beta_e(t) - R_C [\beta_C(t) - \beta_L]\]  
(5.1)

\[
\dot{\beta}_H(t) = -\frac{\kappa_H}{C_H} \beta_H(t) + \frac{\kappa_H}{C_H} \beta_e(t) - R_H [\beta_H(t) - \beta_L]\]  
(5.2)

\[
\dot{\beta}_e(t) = \frac{\kappa_C}{C_e} \beta_C(t) + \frac{\kappa_H}{C_e} \beta_H(t) - \frac{\kappa_C + \kappa_H}{C_e} \beta_e(t) - R_e [\beta_e(t) - \beta_L] + R_{CL} [\beta_{CL}(t) - \beta_e(t)]\]  
(5.3)

with the heat capacities as the Curie constants \(C_I = \frac{N_i}{4} \gamma_i^2 \hbar\) (as defined in equation...
2.100 in section 2.3.2), the number of spins \( N_i \), and the coupling constants \( \kappa_C \) and \( \kappa_H \) between NZ and both nuclear reservoirs defining the thermal coupling rate constants via:

\[
k_i = \frac{\kappa_i}{C_C}
\]

by normalizing the coupling constants to the \(^{13}C\) heat capacity. With this and using the polarization enhancement factors \( \epsilon_i = \frac{\beta_i}{\beta_L} \) (with \( \beta_L \) staying constant due to its large capacity) one can rewrite equations 5.1 - 5.3 in matrix form as:

\[
\dot{\epsilon}(t) = \left( \begin{array}{c}
\dot{\beta}_C(t) \\
\dot{\beta}_H(t) \\
\dot{\beta}_L(t)
\end{array} \right) = \left( \begin{array}{ccc}
-k_C - R_C & 0 & k_C \\
0 & -C_C k_H - R_H & \frac{C_C k_H}{C_L} \\
\frac{C_C}{C_L} k_C & \frac{C_C}{C_L} k_H & -R_{CL} - R_e - \frac{C_C}{C_L}(k_C + k_H)
\end{array} \right) \cdot \epsilon(t)
\]

\[
+ \left( \begin{array}{c}
R_C \\
R_H \\
R_e + R_{CL} \epsilon_{CL}
\end{array} \right).
\] (5.5)

For CZ and HZ the ratios of heat capacities simplify to the product of the ratio of the gyromagnetic ratios and the ratio of their molarities chosen in a given sample. For the capacity \( C_e \) of NZ another assumption has to be made: Since NZ represents the broadened EPR line its heat capacity is assumed to be equal to the Curie constant of a spin-1/2 system with a Zeeman splitting according to the electron EPR line width of \( \approx 300 \) MHz. Therefore:

\[
C_e = \frac{N_e}{4} \gamma_N^2 \hbar \quad \text{with} \quad \gamma_{NZ} = \frac{300}{35} \gamma_C
\]

with the \(^{13}C\) Larmor frequency being 35 MHz in our system.
5.2. Solution of the differential equations and model fitting

The kinetics assumed in the model lead to a set of three coupled differential equations with seven parameters shown in equation 5.5:

\[ R_C, R_H, R_e, k_C, k_H, R_{CL}, \text{ and } \epsilon_{CL}. \]  

The core of the solution and parameter optimization is the numerical solution of the differential equations for a chosen set of seven parameters with boundary conditions given by the starting conditions of the kinetic model. All equation-solving and optimization steps were realized with MATLAB.

For each given sample, the numerical solution routine (function \textit{ode15s}) utilizes an additional unique set of three fixed parameters defining the relative heat capacities of the three spin systems, normalized to the heat capacity of the carbon spins. For situations in which microwave irradiation is turned off, the coupling parameter \( R_{CL} \) is set to zero.

For parameter optimization, numerical solutions of the model were fitted to experimental data. For this purpose, the algorithm (based on the function \textit{fminsearch}) fitted the model simultaneously to 12 data sets: the polarization enhancement build-up and decay curves of protons and carbons of three different samples (Sample A, C, and D in table 5.1; \( 2 \times 2 \times 3 = 12 \) curves) each with the appropriate starting boundary conditions. The sample compositions are summarized in table 5.1. All time-course data were acquired with four-step phase-cycled averaged FIDs, each with a 1° or 3.6° excitation pulse for \(^1\text{H}\) and \(^{13}\text{C}\), respectively.

The fitting was realized by minimizing the sum of the 12 norms of the differences between data points and model predictions, henceforth referred to as the goodness of the fit. Finally, the minimization routine was run 150 times with varying randomly chosen starting sets of the seven parameters to minimize the risk of finding local minima.
5.3 Results and Discussion

With 150 randomly chosen starting values of parameters given in equation 5.6 the fitting process gives 150 similar solutions for the set of parameters. Of these, 108 solutions within 4% less goodness compared to the best fit were selected for further processing. The set of parameters with the best fit is given in table 5.2 and the resulting modeled course of enhancements for all 12 data sets used for the fitting is shown in figure 5.3.

Table 5.2. Parameters of the best fit. The error given for each parameter is the standard deviation of the 108 solutions within 4% less goodness compared to the best fit.

The long relaxation time of the electronic non-Zeeman reservoir $R_e$ is striking in this fit. Abragam and Goldman argue [10] that a coupled system of one nuclear Zeeman bath and an electron non-Zeeman bath relaxes with a common rate of $T_{1,n} = T_{1,e} \cdot \frac{(H_Z)}{(H_{NZ})}$. Herein, the ratio of the expectation values of the total nuclear Zeeman and electronic non-Zeeman Hamiltonians should be equal to the ratio of heat capacities. From this, one would expect the relaxation rate $R_e$ to be much faster than the nuclear Zeeman relaxation rates, between $(0.10 \text{ s}^{-1})$ (above relation applied to $n = ^1\text{H}$) and $(600 \text{ s}^{-1}) (n = ^{13}\text{C})$. This is not the case in the best fit shown in table 5.2, however, the variance on this parameter is large and almost equal results are obtained for values

<table>
<thead>
<tr>
<th>Sample</th>
<th>Solvent deuteration</th>
<th>Sample deuteration</th>
<th>Solvent $(1/1)_\text{vol}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0%</td>
<td>0%</td>
<td>glycerol/H$_2$O</td>
</tr>
<tr>
<td>B</td>
<td>20%</td>
<td>42%</td>
<td>glycerol/D$_2$O</td>
</tr>
<tr>
<td>C</td>
<td>50%</td>
<td>58%</td>
<td>glycerol-d$_3$/D$_2$O</td>
</tr>
<tr>
<td>D</td>
<td>100%</td>
<td>85%</td>
<td>glycerol-d$_8$/D$_2$O</td>
</tr>
</tbody>
</table>

Table 5.1. Sample compositions. All samples hold 4.5 M $[^{13}\text{C}]$urea and 50 mM TEMPO
down to $T_e = 10$ s such that the obtained value for $R_e$ is not assumed to be unrealistic but rather unsubstantial.

Parameter correlations were analyzed assuming linear correlations. This assumption was found to be a good approximation since only the small range of values around the best fit was considered. The full set of Pearson’s correlation coefficients shows mutual correlations of 2 groups of variables if the threshold for correlation is set to 75%: group I: 1,7 (positive) and 4,5 (positive) and 1,4 (negative); group II: 2,3 (negative). Parameter 6 is additionally weakly correlated to the first group. These correlations are a result of the lack of data necessary to deterministically fit the model, i.e., the missing spin temperature course of the NZ reservoir.

The fitted common set of parameters solves the model simultaneously for the 3 samples A, C, and D with different deuteration degree (figure 5.3) by modification of the heat capacity of the proton bath solely. With the fitted set of parameters furthermore the behavior of the fourth sample (B) with a different deuteration degree could be predicted both in build-up and relaxation speed as well as in steady-state DNP enhancement on both nuclei as shown in figure 5.4. For this, only the model heat capacity has to be modified corresponding to the actual molarity of proton nuclei in the sample.

The model predicts for a sample with 1M $^1$H concentration a build up on the order of 1 s for protons while carbons are not sped up dramatically compared to sample D. With regard to experiments utilizing cross polarization from protons to carbons such a sample however would be unsuited since the low concentration ratio of protons to carbons of 1/4 would lead to low CP efficiency. The measured build-up rates $\tau$ of $^1$H and $^{13}$C and their common steady-state DNP enhancement values of samples A - D are plotted in figure 5.5. In the context of the combination of DNP with CP, this plot shows that not only the achieved common DNP value increases with increasing deuteration but furthermore the $^1$H build-up time decreases, essentially accelerating DNP-CP experiments.

The model correctly predicts the behavior of both $^1$H and $^{13}$C polarization after arbitrary experimental preparation of both nuclear spin temperatures, with and without microwave irradiation (figure 5.6). Specifically, it predicts that after a CP pulse the $^{13}$C enhancement tends to re-equalize with the $^1$H enhancement within the thermal mixing time $T_{TM}$ (figure 5.6 a). This time constant depends on the coupling strength of NZ to both nuclear Zeeman baths and is in general faster than the nuclear $T_1$ (also
Figure 5.2. Correlation plots of the 108 best fits. Plotted are pairwise the parameters: $1 = R_C$, $2 = R_H$, $3 = R_\alpha$, $4 = k_C$, $5 = k_H$, $6 = R_{CL}$, and $7 = \varepsilon_{CL}$ as indicated in the correlation coefficients ($r(x\text{-coordinate},y\text{-coordinate})$). Intensities in the given color code correspond to the inverse of the goodness of the fits. Axis units are $s^{-1}$, unitless for parameter $7 = \varepsilon_{CL}$. 

\begin{align*}
r(1,2) &= -0.037 \\
r(1,3) &= 0.060 \\
r(1,4) &= -0.961 \\
r(1,5) &= -0.895 \\
r(1,6) &= -0.467 \\
r(1,7) &= 0.928 \\
r(2,3) &= -0.861 \\
r(2,4) &= -0.047 \\
r(2,5) &= -0.073 \\
r(2,6) &= 0.504 \\
r(2,7) &= -0.282 \\
r(3,4) &= -0.034 \\
r(3,5) &= 0.010 \\
r(3,6) &= -0.517 \\
r(3,7) &= 0.362 \\
r(4,5) &= 0.936 \\
r(4,6) &= 0.377 \\
r(4,7) &= -0.880 \\
r(5,6) &= 0.283 \\
r(5,7) &= -0.784 \\
r(6,7) &= -0.727
\end{align*}
Figure 5.3. Experimentally obtained $^1$H and $^{13}$C enhancement courses for samples A, C, and D used to fit the model parameters. The simulated enhancement courses by the model using the best-fit parameters (table 5.2) are plotted as solid lines.
5.3 Results and Discussion

**Figure 5.4.** Model predictions using the best-fit parameters (table 5.2) and experimentally obtained values of the DNP enhancement and decay of sample B. The model used a value for the $^1$H heat capacity that was adjusted corresponding to the actual molarity of $^1$H nuclei in the sample.

**Figure 5.5.** Measured build-up rates $\tau$ of $^1$H and $^{13}$C and the common steady-state DNP enhancement values of Samples A - D at 4.2 K.
clearly apparent in figure 5.6 b and d). Figure 5.6 b shows that at 4.2 K the thermal mixing process is active even without ongoing microwave irradiation. In agreement to the findings by Cox et al. in 1973 [66] it shows that the $^{13}\text{C}$ polarization rises after a saturation train. This behavior is well predicted by the introduced model and clearly suggests that the samples are undergoing thermal mixing.

![Figure 5.6](image)

**Figure 5.6.** Model predictions using the best-fit parameters and experimental values of the $^1\text{H}$ and $^{13}\text{C}$ enhancement courses of sample A after different preparations. For a guide to the eye the DNP build-up data (a,c,d) and decay data (b) are underlayed in light grey. The model predicts well (solid lines) the enhancement course of $^{13}\text{C}$ after a CP pulse at $t = 90$ s (a), the $^{13}\text{C}$ enhancement course after steady-state DNP followed by a single saturation on $^{13}\text{C}$ and microwaves turned off (b), both enhancement courses after a CP pulse at $t = 20$ s (c), and both enhancement courses during DNP build up after a single saturation at $t = 120$ s on $^1\text{H}$ (d).

In figure 5.6 c the CP pulse is applied at a time point such that the resulting $^{13}\text{C}$ polarization equals the steady-state DNP enhancement. Here, the model correctly predicts the following decrease of polarization to re-equalize both carbon and proton enhancements. This shows that it is neither straightforward nor enduring to lift
the carbon polarization to its steady-state DNP enhancement with a single DNP-CP pulse. Finally, figure 5.6 d illustrates how the $^{13}$C polarization is effected by (partial) saturation of the $^1$H polarization as will occur during the CP step. The $^{13}$C spin temperature clearly depletes until it re-equalizes with the recovering $^1$H spin temperature.

It is worth mentioning that the model also correctly predicts the initial DNP build-up behavior of both spin baths. While the $^1$H polarization builds up in a mono-exponential manner, the $^{13}$C polarization was found to have an initial damped build-up rate (figures 5.3, 5.4). In the terminology of the spin-thermodynamic model the reason for this is the much weaker coupling between CZ and NZ compared to the coupling between HZ and NZ.
6. The influence of sample parameters on dissolution DNP

The large majority of dissolution DNP experiments nowadays is done using the trityl radical OX063 to polarize pyruvic acid. Furthermore, for methodological developments and research, often derivatives of the TEMPO radical are used to polarize small organic molecules (for example glycine [24, 29], acetate [33], urea [22, 73]) or the solvents [98]. For this reason, the influence of the radical concentration and pH as well as sample temperature of similar systems on dissolution DNP experiments will be discussed in this chapter.

6.1. Pyruvate/trityl-based samples

6.1.1. Solid-state DNP and $T_1$

During the process of dissolution, the sample unavoidably is being heated immediately before being dissolved. This is due to the necessity of coupling and sealing warmer dissolution hardware components (in our case the grabber and the dissolution stick) to the sample container.

To be able to estimate the extent of polarization losses during this period, a series of $^{13}$C $T_1$ data was acquired on samples of [1-$^{13}$C]pyruvic acid doped with 0, 5, 10, and 15 mM trityl. The experiments were conducted using the probe 2 in combination with the NMR stick (see section 3.5.2). The system temperature was stabilized at various temperatures between 1.4 K and 70 K while at each temperature $T_1$ experiments were conducted successively on the samples using the revolver rotation mechanism. The pulse scheme used was a saturation recovery sequence using aperiodic saturation as described in [99, 100]. Signal intensities (peak integrals) were fitted with mono-exponentials.
6.1.2. Liquid-state $T_1$ dependence on pH

The applicability of the dissolution DNP method in combination with solution-state NMR or MRI techniques is essentially determined by the solution-state $T_1$ relaxation rate of the polarized nuclei. It has been shown that for polarized amino acids the polarization loss during shuttling in low field is strongly dependent on pH and increases considerably for basic solutions [32].

Over a period of 2 years the solution-state $T_1$ values of polarized and dissolved [1-$^{13}$C]pyruvic acid samples were observed in numerous referencing phantom experiments in our lab. In each experiment the samples were shuttled to a 9.4 T MRI after dissolution and the decaying polarization was monitored with low-flip angle measurements ($4^\circ$). The experiments were conducted by varying teams mainly composed by Marcin Krajewski, Kilian Weiss, Giorgos Batsios, Lukas Wissmann, Julia Busch, and me. The polarized samples were neat pyruvic acid doped with 13.5 to 15 mM trityl and 1.5 mM Gd with a dissolution ratio of $\sim 1/160$ (only 5 samples were dissolved with $\sim 1/320$, mainly having neutral pH). They were dissolved in a buffered solution (tris + NaCl + EDTA) and mixed with neutralizing NaOH immediately after dissolution next to the DNP magnet before carrying them manually to the MRI. Figure 6.3a shows the correlation of $T_1$ values and the pH values that were measured after the solution-state acquisition had finished.

Furthermore pH-dependent relaxometry was carried out in a 200 MHz solution-state NMR probe. Samples of 83 mM [1-$^{13}$C]pyruvic acid in the tris-buffer solution were prepared to mimic the dissolved pyruvic acid solution (no trityl radicals, 5% D$_2$O added). Samples of different pH were prepared from the same stock by adding certain amounts of NaOH to achieve pH values of: 1.7 (no NaOH), 2.1, 3.9, 6.8, 7.7, 9.4, and 12.3. Saturation recovery measurements were conducted while retaining the sample temperature at constant 310 K (to mimic body temperature).

6.1.3. Results and discussion

Solid-state DNP and $T_1$

Figure 6.1 shows the measured $T_1$ relaxation rates as function of the temperature. Due to excessive relaxation times of the 0 mM and 5 mM samples no data has been acquired at 1.4 K for these samples. Figure 6.1 reveals a strong temperature depen-
dence of all samples, including the one without trityl. This points to the fact that, for the investigated samples, there is a relaxation pathway alongside the relaxation via the paramagnetic radicals that contributes strongly to the $T_1$ relaxation. The source of this is assumed to be the methyl rotations of the pyruvic acid methyls. Furthermore, at temperatures around $4 - 8 \text{ K}$ there appears a range of fast relaxation for all samples, again pointing to another source of relaxation alongside the paramagnetic relaxation.

![Figure 6.1](image)

**Figure 6.1.** Longitudinal relaxation times of [1-$^{13}$C]pyruvic acid doped with 0, 5, 10, and 15 mM trityl as a function of temperature. The error on all data points is $\sim 10\%$ arising from the fitting error. However, the reproducibility of the measurements upon repeated sample freezing has been shown to be less accurate than these 10%.

The fast relaxation both at $4 - 8 \text{ K}$ and at higher temperatures shows the importance of a fast dissolution protocol. For this reason, the dissolution protocol had to be optimized by $i$) reducing the time of thermal contact between the dissolution hardware and the sample container to below 5 s (of which only $< 1$ s is the contact between dissolution stick and sample container) and $ii$) by precooling of the dissolution components (as is achieved by introduction of the cold grabber described in section 3.5.7).
Figure 6.2. DNP build-up times, $T_1$ relaxation times, and steady-state DNP enhancements at 3.47 K on samples of [1-13C]pyruvic acid with trityl concentrations ranging from 5 mM to 25 mM. The different symbols and colors group the data points into groups acquired during the same experimental session and prepared from the same stock solutions.
Further samples of [1-\textsuperscript{13}C]pyruvic acid with trityl concentrations ranging from 5 mM to 25 mM were measured at 3.47 K. In these experiments $T_1$ values were extracted from mono-exponential fits to the decay curves after DNP enhancement (figure 6.2b). From the same DNP build-up and decay experiments build-up rates and steady-state DNP enhancement values were measured on those samples (figure 6.2a and c). The large error bars on figure 6.2c arise from the low reproducibility of DNP enhancements upon reloading the system with the same samples. This is mainly due to the fact that in these experiments the samples were scanned in the dissolution port position using the NMR stick. The bump of DNP enhancements around 16 mM thus has to be taken with care and understood as tendency.

**Liquid-state $T_1$ dependence on pH**

The correlation of the solution state $T_1$ with the sample pH both measured in 9.4 and 4.7 T are shown in figure 6.3. Both figures 6.3b) and a) show a similar dependence. The data sets indicate the importance of neutral pH during acquisition in the MRI/NMR after dissolution and hence care has to be taken to adjust the pH of the dissolved sample by adding the correct amount of base immediately after dissolution.

![Figure 6.3](image-url)  
**Figure 6.3.** Correlation of solution-state $T_1$ and sample pH ($T_1$ values are given with 10% error estimated from the monoexponential fitting variance). a) $T_1$ after dissolution DNP experiments measured in a 9.4 T MRI. All samples contain dissolved [1-\textsuperscript{13}C]pyruvic acid (final concentration of $\sim$ 90 mM) and traces of trityl radical ($< 100 \mu$M) in a tris buffer. b) $T_1$ measured in a 4.7 T at 310 K of samples containing 83 mM [1-\textsuperscript{13}C]pyruvic acid in tris-buffer solution (without trityl radicals, 5% D$_2$O added).

For in-vivo MRI experiments the pH has to be adjusted roughly to physiological pH 7.3 – 7.4 [101],[102, p. 146]. The presented data shows that this is the optimum region
concerning $T_1$ as well.

Low-field pH-dependent relaxometry on pyruvic acid samples would help understanding the relaxation dependence during the shuttling processes. Similar low-field relaxometric data has been published on $[1^{-13}\text{C}]$acetate doped with up to 2.5 mM of the TEMPOL radical by Mieville et al. [103]. The relaxation pathways and their strength however strongly depend on the molecule of interest, the paramagnetic dopand, and the solvent. Therefore, care has to be taken when attempting to apply the findings of Mieville to pyruvic acid samples.

6.2. TEMPO-based samples

Samples doped with the TEMPO radical were chosen in this work for the combination of dissolution DNP with CP. For this reason, samples of 4.2 M $[^{13}\text{C}]$urea in (1/1)$_{\text{vol}}$ glycerol-d3/D$_2$O with radical concentrations between 20 – 70 mM were analyzed regarding their solid-state DNP values, CP efficiency, dissolution efficiency, and solution state $T_1$.

6.2.1. Solid-state DNP enhancement

Samples containing 30, 45, and 70 mM were polarized in the probe 1 at single shot temperatures. Note that in this probe the temperature sensor mounted on the probe reads 1.5 – 1.7 K during microwave irradiation whereas the temperature sensor mounted on the cryostat remains at its low temperature reading (1.2 – 1.3 K). Thus, the exact temperature during these experiments cannot be determined more accurately than giving the range 1.3 – 1.7 K or stating < 1.7 K. The $^{13}\text{C}$ NMR signal intensity was followed with low-flip angle measurements ($< 4^\circ$) every 30 s without microwave irradiation. After having acquired a large enough amount of thermal equilibrium reference spectra the microwaves were turned on to the optimum frequency (~ 93.900 GHz, depending on the sample) and field strength (120 mW) previously determined. After reaching the DNP steady state, the microwaves were switched off to determine the $T_1$ relaxation rate.
6.2.2. CP efficiency

For samples containing 30 and 70 mM TEMPO the CP transfer was optimized and compared at single-shot temperatures (1.3 – 1.7 K) and 4.2 K in probe 1. The CP transfer was done using the AHP pulses with a maximum rf-field amplitude and CP mixing field strength of 100 kHz.

6.2.3. Dissolution efficiency

On the probe 2 the dissolution efficiency was compared for the urea samples containing 20, 30, 40, 60, and 70 mM TEMPO with and without CP following the DNP at 1.35 K. The experiments were conducted following the procedure described in section 4 in combination with automatic shuttling to a 7 T NMR spectrometer. Microwave frequency and irradiation times were set to the optimum for each sample and the CP sequence was used with AHP pulses with a maximum field strength and mixing field of 30 kHz. The dissolution efficiency was calculated as the ratio between the $^{13}$C polarization in the liquid state (back extrapolated to time point $t = 0$ after dissolution, see section 4) and the $^{13}$C polarization measured immediately before dissolution (for the DNP-CP experiments after the CP pulse). Thereby, the polarization in the liquid state can be determined accurately since the thermal equilibrium data has a high enough SNR. The solid-state polarization values without CP were assumed to correspond to the ones quantified in the probe 1 at single shot temperature, i.e. with $\varepsilon \sim 80$. The solid-state polarization after the CP pulse was calculated by multiplying the corresponding observed CP factor with the plain DNP polarization value.

6.2.4. Results and discussion

Solid-state DNP enhancement

The solid-state DNP enhancements of the samples containing 30, 45, and 70 mM TEMPO as well as the time constants of the mono-exponential fits to the DNP build-up and decay curves are shown in figure 6.4. For the given range of radical concentrations the enhancement does not change considerably. The time constants however increase by 500% ($\tau$) and 1200% ($T_1$) when reducing the TEMPO concentration from 70 to 30 mM.
Comparable experiments were published by Kurdzesau et al. on sodium acetate doped with 17, 33, and 50 mM TEMPO [29]. While for the build-up time similar values were found, the DNP enhancement at 33 mM in their publication is twice as high as at 17 and 50 mM, both comparable to the results shown here.

![Figure 6.4](image)

**Figure 6.4.** Solid-state $^{13}$C DNP build-up rate, steady-state enhancement, and $T_1$ relaxation rate at 1.3 – 1.7 K of samples containing 4.2 M [$^{15}$C]urea in (1/1)$_{\text{vol}}$ glycerol-d3/D$_2$O doped with 20, 45, and 70 mM TEMPO.

**CP efficiency**

For CP the most important parameter to be optimized when changing the radical concentration was found to be the CP mixing time. Figure 6.5a shows for both samples the CP transfer as a function of the mixing time at single-shot temperature. It shows that the optimum mixing time shifts strongly from ~ 2000 $\mu$s to ~ 750 $\mu$s when going from 30 to 70 mM TEMPO concentration. Furthermore the achievable CP factor is reduced as shown in figure 6.5b for both temperatures.

To investigate the source of the reduced CP efficiency at large radical concentrations $T_{1p}$ measurements were conducted on both samples at both temperatures with the same protocol as described in section 4.3.2. The $T_{1p}$ data were fitted with exponential decay curves and the corresponding time constants are plotted in figure 6.6. The
$T_{1,\rho}$ values decrease strongly for increasing TEMPO concentration. This enhanced relaxation rate in the rotating frame explains the efficiency loss of the CP transfer for higher radical concentrations seen in figure 6.5b. Additionally plotted in figure 6.6 are the optimum mixing times for the AHP CP sequence, decreasing with increasing TEMPO concentration in the same manner and once more emphasizing the need to optimize this parameters upon changes of the radical concentration.
Figure 6.5. a) The CP transfer as function of the mixing time at < 1.7 K for the samples containing 30 and 70 mM TEMPO. b) The optimized CP factors for both samples at < 1.7 K and 4.2 K using the AHP pulses CP with 100 kHz mixing field strength.

Figure 6.6. $^{13}$C $T_{1p}$ relaxation times (⋆) and optimum CP mixing times (□) for the samples containing 30 and 70 mM TEMPO at < 1.7 K and 4.2 K.
Dissolution efficiency

Figure 6.7a shows the calculated dissolution efficiencies for all samples (other than the 20 mM sample on which no DNP-CP experiment was conducted). The data shows a clear tendency on all samples of decreasing dissolution efficiency with increasing radical concentration. The drop in efficiency from the 30 to 70 mM sample is as large as 1/3.2. In figure 6.7c the solution-state $^{13}$C $T_1$ relaxation times are plotted as acquired by following the decaying hyperpolarized NMR signals after the dissolutions.

Figure 6.7. The dissolution efficiency (a) and final reached $^{13}$C polarization levels (b) upon dissolution DNP-CP experiments conducted on samples containing 4.2 M $^{[13]}$C urea in (1/1)$_{vol}$ glycerol-d3/D$_2$O with radical concentrations between 20 – 70 mM. Additionally the solution-state $T_1$ values are plotted in c) as acquired during the relaxation of the hyperpolarized samples in the 7 T spectrometer.
Together with the loss in CP transfer efficiency with larger radical concentrations seen in figure 6.5 the final solution state DNP-CP $^{13}$C polarization shown in figure 6.7b reveals a strong inverse dependency on the radical concentration.

The dependence of the dissolution efficiency on the radical concentration might be a unique feature of the experimental setup chosen in these experiments, i.e. the exact pathway of the dissolved sample through the low-field area between the DNP magnet and the NMR magnet. Furthermore, the speed of the shuttling might be a crucial parameter in these experiments in the sense that it might influence the relative differences in dissolution efficiencies observed at different radical concentrations.
Conclusion

In this thesis a cryogenic multi-sample DNP system was realized with heteronuclear NMR, EPR, and dissolution capabilities. Dissolution DNP was combined with a modification of the Hartmann-Hahn cross polarization technique using adiabatic half-passage pulses. Finally, a spin-thermodynamic model was applied and the impact of sample parameters on the dissolution DNP-CP method was measured to improve the overall efficiency of dissolution DNP-CP experiments.

Instrumentation

In chapter 3, the realization of the DNP setup is described. The cryogenic system was designed to fit wide-bore NMR magnets and is therefore transferrable between compatible magnets.

Two DNP probes have been realized: a single-sample probe allowing static heteronuclear solid-state NMR experiments with high sensitivity and rf-field strengths up to 100 kHz and a multi-sample DNP probe with low-sensitivity NMR, EPR and dissolution capabilities.

The revolver-style sample changer of the multi-sample probe has been shown to reliably allow exchange of samples between the DNP, CP, and dissolution sites at the operating temperature and pressure ranges of the system. The multi-sample probe has been found to be highly convenient to conduct series of solid-state DNP experiments with varying sample compositions, since the time-consuming changing of samples can be avoided. Furthermore, conducting multiple dissolution DNP experiments during one working day is eased by the possibility of a single loading procedure of all samples at the beginning of the working day.

The incorporation of an oversized microwave cavity allows efficient microwave irradiation with minimized heating of the sample space. An EPR coil allows longitudinal detected EPR experiments down to 4-10 K which is important for testing DNP
Conclusion

in combination with new radicals or mixtures of radicals. The presented dissolution DNP system has proven to reach $^{13}$C polarization levels of up to 45% in the solid state and 33% in the solution state.

For the purpose of increasing the repetition rate of subsequent dissolutions, the multi-sample probe has shown the need for improvements. Although simultaneous polarization of all 6 samples was shown to be possible, the dissolution of one sample means losses in polarization of the remaining samples and makes dissolutions DNP experiments with a high repetition rate unfeasible. This problem could be addressed by making the dissolution conductible under vacuum conditions.

**Dissolution DNP-CP**

In chapter 4, aspects of the combination of CP with dissolution DNP are discussed. It is concluded that thermal mixing is the most favorable mechanism for DNP-CP experiments while emphasizing two drawbacks of this mechanism: i) the necessity of large-line width radicals reduces the achievable direct DNP enhancements and ii) the thermal mixing between the $^1$H and $^{13}$C Zeeman reservoirs leads to the demand of minimizing the delay between CP and dissolution to $\ll T_{TM}$.

A partial saturation method for calibration of rf-flip angles is introduced and shown to allow time-efficient estimation of the $B_1$-field strength when using slow-relaxing samples. It is, therefore, a convenient method for rf-field strength estimation in low-temperature DNP or NMR experiments.

To allow efficient application of the CP method under the limited rf-field strengths available in the dissolution DNP probe, it is shown that adiabatic half-passage pulses are able to enhance the Hartmann-Hahn CP transfer efficiency, especially at low rf-field strengths. The DNP-CP technique using adiabatic half-passage pulses is shown to allow acceleration of the polarization build up while reaching higher final $^{13}$C polarization levels. It is shown that the solid-state CP enhancement can be transferred to the solution state via dissolution.

**A spin-thermodynamic model of thermal mixing**

In chapter 5, a spin-thermodynamic model based on the thermal mixing mechanism is applied to TEMPO-based samples. By varying the thermal capacity of the proton
Zeeman bath, the model correctly predicts the effect of solvent deuteration and provides an intuitive understanding of the reason for the enhanced DNP efficiency upon sample deuteration. The presented model, furthermore, correctly predicts the course of spin temperatures after various preparations of the nuclear polarizations.

The successful prediction of the dynamics of the spin system during DNP experiments is understood as an indication for thermal mixing to be the dominant mechanism on both $^1$H and $^{13}$C in TEMPO-based samples.

**The influence of sample parameters on dissolution DNP**

In chapter 6, solid-state $T_1$ and DNP performance values are presented for trityl-doped pyruvic acid samples. The shown data emphasizes the importance to minimize the time of sample exposure to hot dissolution components during the dissolution procedure.

Solution state $T_1$ values as a function of the sample pH are shown for the commonly used trityl-doped pyruvic acid sample at 9.4 and 4.7 T. The data indicates that longest $T_1$ values are reached at neutral pH.

The DNP, CP, and dissolution efficiencies of TEMPO-doped samples are presented as a function of radical concentration. A significant decrease of the overall efficiency of the dissolution DNP-CP experiment towards larger radical concentrations is observed for the given sample compositions and experimental protocol.

The discussions throughout this thesis additionally lead to the conclusion that for TEMPO-based samples the dominant DNP mechanism is thermal mixing, both on $^1$H and $^{13}$C. This conclusion arises once from the theoretical discussion given in section 2.2 concluding that the DNP enhancement is independent of the nuclear $\gamma$ for thermal mixing while being inverse dependent for the solid effect, while the data presented in section 4.4 shows that the experimental enhancement reached is equal on both $^1$H and $^{13}$C. The same argument holds for the cross effect, whose contribution has been shown to drop even below the solid effect below 20 K for a similar system [53]. Additionally, equal polarization levels of both nuclei in similar systems using TEMPO have been reported [29], whereas for the trityl radical the enhancement on $^{13}$C has been reported to be $>10$ fold compared to the $^1$H enhancement [27]. Second, the possibility of fitting and predicting experimental DNP data with the spin-
thermodynamic model presented in chapter 5 indicates that thermal mixing is the dominant mechanism.
Outlook

To push the dissolution DNP method towards the overall aim to which this work was directed, i.e., the achievement of large solution-state polarization values at a high repetition rate, further work has to be done on the hardware as well as on the methodological side.

The dissolution DNP system presented in chapter 3 has shown to allow operating temperatures of down to \( \sim 1.3 \) K. This is a value similar to what is reached by other published dissolution DNP systems [22, 24, 25, 104] and possible to be lowered considerably only with much more dedicated cryostat designs [28, 84]. A problem arising from the actual design of the presented multi-sample probe is the depletion of polarization of the remaining samples upon dissolution of one sample. To tackle this problem, the design presented by Marcin Krajewski [85] should be supported and advanced. It is based on multiple independent dissolution paths that couple and seal each to one of the simultaneously polarized samples similar as in [84].

To enhance the repetition rate of dissolution DNP experiments, it is shown in chapter 4 that DNP-CP is a possible complementing approach to the multi-sample design. The lack in achieved \(^{13}\)C polarization values, however, makes further developments on this technique necessary. On the hardware site, the group of Geoffrey Bodenhausen (EPFL, Lausanne) recently showed [95, 105], that applying the DNP-CP technique in a magnetic field close to 7 T can lift the final reached polarization to similar values as achieved for trityl-based samples in common 3.4 T dissolution DNP systems but with higher build-up rates. Therefore, the development of a high-field dissolution DNP system allowing heteronuclear NMR experiments would be promising.

On the methodological site, further investigations should be conducted to enhance the efficiency of the DNP-CP technique. As emphasized in section 3.5.5 and 4.5, rf-limitations are often encountered in dissolution DNP probes. CP techniques should thus be investigated allowing efficient polarization transfer at lower rf-field strengths.
A method recently suggested by Lee and Khitrin [106, 107] applies adiabatic demagnetization and remagnetization in the laboratory frame (ADLF/ARLF), a technique based on adiabatic demagnetization in the rotating frame [108] similar to the "total CP" experiment [109]. The advantage of full adiabatic CP techniques is the theoretical increase of the CP transfer factor by $\sqrt{N_1 / N_Q}$ over the Hartmann-Hahn CP such that $^1$H to $^{13}$C enhancements of up to 15-fold have been reported in static powder adamantane [110]. Using the approach chosen by Lee and Khitrin, furthermore, allows the experiment to be conducted at much lower rf-field strengths, e.g., below 10 kHz in their case. Further research along this line could both, improve the final polarization values as well as reduce the demands on rf-field strengths.

It is discussed in section 4.5 that large EPR line widths allow the polarization of $^1$H via thermal mixing but reduce the DNP enhancements reached for all participating nuclei. In DNP-CP experiments it is, therefore, beneficial to use radicals with line widths larger but similar to the $^1$H Larmor frequency. Lumata et al. investigated the usage of galvinoxyl for the use of DNP and showed that its line width is intermediate to the one of trityl and TEMPO [93]. Investigations on the usage of galvinoxyl or radicals with similar line widths for DNP-CP experiments could further increase the DNP-CP efficiency.

The spin-thermodynamic model presented in chapter 5 could be extended by including predictions for the rate constants. Alternatively, it could be used to gain information about the correlation between sample parameters and the rate constants. Further improvements in this direction could be achieved if the inverse spin temperature of the electron non-Zeeman reservoir could be accessed experimentally, e.g., by line shape analysis. These investigations should be directed to solving the question if it is possible to enlarge the thermal coupling between the electron non-Zeeman and the $^1$H Zeeman reservoir while reducing the corresponding coupling to the $^{13}$C reservoir. This way, faster $^1$H DNP and thus DNP-CP to $^{13}$C could be achieved and multiple-contact time CP could be applied more efficiently.

The standard sample used in dissolution DNP today is $[1-^{13}$C] pyruvic acid. Therefore, all further developments of the DNP-CP technique should be focused on optimizing the efficiency on this sample. The results shown in section 6.2.4 on the dissolution efficiency of TEMPO-based samples are alerting concerning the usage of larger radical concentrations. Compared to the results published by the Bodenhausen group
[95], the efficiency achieved in the experiments presented here are low. The reason for this should be investigated to avoid similar losses on pyruvic acid based samples. Measurements of the $T_1$ values of a suited sample as a function of low magnetic fields would provide valuable information in the context of such investigations. A promising approach should be the scavenging of the TEMPO radicals upon dissolution as suggested by Mieville et al. [103, 111]. With their approach, they are able to extend, both, the $T_1$ and $T_2$ relaxation times in the solution state at high and low (2 mT) magnetic fields.

The placement of the DNP project within the group of solid-state NMR at the ETH finally stimulates the application of solid-state DNP as a complementing technique to MAS NMR. A current open problem of the research group is the determination of the torsion angle between the two phenyl rings of congo red when bound to an amyloid fibril. Similar to the work presented by Potapov et al. [112], one can use static DNP-enhanced double-quantum and single-quantum spectra (DOQSY) [113] to measure CSA tensor correlations. For this method to work, however, the spectral resolution should be large enough to resolve the CSA tensors. The development of the high-field DNP system suggested previously could support such a project.
Appendices
A. Cryogenic heat flow

The heat flow through a small temperature difference is given by the general formula:

$$\dot{Q} = -\sigma(T) \cdot A(x) \cdot \frac{dT}{dx}. \quad (A.1)$$

The heat conducted through an object in $x$-direction from a plane at $x_1$ at temperature $T_1$ to $x_2$ at $T_2$ thus can be calculated [114] as:

$$\dot{Q} = -G \left[ \Sigma(T_2) - \Sigma(T_1) \right] \quad (A.2)$$

where $G$ is a geometry function defined by

$$G = \left[ \int_{x_1}^{x_2} \frac{1}{A(x)} dx \right]^{-1} \quad (A.3)$$

with the variable cross section $A$. $\Sigma$ is the integrated thermal conductivity

$$\Sigma(T) = \int_{0}^{T} \sigma(T')dT' \quad (A.4)$$

with the temperature-dependent thermal conductivity $\sigma$.

For a uniform body in $x$-direction with cross-section $A$ the geometry factor simplifies to

$$G = \frac{(x_2 - x_1)}{A} \quad (A.5)$$

so that the heat flow over $L = x_2 - x_1$ can be calculated with the formula

$$\dot{Q} = -\frac{A}{L} \left[ \Sigma(T_2) - \Sigma(T_1) \right]. \quad (A.6)$$

A further simplification could be done by the assumption of $\sigma =$constant. For most materials this is a bad approximation. Especially in liquid-helium applications in
general it does not hold since large temperature differences are achieved. However, for parts of the cryogenic systems discussed in this work that experience only modest temperature differences it might be applicable and one can use:

$$\dot{Q} = - \frac{A}{L} \sigma \Delta T.$$  \hfill (A.7)

To calculate the heat flow through a specific material its exact $\sigma(T)$ has to be known. This, however, depends strongly on the fabrication process, which means that the thermal conductivity functions given in the literature should only be used for estimations. For the purpose of this work this is sufficient. Figure A.1 shows an overview of some common materials (source: Lake Shore Cryotronics, "Cryogenic Reference Tables"). For the same material figure A.2 gives the integrated thermal conductivities.

To calculate the heat conducted from room temperature to $< 4 \text{ K}$ the term

$$[\Sigma(\sim 300\text{K}) - \Sigma(< 4.2\text{K})]$$

can be approximated by $\Sigma(300\text{K})$. Therefore, equation A.6 can be simplified to

$$\dot{Q} = - \frac{A}{L} \Sigma(300\text{K}).$$  \hfill (A.8)

Additionally to the values shown in figure A.2 the following values shall be given:

1. Silver: $\Sigma(300\text{K}) \approx 100\,000$ (drawn) - $360\,000$ (annealed) $\frac{W}{m}$ [115],

2. Carbon fibres - A: $\Sigma(300\text{K}) \approx 100 - 7500$ (mean: 1500 $\frac{W}{m}$) (data calculated from [116] using $\Sigma(300\text{K}) = \frac{1}{2}300 \cdot \sigma(300\text{K})$ by linearly approximating and extrapolating the time dependence given).

3. Carbon fibres - B: $\Sigma(300\text{K}) \approx 900\,W/m$ (data calculated as above, from [117])
Figure A.1. Thermal conductivities of selected materials. Source: Lake Shore Cryotronics, "Cryogenic Reference Tables"
Figure A.2. Integrated thermal conductivities of selected materials. Source: Lake Shore Cryotronics, "Cryogenic Reference Tables"
A.1. Heat flow through a succession of materials

For electrical cryogenic components low thermal and high electrical conductance is desired. This demand can be addressed by using compromising materials which have medium thermal and electrical conductivities (for example CuBe). Another approach is the succession of different materials over the entire conducting path. The estimation of the resulting heat flow of a succession of two materials $M$ (warm end at $T_2$) and $N$ (cold end at $T_1$) of length $m$ and $n$ ($L = m + n$) shall be given here.

The heat flow through both materials is given with equation A.6

\[
\dot{Q}_m = -\frac{A_m}{m} [\Sigma_m(T_2) - \Sigma_m(T_x)] \quad (A.9)
\]

\[
\dot{Q}_n = -\frac{A_n}{n} [\Sigma_m(T_x) - \Sigma_n(T_1)] \quad (A.10)
\]

with the temperature at the junction $T_x$. To conserve energy, both heat flows have to be equal:

\[
\frac{A_m}{m} [\Sigma_m(T_2) - \Sigma_m(T_x)] = \frac{A_n}{n} [\Sigma_n(T_2) - \Sigma_n(T_x)]. \quad (A.11)
\]

Equation A.11 can be solved numerically for the junction temperature $T_x$ if both integrated thermal conductivities $\Sigma_i$ are known. With $T_x$ the heat flow can be calculated using equation A.6.
B. Cavity dimensions

The exact dimensions of the microwave cavity of probe head 2 are given in the following. These dimensions were used for the simulations shown in figure 3.8 b.
Figure B.1. Technical drawing of the upper part A of the microwave cavity of probe 2 (by Andreas Hunkeler).
Figure B.2. Technical drawing of the upper part B of the microwave cavity of probe 2 (by Andreas Hunkeler).
Figure B.3. Technical drawing of the lower part of the microwave cavity of probe 2 (by Andreas Hunkeler).
Bibliography


Acknowledgement

This thesis is in great parts a result of close teamwork and would not have been realized without the help of my coworkers. I want to thank everyone who contributed to this work, specifically addressing the following people:

My supervisor and mentor Prof. Matthias Ernst who supported me in all stages of the project. With great patience he gave me the time and support to study DNP and NMR while simultaneously fighting with the hardware development. His guidance and trust were my major motivation throughout this project.

My co-examiners Prof. Gunnar Jeschke and Prof. Sebastian Kozerke for reviewing and improving this thesis with their constructive feedback. Additionally, leading the DNP project from the imaging side, Prof. Kozerke was like a second supervisor to me. I thank him for the continuous support and stimulation to push further the development of the DNP hardware.

The head of the research group Solid State NMR Prof. Beat H. Meier for allowing me to participate in the DNP project, which was mainly situated in his laboratory.

Dr. Marcin Krajewski with whom I realized the development of the revolver and cryogenic system while profiting from his direct supervision. I want to thank him for his patience in helping me overcome all technical obstacles and keeping up his humor at any stage of the projects or day and nighttime.

Andreas Hunkeler not only for building both probes as the groups mechanic. Also he was always available and reliable in hardware-related ‘emergency’ situations. Finally, sharing the hobby of photography he became a friend and our Timelapse-Dolly project connects us even beyond the ETH.

The electricians Alex and Oli for designing and realizing the electrical circuitries and for the common days in the mountains. Also René Tschaggelar for his help in designing the microwave circuit.

The remaining DNP team consisting of Kilian, Andreas, Georgios, Lukas, Julia, and Patrick for the dedicated effort in establishing workflows and helping to reach
the desired performance of the DNP system. Especially Kille was not only an integral part of the initial trio during the implementation. He also helped me enjoy countless nights both in the Kabuff and in the nightlife of Zürich.

Further staff of the LPC contributed in different ways. Gabriele was always willing to both help with administrativ issues as well as cheering me up with entertaining small talk. The chemists Riccardo, Guido, and Fabienne helped providing the samples.

The PhDs and postdocs in the Meier lab for always being open for a coffee, discussions on research or teaching assistance, a round of crazy-ball or the weekly football matches. Anders dared to use the DNP setup for non-DNP research. I enjoyed the puzzling and often amusing work on the Haupt project with him.

The ‘Spalter’ lunch group with Rosi, Andreas, Oli and Alex guaranteed the daily escape from the turbulences in the project. I gained profound inside into the swiss culture in this round and to them I owe a good deal of my rudimentary skills in Züridütsch.

Lilli stands by me and bears me. I am deeply grateful for her love and patience in all phases of the PhD and for the energy and time she was willing to invest upon my decision to move to Zürich.

Finally, it is my roots in the first place that allowed me to find my way. With their unconditional support my parents gave me the will and self-confidence to go this way. This thesis is dedicated to my family.
Curriculum Vitae

Name: Michael Batel

Date of birth: June 25, 1982

Place of birth: Lindenfels (Federal Republic of Germany)

Nationality: German

Education

Sep. 2008 – present  Ph.D. studies supervised by Prof. Matthias Ernst at the laboratory of physical chemistry at ETH Zürich (Zürich, Switzerland)

Aug. 2007 – Aug. 2008  Diploma thesis at the DKFZ (Heidelberg, Germany)

Sep. 2002 – Aug. 2008  Diploma studies in physics at the University of Heidelberg (Heidelberg, Germany)

March. 2005 – July 2005  Student exchange at the University of Zagreb (Zagreb, Croatia). Majors: solid-state physics, croatian


Aug. 1999 – June 2000  US High School Diploma during a student exchange at Hermon High School (Hermon, Maine, USA)
Work Experience

Sep. 2008 – present
ETH Zürich Teaching assistant in the laboratory of physical chemistry

March 2010
Kyoto University Visiting researcher fellowship

Nov. 2007 – June 2008
DKFZ Heidelberg Student assistant

DWM GmbH Merchandiser at Vobis, Heidelberg
List of Publications


K. Weiss, A. Sigfridsson, L. Wissmann, J. Busch, M. Batel, M. Krajewski, M. Ernst, and S. Kozerke, 2013. Accelerating hyperpolarized metabolic imaging of the heart by exploiting spatiotemporal correlations. *Nmr in Biomedicine* Published online 2013