Triple resonant electromagnetic structures for polarization transfer in DNP

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Triple resonant electromagnetic structures for polarization transfer in DNP

Ph.D Thesis
Mohammed M. Albannay

Kgs. Lyngby, May 2019
Triple resonant electromagnetic structures for polarization transfer in DNP

Submitted in fulfillment of the requirements for the degree of Doctor of Philosophy at the Technical University of Denmark.

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Abstract

Despite, its low inert sensitivity, it is irrefutable that nuclear magnetic resonance (NMR) is extremely useful for both analytical spectroscopy and imaging. As the study of magnetic resonance evolved, detection instruments improved and magnets increased yielding modest improvements to sensitivity. Ultimately, it is the polarization of nuclear spins between Zeeman energy levels that dictate the NMR signal intensity.

Several hyperpolarization methods exist in aiding to increase nuclear spin polarization but it is dynamic nuclear polarization (DNP) the offers the most versatility in application to an exhaustive range of nuclear spins. The method relies on transferring spin polarization from unpaired electrons to nuclear spins facilitated my irradiation at the electron resonant frequency.

In 2003, a technique emerged based on DNP to produce polarized liquid-state solutions. The technique involves cooling a sample to approx. 1 K in a high magnetic field (≥ 3.35 T) where electron spin polarization is very high and rapidly dissolving the sample with a hot solvent to produce the solution. Dissolution dynamic nuclear polarization enabled real time surveillance of metabolic conversions in both spectral and spatial dimensions, finding employment in the study of cancer progression and response to therapy.

Polarizer systems have since rapidly evolved to primarily reach higher nuclear polarization levels, but also increase sample throughput, limit dependence on cryogenics and incorporate automation. The latest polarizer design realizes a variable field (up to 10.1 T) cryogen-free polarizer system. This thesis serves to investigate the development of instruments to improve the polarization process in a system of that type. Herein a probe is developed facilitating the ability to perform double resonance solid-state DNP experiments with dissolution capabilities. Moreover, the design is optimized to minimize static heat load, manufacturing complexity and cost.

To improve throughput another probe capable of performing cross-polarization is developed, yielding 27% $^{13}$C polarization with a 12 min build-up time that is twice the direct $^{13}$C polarization and 4.4 times faster. Dissolution compatible coil geometries are explored. Techniques to design single and double resonant detection circuits including methods to evaluate their sensitivity is discussed. In low pressure environments arcing is probable due to high voltages during pulsing. As such, arc detection methods and mitigation strategies are explored and experimentally verified.

Microwave power in solid-state sources is increasingly scarce at higher magnetic fields. To combat this limitation and greater transmission losses, two microwave strategies were
designed and experimentally verified. A process is described to reduce waveguide attenuation due to conductive loss thereby doubling the delivered power. A chamfer and reflector are designed, fabricated and tested to increases the microwave field density across the sample volume resulting in an equivalent 1.3 dB increase in power.

A compact two channel benchtop spectrometer is developed, suitable for use up to 450 MHz. This, in part, aids the deployment of polarizer without the need of a traditional full-rack spectrometer. Sensitivity tests indicate the bench spectrometer achieves 90% and 50% the signal-to-noise ratio value of that from a dedicated full rack spectrometer for $^1$H and $^{13}$C spectra measured at 6.7 T.
Resumé

Der eksisterer mange forskellige spektroskopiske metoder, hver med deres egne styrker og svagheder. På trods af sin umiddelbart lave følsomhed, er det unægteligt at nuklear magnetisk resonans (NMR) har været til stor nytte for analytisk spektroskopi og medicinsk billeddiagnostik. Som feltet magnetisk resonans har udviklet sig, har bedre instrumenter og stærkere magnete resulteret i beskedne forbedringer af sensitiviteten. Ultimativt er det polariseringen af de nuklære spin mellem Zeeman energiniveauerne der dikterer intensiteten af NMR signalet.

Der eksisterer flere forskellige hyperpolariseringsmetoder, der forstærker intensiteten af signalet ved at øge polariseringen af de nuklære spin. Af disse metoder tilbyder dynamisk nuklear polarisering (DNP) den højeste versatilitet, i det den kan anvendes på en adskillige forskellige typer af nuklære spin. Denne metode fungerer ved at overføre spin polarisering fra uparrede elektroner til nuklære spin, facilitet af bestråling ved elektron resonans frekvensen.

I 2003 udvikledes en teknik baseret på DNP der tillod produktionen af polariserede opløsninger. Denne teknik fungerer ved at køle en prøve til ca. 1 K i et stærkt magnetfelt ($\geq 3.35$ T), hvor polariseringen er meget høj for elektron spin, og efterfølgende opløse hastigt ved hjælp af et opvarmet solvent, for derved at producere den polariserede opløsning. Såkaldt opløsnings DNP har tilladt overvågning af metabolske processer i realtid, i både spectrale og spatielle dimensioner. Dette har været relevant inden for for overvågning af kræft og monitorering af terapiresponser.

Polarisator systemer har siden oplevet en hastig udvikling, primært for at opnå højere polarisering, men også for at øge prøve gennemløbet, reducere afhængigheden af cryogener og inkorporere automatisering. De nyeste polarisator design muliggør et cryogen-frit polarisator system med varierende felt (op til 10.1 T). Denne afhandling undersøger udviklingen af instrumenter med det formål at forbedre polariseringsprocessen i systemer af denne type. Heri udvikles en probe der faciliterer muligheden for at udføre dobbeltresonans faststof DNP eksperimenter med kapacitet for opløsningsprocessen. Designet bliver yderligere optimeret til at mindske den statiske varmebelastning, kompleksiteten af fremstillingen og omkostningerne.

Krydspolarisering bliver implementeret, hvilket resulterer i et udbytte på 27 % $^{13}$C polarisering efter 12 minutters akkumulering, hvilket er dobbelt så højt som ved direkte $^{13}$C polarisering og 4.4 gange så hurtigt. Spoletyper der er kompatible med opløsningsprocessen
bliver undersøgt. Teknikker til at designe kredsløb til detektion af enkelt- og dobbeltreso-
nans, samt metoder til at vurdere deres sensitivitet bliver diskuteret. Ved lavt tryk er der
en øget risiko for elektrisk afladning, grundet den høje spænding under pulseringen. Der-
for bliver metoder til at detektere og mitigere afspænding udforsket og eksperimentielt
verificeret.

Kraften fra solid-state mikrobølge kilder bliver betragteligt dæmpet i stærke magnetiske
felter. For at bekæmpe denne begrænsning og transmissionstab, bliver to forskellige mikrobølge
strategier designet og eksperimentielt verificeret. En proces bliver beskrivet der reducerer
dæmpningen af bølgelederen, hvorved den leverede kraft fordobles. Et spejl og en reflek-
tor bliver designet, fabrikeret og tested for at øge densiteten af mikrobølgefeltet hen over
prøven, hvilket resulterer til en stigning i kraft svarende til 1.3 dB.

Et kompakt to-kanals spektrometer bliver udviklet, der er velegnet til analyse op til 450
MHz. Dette faciliterer etableringen af en polarisator der er uafhængig af det traditionelle,
ophængte NMR spektrometer. Undersøgelser af sentiviteten indikerer at det kompakte
spektrometer opnår hvad der svarer til 90 % og 50 % af SNR værdien af et ophængt NMR
spektrometer for respektivt.
This thesis was prepared at the Center for Hyperpolarization in Magnetic Resonance part of the Department of Health Technology (formerly part of the Department of Electrical Engineering) at the Technical University of Denmark, including a 5 weeks external research stay at the Cancer Research UK/Cambridge University, England, UK. The thesis was submitted in conformity with the requirements for the degree of Doctor of Philosophy at the Technical University of Denmark.

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The thesis was submitted for assessment on May 31st 2019 and successfully defended on July 8th 2019.

The thesis investigates the development of dissolution dynamic nuclear polarization instruments for high-field cryogen-free polarizer systems.

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Kgs. Lyngby, May 2019

Mohammed M. Albannay
Contribution

Journal publications


Conferences


This thesis came to fruition as a result of scientific curiosity and close collaboration with my colleagues at HYPERMAG. I wish to thank and recognize all members past and present for shaping my development, specifically addressing the following people:

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helped me navigate DTU and Copenhagen in my early days but also served to be my writing partner as we both prepare to submit our thesis.

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This project is part of a larger consortium (EUROPOL ITN) consisting of 18 Ph.D. students distributed all across Europe. Collectively we shared knowledge, experiences and research skills. It was a pleasure working with them all and meeting them at conferences, meetings and secondments.

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# Nomenclature

## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC</td>
<td>analouge to digital converter</td>
</tr>
<tr>
<td>CP-DNP</td>
<td>cross-polarization in combination with DNP</td>
</tr>
<tr>
<td>dDNP</td>
<td>dissolution dynamic nuclear polarization</td>
</tr>
<tr>
<td>DNP</td>
<td>dynamic nuclear polarization</td>
</tr>
<tr>
<td>DNP-NMR</td>
<td>NMR in combination with DNP</td>
</tr>
<tr>
<td>ESR</td>
<td>electron spin resonance</td>
</tr>
<tr>
<td>FWHM</td>
<td>full width at half maximum</td>
</tr>
<tr>
<td>HPA</td>
<td>high power amplifier</td>
</tr>
<tr>
<td>IMPATT</td>
<td>impact ionization avalanche transit-time</td>
</tr>
<tr>
<td>LNA</td>
<td>low noise amplifier</td>
</tr>
<tr>
<td>MR</td>
<td>magnetic resonance</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclaeer magnetic resonance</td>
</tr>
<tr>
<td>PCB</td>
<td>printed circuit board</td>
</tr>
<tr>
<td>PTFE</td>
<td>polytetrafluoroethylene</td>
</tr>
<tr>
<td>RF</td>
<td>radio frequency</td>
</tr>
<tr>
<td>SNR</td>
<td>signal-to-noise-ratio</td>
</tr>
<tr>
<td>SSS</td>
<td>solid-state source</td>
</tr>
<tr>
<td>T/R</td>
<td>transmit/recieve</td>
</tr>
<tr>
<td>TEMPOLO</td>
<td>4-hydroxy-2,2,6,6-tetramethylpiperidin-1-oxyl</td>
</tr>
<tr>
<td>TM</td>
<td>tune and match</td>
</tr>
<tr>
<td>VCO</td>
<td>voltage-controlled oscillator</td>
</tr>
<tr>
<td>VES</td>
<td>vacuum electron source</td>
</tr>
<tr>
<td>VTI</td>
<td>variable temperature insert</td>
</tr>
<tr>
<td>YIG</td>
<td>yttrium iron garnet</td>
</tr>
</tbody>
</table>

## Physical constants

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\gamma$</td>
<td>spin gyromagnetic ratio</td>
</tr>
<tr>
<td>$\hbar$</td>
<td>Plank constant divided by $2\pi$</td>
</tr>
<tr>
<td>$\mu$</td>
<td>permeability of free space</td>
</tr>
<tr>
<td>$k_B$</td>
<td>Boltzmann constant</td>
</tr>
</tbody>
</table>
Symbols

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_c$</td>
<td>Attenuation due to conductive losses</td>
</tr>
<tr>
<td>$\mu_I$</td>
<td>Nuclear magnetic moment</td>
</tr>
<tr>
<td>$\nu$</td>
<td>Nutation frequency</td>
</tr>
<tr>
<td>$\omega$</td>
<td>Larmor frequency</td>
</tr>
<tr>
<td>$\tau_{\text{DNP}}$</td>
<td>DNP build-up time constant</td>
</tr>
<tr>
<td>$\epsilon_{\text{DNP}}$</td>
<td>DNP enhancement</td>
</tr>
<tr>
<td>$\epsilon_r$</td>
<td>Relative dielectric constant</td>
</tr>
<tr>
<td>$B_0$</td>
<td>Static magnetic field</td>
</tr>
<tr>
<td>$B_1$</td>
<td>Linearly polarized magnetic field</td>
</tr>
<tr>
<td>$I$</td>
<td>Nuclear spins</td>
</tr>
<tr>
<td>$k$</td>
<td>Thermal conductivity</td>
</tr>
<tr>
<td>$m$</td>
<td>Quantum number</td>
</tr>
<tr>
<td>$Q$</td>
<td>Heat flux</td>
</tr>
<tr>
<td>$S$</td>
<td>Electron spins</td>
</tr>
<tr>
<td>$T$</td>
<td>Temperature</td>
</tr>
<tr>
<td>$T_1$</td>
<td>Spin–lattice relaxation time</td>
</tr>
<tr>
<td>$T_2$</td>
<td>Spin-spin relaxation time</td>
</tr>
</tbody>
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Chapter 1

Introduction

1.1 Why, what and how of DNP?

The birth of nuclear magnetic resonance (NMR) [1] has paved the way for spectroscopy and imaging (MRI). NMR spectroscopy is a powerful analytical technique that provides information about molecular structures, their dynamic processes, and chemical reactions. MRI is a non-invasive and non-ionizing diagnostic technique that has found great success in clinical neurology, cardiology, and oncology, to name a few. However, despite their success, both techniques suffer from inherently low sensitivity, which leads to extended acquisitions (in order to average) and poor time resolution. Alas, thermal energy at room temperature will inevitably dwarf the NMR signal induced by a precessing nuclear magnetic moment, yielding a poor signal-to-noise ratio (SNR).

In a static magnetic field ($B_0$) NMR active spins populate energy eigenstates according to the competing magnetic and thermal energies. It is the difference in spin population between energy levels that define the degree of polarization, and by extension the intensity of observed NMR signal. At thermal equilibrium, the spin population follows a Boltzmann distribution, resulting in a few participating spins per million at room temperature and typical magnetic field strengths [2]. Technological improvements in instrumentation prevailed over the years, introducing cryogenic probes for spectroscopy and higher magnetic fields for both NMR techniques. Indeed, the 2–10 fold improvement is appreciated, but only with hyperpolarization did the field of NMR observe drastic improvement in SNR.

Hyperpolarization entails creating a non-equilibrium polarization by forcing nuclear spins to a single Zeeman level, thus significantly increasing the population difference. This state is non-permanent, and population spins will subsequently undergo relaxation and redistribution to thermal equilibrium. Many hyperpolarization methods exist, including brute-force polarization [3, 4], spin exchange optical pumping [5, 6] and parahydrogen-induced polarization [7, 8]. The aim of each method is to achieve an enhancement of the nuclear polarization of interest above thermal equilibrium at the moment when exploiting the NMR signal. Among the different methods and widely adopted is dynamic nuclear polarization (DNP). The method relies on polarization transfer from electrons to nuclear spins.
DNP in metals was first theorized by Overhauser [9] and experimentally verified by Carver and Slichter [10] using an alkali metal suspension in the early 1950s. Shortly after, Abragham extended the method to liquids containing paramagnetic impurities [11]. Today, the Overhauser effect is the only known form of DNP applicable to liquid-state samples. Jefferies proposed DNP in non-metallic dilute paramagnetic solids at low temperature [12]. Abragham and Proctor experimentally confirmed the solid effect soon after in 1958 [13]. Typically a solid-state DNP sample encloses an electron paramagnetic agent (EPA), the substrate bearing the target nuclei and if the molecule was not self glassing, a glassing agent (e.g. glycerol). Initially, nuclear physics utilized the method to create polarized targets for neutron filters and scattering experiments. The method was reserved to low fields due to the need for power frequency sources. Nonetheless, NMR spectroscopy adopted DNP to improve NMR sensitivity. Solid-state DNP experiments continued throughout the 1990s [14–16]. High-field magnets debuted in this time, with the emergence of high-frequency microwave sources.

In 2003, a DNP technique called dissolution DNP (dDNP) [17] successfully produced highly polarized $^{13}$C in liquid-state. The seminal work cooled a solid-state sample to 1.2K in a 3.35 T field, where the electron spins are near unity polarization. Microwave irradiation close to the paramagnetic resonance causes the nuclear spins to redistribute and rise in polarization. The polarization time is not trivial, typically taking 0.5 – 2 hours. Once the desired polarization is reached, the namesake dissolution step takes place using a solvent, spanning a few seconds. The produced result is a hyperpolarized solution with a 10,000-fold enhancement over thermal equilibrium at any feasible magnetic field strength. The polarizer design was subsequently commercialized (Hypersense, Oxford Instruments, Abingdon, UK) with the added feature of automation, which eliminates operator variability in loading and dissolution.

With its overwhelming liquid-state nuclear polarization enhancement, dDNP ushered the field of metabolic MR. When it came to in vitro spectroscopy, dDNP enabled real-time enzyme monitoring [18] and the study of cell metabolism [19, 20]. The technique found primary employment in real time in vivo metabolic imaging [21], where the elevated conversion of pyruvate to lactate is detected in cancer (Warburg effect) [22]. In 2013, metabolic imaging using hyperpolarized pyruvate (administered intravenous) successfully identified and confirmed the tumour locations, size and stage in patients with prostate cancer [23]. Since then, several clinical experiments were conducted, and many more trials have commenced to investigate different cancer types [24]. Beyond diagnosis, the technique supports the surveillance of cancer progression and response to therapy [25].
1.1 Why, what and how of DNP?

Hyperpolarized pyruvate remains the substrate of choice due to its prolonged relaxation times in liquid-state, which typically lasts in the order of 60 s in a 9.4 T field.

Clinical studies are strictly regulated and require several modifications to the original dDNP design. In 2011 a polarizer design aimed at clinical experimentation was published [26]. The polarizer (SPINlab, GE Healthcare, NY, USA) operated at 5 T with a 0.9 K base temperature cooled by a closed cryogen cycle and a cryocooler. Meaning, the polarizer does not need helium resupply nor does it vent helium during operation. The polarizer system is supplied with a single channel spectrometer to monitor polarization build-up. To improve throughput, four independent samples are simultaneously polarized. Sample volumes are increased to 2 mL of solid, to allow for human doses. Ultimately, the most critical addition to the clinical translation was the single-use fluid path and quality control module. A closed plastic fluid path ensures a sterile barrier from any external contaminants or impurities. It attaches to a vial preloaded with the solid-state sample from one end and a filter (to remove the radical post dissolution) and quality control module at the other. The control module checks for several parameters (pH, radical removal, concentration of bioprobe, temperature, volume and polarization) before releasing the hyperpolarized solution. Again, the polarizer automation minimizes operator variability and introduces the warm sample into the cryostat following an optimum actuated profile to minimize thermal loading.

Since then, preclinical polarizers have undergone rapid development [27], aiming for greater system automation and cryogen-free consumption. Cryocoolers began to replace boiling helium cryostats. Homemade polarizers based on a closed cryogen cycle emerged with a variable superconducting magnet capable of investigating DNP at multiple magnetic field strengths and temperatures [28–30]. Though, optimal magnetic field and temperature conditions for DNP are not evident. Although, polarization benefits have been observed at increasingly higher magnetic fields strengths for the two widely adopted radicals, trityl [29, 31, 32] and nitroxide [33, 34]. This was primarily facilitated by the availability of compact solid-state microwave sources with reasonable power outputs and low loss transmission waveguides. Higher throughput strategies included parallel polarization of multiple samples [35] and a promising technique combining cross-polarization with DNP (CP-DNP), although only the latter has been attempted in a cryogen-free system [28]. In CP-DNP faster polarizing $^1$H spins transfer their polarization to $^{13}$C spins with the aid of RF pulses. The technique relies on commercially available and economically priced nitroxide radicals to achieve up to 70% $^{13}$C polarization in 20 minutes at 6.7 T [34].
Producing and transporting hyperpolarized samples from a centralized location is possible, envisaging dissolution outside the polarizer. A proof of concept has been published, proposing the use of nitroxide radical impregnated microcrystals of $^{13}$C substrates [36]. The sample achieves modest polarization and an extended $^{13}$C relaxation of many hours when stored in a liquid helium dewar at a static field of 1 T. At the same time, an alternative approach was published utilizing ultraviolet-generated radicals [37]. A high concentration of radicals can be created ex-situ in liquid nitrogen and yield efficient DNP [38]. The radicals swiftly quench at a temperature slightly above liquid nitrogen, thus promoting a prolonged hyperpolarization lifetime of many hours.

1.2 Thesis Aim

This thesis aims to contribute to the development of cryogen-free polarizer instrumentation. At the time of formulating this thesis, a polarizer based on a commercially available cryogen-free variable temperature cryostat (Cryogenic limited, London, UK) was in development at the group. The enclosed superconducting magnet is capable of continuously cycling up to 10.1 T but is discretized to 3.35, 6.7 or 10.1 T due to the availability of microwave sources at the corresponding electron spin resonance (ESR) frequencies. Operators can investigate DNP at one magnetic field strength and observe relaxation at another, across a range of temperatures. Catering for a wide operational bandwidth, especially at higher field strengths, is challenging and defines the primary design criteria in this work.

Due to the limited cryocooler ‘cooling power’, a dDNP probe is designed to minimize static heat load (temperature gradient $\approx 295$ K) as well as manufacturing complexity and cost. The probe is responsible for centering the sample in the homogeneous region of the magnet and provide sample access to microwave irradiation, RF circuitry and dissolution. At 3.35 T the ESR frequency is approx. 94 GHz but rises to 282 GHz at 10.1 T. Compact source powers are limited at higher frequencies, encouraging the investigation of strategies to improve microwave delivery to the sample.

It is essential to monitor the polarization to determine the DNP efficiency. Consequently, a compact benchtop spectrometer was developed to enable NMR capabilities and provide the polarizer autonomy, regardless of the surrounding environment. The cryostat cannot accommodate multiple samples for parallel DNP. Therefore CP-DNP was explored to accelerate the polarization of $^{13}$C in a large sample. Great emphasis was placed on realizing efficient double resonant circuits and NMR coil geometries that could sustain the demanding high-powered excitation pulses by CP-DNP.
1.3 Outline

All preliminary information required to understand the work conducted in the thesis is consolidated to Chapters 1 and 2. An overview of DNP and its underlying mechanisms are briefly summarized in Chapter 2. The preliminaries continue to discuss dDNP polarizer state-of-the-art. Once an overview has been established, Chapter 3 details the polarizer system used throughout this body of work, including microwave sources and experimental methods. A thorough description and design of the dDNP probe is also enclosed, including a thermal analysis of its static heat load. Chapter 4 explores the procedure for designing efficient single and double resonant NMR circuits. Different coil geometries are considered including circuit configurations to realize a double resonant circuit capable of CP-DNP and suitable for large samples. Technical challenges of sustaining high powered excitations in a helium cryostat are investigated, including techniques to mitigate arcing. A study of a low-loss waveguide is available in Chapter 5, where the guide was subsequently fabricated and verified using DNP-NMR. Moreover, an augmented cavity is designed using numerical electromagnetic (EM) simulations and verified using DNP-NMR to enhance microwave field density across the sample volume. A two channel benchtop spectrometer is retrofitted to provide the capability of a traditional full-rack spectrometer in a smaller form factor. Found in Chapter 6 are the circuit designs, component characterizations and performance results for both benchtop and full rack high-resolution spectrometers. Conclusions and perspectives are reported in Chapter 7.
Chapter 2

Preliminaries

This chapter provides the preliminary information to place into context the contributions of this thesis. The principles of spin polarization and DNP mechanics are briefly introduced, followed by a chronological presentation of polarizer designs and cryogenic management since 2003.

2.1 Spin polarization

Spin is a form of angular momentum, intrinsic to elementary particles. Classically electron spin is denoted by $S$ and nuclear spin by $I$. However, the scope of this overview applies to both, and it is sufficient to interchange them. Spin is a vector quantity with a magnitude characterized by the quantum number:

$$|I| = h[ I(I + 1) ]^{1/2}$$  \hspace{1cm} (2.1)

where $h$ is the Plank constant divided by $2\pi$. The orientation of spin in space is quantized. Consequently, the observed values for $I$ along a given direction (usually the $z-$axis) are given by $I = hm$, where the quantum number $m = [-I, -I + 1, \ldots , I - 1, I]$. The presence of spin angular momentum entails a magnetic moment [2]:

$$\mu = \gamma hm = \gamma I$$  \hspace{1cm} (2.2)

where $\gamma$ is the gyromagnetic ratio, unique to the spin species. In the presence of a static magnetic field ($B_0$), the energy of the magnetic moment is given by the product:

$$E = -\mu \cdot B_0$$  \hspace{1cm} (2.3)

Since $I$ can only assume integer or half-integer values, the interaction between the magnetic moment and field will result in a total of $2I + 1$ permitted energy levels, known as Zeeman levels. The energy value characterizes the levels:

$$E_m = -\gamma hmB_0 = -\hbar \omega m$$  \hspace{1cm} (2.4)
where $\omega = \gamma B_0$ represents the spin Larmor frequency. It is worth noting that the magnetic moment is not statically aligned to the field $B_0$, but rather precesses along the field axis with an angular frequency $\omega$. The relative population of spins distributed across Zeeman level $m$ follow a Boltzmann distribution \[39\]

$$P_m = \frac{\exp(-E_m/k_B T)}{\sum_m \exp(-E_m/k_B T)} \tag{2.5}$$

where $k_B$ and $T$ denotes the Boltzmann constant and temperature, respectively. Typically, the energy levels are not equally populated, leading to the rise of a bulk magnetic moment. In NMR the SNR is directly proportional to the bulk magnetic moment. Given a spin assembly with $I = 1/2$ and thus two Zeeman levels ($m \pm 1/2$), the polarization is expressed as:

$$\text{Pol} = \frac{N^+ - N^-}{N^+ + N^-} = \tanh \left( \frac{\gamma \hbar B_0}{2k_B T} \right) \tag{2.6}$$

where $N^+$ and $N^-$ denote the spin population in two energy levels, respectively. From Equation 2.6, it is evident that the polarization between two energy levels is very small for feasible field strengths at room temperature. This is the origin of poor sensitivity articulated in Chapter 1. Ultimately, the measured resonance signal is directly proportional to the polarization of a spin assembly (i.e., the difference in populations between the two levels).

### 2.2 Principles of dDNP

In principle, any molecules containing an NMR sensitive nucleus ($I \neq 0$) can be polarized via DNP. Generally, the process entails creating an assembly of highly polarized electron spins by cooling the electrons to about 1 K in a magnetic field of several teslas (dDNP conditions). Microwave irradiation close to the ESR frequency, facilitate the transfer of electron spin polarization to nuclear spins.

Specifically, there are several identified mechanisms for polarization. The solid effect envisages a single electron spin coupled to a single nuclear spin. The hyperfine coupling between the two spins results in four energy levels separated by $\omega_S \pm \omega_I$. In this regime, microwave irradiation at sum or difference frequency causes simultaneous energy level transitions for both electron and nuclear spins. This action transfers the electron spin polarization to nuclear spins. Next, the cross effect and thermal mixing involves two coupled electron spins and one nuclear spin. In this mechanism, there are 8 energy levels due to the interaction between the two electron spins (dipolar coupling) and coupling between the electron spins and the nuclear spins (hyperfine coupling). Microwave irradiation causes
simultaneous energy level transitions, causing the transfer of polarization to nuclear spins. Note, the ESR frequencies should be separated by the nuclear Larmor frequency such that $\omega_I = |\omega_{S1} - \omega_{S2}|$.

A description of DNP mechanics based on spin temperature contributed to establishing a general model to describe polarization transfer [40–42]. Based on Equation 2.6, a temperature can be assigned to spins for any polarization. For example, Pol = 0% corresponds to an infinite spin temperature, while unity polarization approaches absolute zero. Spin temperature can be positive or negative, depending on the polarization sign. In thermal mixing, the spin temperature can be different from the lattice spin temperature during microwave irradiation. In this regime, nuclear and electron spins are in thermal contact through a series of electron-electron-nuclear cross-relaxation actions. This is akin to all electron spins satisfy the condition $\omega_I = |\omega_{S1} - \omega_{S2}|$ in the cross effect. Once the conditions change the nuclear spins temperature, equilibrate with the electron spin temperature. Microwave irradiation first perturbs the electron spin temperature. By way of cross-relaxation, the nuclear and electron spins temperature equilibrate yielding a higher nuclear polarization.

Strictly speaking, the cross effect or thermal mixing are the primary polarization transfer mechanisms under dDNP conditions. The solid effect requires powerful microwave irradiation to be effective. This would not be applicable for dDNP due to the likelihood of physically heating the sample. Instead, the other mechanisms rely on spin diffusion to efficiently interact with microwave irradiation. Spin diffusion is the process of transporting polarization across an assembly of spin particles by dipolar coupling. In dDNP, this is in part ensured by the sample formulation. As mentioned in Chapter 1, an EPA needs to be dissolved in an amorphous glassy structure that allows for a random distribution of unpaired electrons across the sample. Naturally, higher concentration of nuclei promotes faster polarization due to more efficient spin-diffusion [43]. Choice of EPA also plays a role in DNP effectiveness depending on the nucleus of interest. It is advantageous to use an EPA with an ESR linewidth that exceeds the Larmor frequency of the nuclear spins to promote the cross-effect or thermal mixing.

Once the desired polarization is achieved, the sample is dissolved within a few seconds using a heated solvent, while still inside the cryostat. At this juncture, the hyperpolarized solution is to be swiftly delivered for application; all the while DNP enchantment is diminishing. Spin-lattice relaxation time ($T_1$) redistributes nuclear spins back to thermal equilibrium. The nuclear spins do experience relaxation in the cryostat, however, solid-state $T_1$ is orders of magnitude longer [4]. Many parameters influence $T_1$, including the
magnetic field, temperature, and chemical environment. Transporting the hyperpolarized solution through zero field regions destroys the hyperpolarized nuclear population either by relaxation or non-adiabatic transfer and are faithfully avoided [44]. Another strategy involves the use of deuterated sample ingredients during formulation and scavenging the EPA after dissolution [45].

A brief overview of dDNP is illustrated in Figure 2.1. The magnetic moment of electrons is 658 times greater than $^1\text{H}$. Meaning, unit electron spin polarization can be attained at moderate magnetic fields and about 1 K. Considering, at room temperature, in a 3 T MR scanner, the $^1\text{H}$ polarization becomes $10 \times 10^{-6}$, while $^{13}\text{C}$ polarization is only to $2.5 \times 10^{-6}$. That is, a theoretical enhancement of 400,000 and 100,000 times, respectively, if unity polarization could be achieved.
Figure 2.1: The principles of dDNP. (a). At room temperature and 3 T, $^{13}$C polarization is low (depicted in b). However, electron polarization is significantly higher due to 2700 times stronger magnetic moment. When the sample is cooled, the electronic polarization reaches near unity. Irradiating with microwaves close to the ESR frequency of the electron spins initiates the DNP process, thereby enhancing nuclear polarization (depicted in c). This process is slow at low temperatures and takes typically 60-120 minutes. When the sample is polarized, the superheated solvent dissolves the sample within seconds, and a hyperpolarized solution is obtained at pathological temperatures. The hyperpolarized nuclear spins relax to thermal equilibrium with $T_1$. (d) The thermal spectrum after 65 h of averaging is shown along with (e) a hyperpolarized $^{13}$C spectrum of urea at room temperature at 9.4 T obtained in a single transient. Figure adapted from [46].
2.3 The evolution of dDNP polarizers

The first dDNP polarizer appeared in 2003 [17], based on a wide bore 7 T magnet and cryostat (Figure 2.2). The cryostat was furnished with variable temperature insert (VTI) connected to an in situ liquid helium dewar via a capillary tube. Liquid helium flow is externally regulated by a needle valve. The VTI base temperature reaches 1.2 K and is sustained by external pumps. The magnet was charged to 3.35 T (due to, at the time, readily available microwave sources at 94 GHz) and shimmed to achieve a homogeneity better than 50 ppm over the sample region.

A probe is inserted into the cold VTI and designed to minimize the overall static heat load. The probe consists of a perforated fibreglass sample tube terminated into a cylindrical overmoded microwave cavity. Microwaves are delivered via a rectangular WR-28 stainless steel waveguide. In the cavity, a saddle coil accessed via a UT85-SS-CuBe coaxial cable measures the NMR signal. The sample is prepared in a cup and loaded into the probe via a polytetrafluoroethylene (PTFE) sample holder tube. Helium submerges the sample during DNP and the holder is sealed with a septum. Before dissolution, the VTI is repressured and the sample lifted by 10 cm from the helium bath. The dissolution wand consisting of two enclosed PTFE tubes slides into the sample holder and tightly connects to the sample cup. Injected boiling water dissolves the sample and transports the solution out of the cryostat.

In 2005, the first in vitro polarizer based on the original design became commercially available (Hypersense, Oxford Instruments, Abingdon, UK). The polarizer allowed early adopters to begin developing metabolic MR studies using a proprietary trityl radical (AH111501, GE Healthcare, Oslo, Norway) as a source of unpaired electrons for [1−13]Cpyruvic acid samples [47, 48]. The loading process became automated using pneumatics and a programming logic controller. The sample volume has increased to 250 µL, and helium chase gas expedites the dissolution time. Several system upgrades have emerged, e.g. employing larger pumps to lower the base temperature from 1.4 K to 1.2 K and modify the dissolution apparatus to handle larger volumes [49]. Other home built polarizer emerged over time [50–55], all relied on an external helium dewar to flood the VTI, but otherwise, did not significantly deviate in design principles. Nonetheless, some of the deviations highlighted the shortcoming of dDNP that can be addressed technologically, e.g. a probe design for parallel DNP of up to 6 samples with individual dissolutions (Figure 2.3a) [35] or a combined polarizer/NMR magnet that reduces delivery time between dissolution and MRS [55] (Figure 2.3b). Additionally, an infusion pump could expedite the delivery of hyperpolarized solution to an MRI scanner post-dissolution [51].
2.3 The evolution of dDNP polarizers

Figure 2.2: (a) Schematic of first published dDNP polarizer. The cryostat consisted of a modified magnet with a permanently installed VTI. (b) Housed in the VTI is a probe which cantered the sample in the homogeneous region of the magnet. A microwave cavity confines incoming microwave from a (b) microwave source above. Polarization monitoring facilitated by an NMR coil in the cavity. A sample holder mechanically couples to the sample cup and safely delivers it into the microwave cavity. Liquid helium flows to the VTI via a needle valve from the cryostat helium vessel. Pumping on the helium bath reduces the VTI base temperature to about 1 K, as determined by the pressure transducer. (d) Dissolution wand slides into the sample entry port and dissolves the sample using a superheated solvent. Figure adapted from [17].
Selection of magnetic field strengths and temperature needs to be considered with great care. DNP efficiency increases with higher field strength, but yields a slower polarization build-up rate [29, 32]. This dependence is in part due to an increase in nuclear $T_1$ but less significant change in electron $T_1$ [57]. At higher fields, electron relaxation is more likely due to the direct effect. The nuclear $T_1$ is determined by the electron spin and follows typically a $B_0^2$ dependence [58]. As for temperature, DNP enhancement follows a $1/T$ relation [32]. However, beyond a certain point (4 K), it is only the nuclear Boltzmann polarization that benefits from lowering the sample temperature.

Recalling from Chapter 1, a polarizer intended for clinical application was introduced in 2011 [26] and later commercialized (SPINlab, GE Healthcare, NY, USA). The polarizer
2.3 The evolution of dDNP polarizers

Figure 2.4: Preliminary schematic of SPINlab polarizer. Cryostat consists of a superconducting magnet with liquid helium, sorption pump and helium vessel coupled by a thermal bus. Atop the polarizer are 4 gate valves for loading samples using fluid paths and the cryocooler.

encloses a 5 T superconducting magnet that could reach a base temperature of 0.9 K (Figure 2.4). Unlike, its predecessors, a cryocooler provides the ‘cooling power,’. The principle behind its operation is a sorption pump consisting of charcoal that adsorbs helium gas when cooled and releases its when heated. The cryocooler cools the sorption pump to 5-6 K via a thermal switch, causing the helium to be adsorbed to the charcoal. Inversely, helium can be regenerated by decoupling the thermal switch and electrically heating the charcoal to release the helium gas and condense it back into the helium vessel. All samples are enclosed in one meshed cavity, which confines microwave irradiation from a 200 mW microwave source (140 GHz) via a circular stainless steel waveguide. A 3-turn parallel saddle coil coupled to a SS-BeCu coaxial able allows for polarization monitoring using a single channel spectrometer (TRX-I-50-75-300-AWG, SpinCore Technologies, FL, USA).
The final polarizer discussed in this section (Figure 2.5), is that featuring the 10.1 T superconducting variable magnet in a cryogen-free cryostat (Cryogenic Ltd, London, UK) [29]. A 1-W pulse tube cooler (RP-082B2, SHI Cryogenics, Tokyo, Japan) and a compressor (F-70H, SHI Cryogenics, Tokyo, Japan) extract heat from the helium cycle. An oil-free multistage-root pump ACP40, Pfeiffer Vacuum, Aßlar, Germany) reduces the VTI pressure and exhausts into a 100 L tank with helium gas. In turn the buffer gas is charged into the cooling cycle. The charcoal trap filters out any contaminants before the gas is condensed in the helium pot and drawn into the VTI via a manually controlled needle valve. The VTI is 30 mm in diameter, and 400 mm long and houses a probe similar to that discussed in the following chapter, but shorter. The polarizer is compatible the fluid path from the former polarizer. The airlock insures the VTI remains at low pressure and allows for the sample to be precooled via helium vapor before introduction into the helium bath.

Figure 2.5: (a) Schematic of the cryostat with the 10.1 T variable magnet. A cold head and compressor provide the cooling power to the magnet and helium cooling circuit. 100 L of helium gas from a cylinder is charged into the closed cooling circuit. The cold head condenses the helium gas into the helium pot. A needle valve controls the flow of liquid helium into the VTI. A dry pump reduces the vapor pressure in the VTI, and the exhaust of the pump is buffered by tanks before entering the cryostat through a charcoal trap. The interior of the DNP probe is isolated from the VTI with a separate helium gas volume of 2 L at 2 bar. Sample loading into the DNP probe is through an airlock. Figure adapted from [29]. (b) Rendered model of polarizer system, figure courtesy of Cryogenic Ltd, London, UK.
Chapter 3

Instrumentation and experimental procedure

In this chapter, the DNP polarizer used for all tests is presented, including all sample formulations and DNP-NMR sequences. The dDNP probe and manufacturing process is described in detail including an analysis of the static heat load. Several microwave sources are characterized and assembled herein.

3.1 DNP system

Magnet and cryostat

The DNP polarizer system used throughout this thesis is similar to that in the seminal dDNP work presented in [17]. The magnet is based on a standard narrow bore 7 T magnet (Magnex Scientific, Oxford, UK). The cryostat consists of a stainless-steel 750 L liquid helium reservoir surrounded by a vapor-cooled radiation shield and a 180 L liquid nitrogen reservoir. This entire assembly is contained in an evacuated stainless-steel vessel. The cryostat is modified to accommodate a VTI 70 mm in diameter, accessible via an ISO-100 top flange. The VTI is a 10 mil thick stainless-steel tube that is thermally coupled to the vapor-cooled shield and nitrogen vessel. A thin capillary couples the VTI interior with the helium vessel and controlled using a needle valve. A stepper motor mechanically operates the needle valve and consequently helium flow using a shaft located in one of the magnet turrets. The magnet (charged to 6.7 T) center is housed in the liquid helium vessel, 800 mm from the top flange and offers a <30 ppm cylindrical (h=40 mm and r=20 mm).

Two vacuum pumps evacuate the VTI atmosphere to reduce the pressure to approximately 1.2 mbar, thus reaching a base temperature of 1.2 K when a probe is present. The pump system consists of a single-stage root vacuum pump (RUVAC WAU251, Leybold, Cologne, Germany) specified to a nominal pumping speed of 253 m³/h, in series with an oil-sealed rotary vane vacuum pump (TRIVAC D40B, Leybold, Cologne, Germany) with a
nominal pumping speed of 46 m$^3$/h. The pumps connect through a KF50 flange regulated by a butterfly valve. When the needle valve is fully open, the VTI pressure rises to 8 mbar.

**Sensors**

The helium vapour pressure determines the helium bath temperature. A transducer (DualTrans, Wenzel Instruments Aps, Denmark) calibrated to the international temperature scale of 1990 (ITS-90) measures the VTI pressure from under the ISO-100. The helium-4 vapor pressure to temperature relation is detailed in [59] and illustrated in Figure 3.1. This value is verified using a Cernox temperature sensor (CX1030, Lakeshore Equipment, CA, USA) which directly measures the bath temperature. The sensor relies on a 4-wire connection to compensate for wire resistance and obtain a $\pm 0.5$ mK accuracy for measurements as low as 1 K.

Three 100 $\Omega$ Allen-Bradley carbon resistors measure the liquid helium level in the VTI. The resistors stack 1 cm vertically apart, with the lowest placed approx. 50 mm above the magnet center. Due to their sensitivity, small size and low cost, Allen Bradley resistors make for ideal sensors to distinguish the presence of liquid helium. A two-step procedure identifies the presence of liquid helium around the resistors. First, a 5V TTL pulse is applied, inducing currents that briefly heat the resistors. Next, the resistor voltage is measured. Change in resistance due to heating is reflected in the trailing voltage profile, which identifies if the resistor is surrounded by vapor or liquid helium [60]. This approach distinguishes four discrete levels of liquid helium inside the VTI. Before commencing any DNP experiment, the needle valve is 80–100% opened to submerge the sample and subsequently the lowest resistor. Once enough helium is present, the needle valve is limited to 22–25%. In automatic regulation mode, the needle valve control adapts to different heat loads (e.g. different dDNP probes or microwave powers) and adjusts to identify the optimum valve setting to maintain the helium level between the lower and middle resistors. If the lowest resistor is no longer submerged, the valve openness increases above the optimum level. Similarly, if the top resistor is in contact with liquid helium, the needle valve openness is reduced below the optimum level. A timer delays automatic regulation to avoid feedback instability. As a safety precaution, the needle valve fully closes if the VTI pressure is above 10 mbar.
Figure 3.1: Helium-4 vapor pressure vs. temperature as expressed by the international temperature scale of 1990 (ITS-90) for temperatures between 0.5—2.1768 K.

Ancillary hardware

A LABVIEW program running on a personal computer controls the polarizer system. Several electronics housed in a 19-inch rack automate operational processes. Two CompactPCI power supplies provide 5, 12, −12 and 27 V to energize control electronics and the microwave power source. Analogue and digital signals for stepper motor control, pressure transducer and helium level sensing are generated and acquired by an I/O card (NI PCI-6025, National Instruments TX, USA). Another I/O device (NI-USB-6525, National Instruments TX, USA) controls the microwave source tuning frequency and power attenuation.

A helium monitor unit (E5011, Magnex Scientific, UK) determines the volume of liquid helium in the magnet’s vessel. The unit consists of a controller module and a length of superconductive wire. The monitor works on the same principles used for helium level sensing with the Allen-Bradly resistor but with higher spatial resolution. The section of wire above the liquid is non-super conducting and presents an ohmic resistance. When investigating the volume of liquid, a voltage pulse is applied, while sequentially reading the voltage across the wire. A reference calibration interprets the reading and reports the present volume level. Polling the helium level causes an excitation current between 80—245 mA to flow through the wire which momentarily leads to liquid boiling; therefore, polling
is limited to every 8 hours. A similar monitoring unit exists to monitor the volume of liquid nitrogen in the vessel.

### 3.2 dDNP probe

#### Design and construction

The dDNP probe is responsible for centring the sample in the homogeneous region of the magnet and provide sample access to microwave irradiation, RF circuitry and dissolution. The probe is designed to minimize manufacturing complexity, cost and static heat loads when in the magnet’s cryostat. A drawing of the probe is depicted in Figure 3.2 with components and assemblies discussed next:

**Top flange**: 304L stainless-steel ISO-100 flange (Kurt J. Lesker company, PA USA), mates with the top of the VTI using a centering ring equipped with an O-ring and four claw clamps. The flange houses multiple connectors; two hermetic bulkhead female-to-female SMA connectors (SF2991-6002, SV microwaves, FL, USA) to access the RF circuitry and two hermetic low voltage connectors (Fischer, St-Prex, Switzerland) for helium level sensing and thermometry. Varnished 32 AWG Phosphor bronze wires are used to connect the two low voltage connectors with the sensors placed on the probe cavity. The wire thickness and material offer low thermal conductivity and high electrical resistivity. Brazed on the ISO-100 is a modified UG387 flange with four additional threaded M2 holes and an O-ring to receive a waveguide at a later stage. O-rings are lightly coated with cryogenic grease (Apiezon N, M & I Materials Ltd, Manchester, UK) to improve their seal under vacuum.

**Sample port**: 304L KF16 flange with an extended butt (QF16-075-LFA, Kurt J. Lesker company, PA, USA) is slotted into the centre of the top flange and tack welded in position. The mate is vacuum brazed to reinforce the joint (silver soldering also viable). The flange butt is tapped with a 15.9 mm drill bit to accommodate the sample tube. A gate valve (01224-KA24VAT, VAT, Switzerland) and airlock adapted from the SPINlab polarizer [26] install above the KF16 flange.

**Sample tube**: 304L stainless-steel tube (Wellington Tube Supplies Ltd, Hayes, UK) (ID = 11.8±0.2 mm, OD = 12.7±0.2mm and h = 790±1 mm) is slotted through the top flange and into the sample port. A weld joint between the top flange and the sample tube wall secures the assembly. Adoption of a stainless-steel sample tube departs from perforated fiberglass tubes, which is often used to reduce surface area and thus heat conduction. However, the durability, ease of machining and poor thermal conduction of 304L stainless steel make it an acceptable substitute.
3.2 dDNP probe

**Baffles:** 316L stainless steel sheets are water cut to produce 4 semi-circle baffles \((r = 68 \pm 0.2 \text{ mm} \text{ and } t = 1 \pm 0.2 \text{ mm})\) and welded to the sample tube. The baffles mitigate black-body radiation towards the sample from the room temperature top flange. There are 3 semi-circle cuts in the baffles to accommodate the sample tube, waveguide and coaxial cable(s). The middle two baffles are spaced 22 mm apart, while 110 mm separate the top and bottom baffles. The top baffle is positioned 145 mm from the top flange.

**Waveguide:** 316L seamless stainless-steel tube (Wellington Tube Supplies Ltd, Hayes, UK) \((\text{ID} = 4.16 \pm 0.2 \text{ mm}, \text{OD} = 4.80 \pm 0.2 \text{ mm} \text{ and } h = 780 \pm 1 \text{ mm})\) is vacuum brazed to a modified UG387 flange hosting an O-ring. Further details about waveguide are discussed in Chapter 5.

**Cavity:** The cavity is a two-part assembly. The first part is a copper ring constituting the cavity upper \((\text{ID} = 27.5 \pm 0.2 \text{ mm}, \text{OD} = 12.9 \pm 0.2 \text{ mm} \text{ and } h = 7 \pm 0.2 \text{ mm})\) is brazed onto the sample tube. Second, the lower cavity is made from a cylindrical copper can \((\text{ID} = 28.0 \pm 0.2 \text{ mm}, \text{and } h = 30.0 \pm 0.2 \text{ mm})\) that tightly fits around the cavity upper and secures to it by two M1 screws. 1 mm offsets the cavity and sample tube isocentres while the waveguide outlet is centred 9 mm in the opposing direction. Helium sensing Allen-Bradley resistors and Cernox temperature sensor are placed on the cavity upper. Two circular grooves milled in the cavity upper and lower \((\text{ID} = 13.0 \pm 0.2 \text{ mm}, \text{OD} = 15.0 \pm 0.2 \text{ mm} \text{ and } h = 1.0 \pm 0.2 \text{ mm})\) accommodate the coil and coil former.

**Sample coil:** Several sample coil geometries were considered in this work and are discussed in Chapter 4. All geometries fit onto a a PTFE coil former \((\text{ID} = 13.0 \pm 0.2 \text{ mm}, \text{OD} = 15.0 \pm 0.2 \text{ mm} \text{ and } h = 32.0 \pm 0.2 \text{ mm})\) which sits in the circular groove in the lower and upper cavity.

**Coaxial cable:** Thermal conductivity and power handling primarily govern the selection of the coaxial cable. Consequently, cables with stainless-steel outer conductors are favoured. A 0.141” semi-rigid coaxial cable (UT141SS-C-P, JYEBAO Co., Taiwan) rated to 347.1 W at nominal conditions (continuous wave, 500 MHz at 20°C) is selected for installation in the dDNP probe. The sample coil is soldered to the coax cable which accesses the cavity via a designated drilled hole in the cavity upper. Alternatively, a 0.85” semi-rigid coaxial cable (UT-085-BeCU, JYEBAO Co., Taiwan) offers less heat loading but is specified to 142.7 W at nominal conditions. The coax cable is fitted with a male SMA connector and couples to the adapter on the top flange.
Figure 3.2: (a) dDNP probe drawing. 1. sample loading port, 2. helium level connector, 3. hepatic SMA connector, 4. ISO-100 flange, 5. UT141SS-C-P coaxial cable, 6. thermometer connector, 7. waveguide, 8. baffles, 9. sample tube, 10. overmoded cavity, 11. PTFE coil former, 12. sample vial (purple), 13. waveguide outlet, 14. Sample coil (green). Not illustrated: Allen-Bradley resistors, Cernox sensor and second hepatic SMA connector (positioned behind component 2.). (b) Modified UG387 waveguide flange and coupling flange.
3.2 dDNP probe

**Leak test**

A leak detector system (L200+, Leybold, Cologne, Germany) comprising of a mass spectrometer, a rotary vane pump (TRICAV D2.5E, Cologne Germany) and a turbo molecular pump (TRICAV TMP 35 LS, Cologne Germany) identify the location and size of a leak in the probe when under vacuum. Preparation begins by connecting the detectors KF40 inlet flange to a corrugated pumping line. The probe is housed in an evacuation chamber made of a stainless-steel tube with an ISO-100 flange and KF25 outlet flange positioned on its side. Before pumping the probe sample and waveguide ports are sealed. The pump line connects to the evacuation chamfer via the KF25 outlet using a KF40 to KF25 taper. All flanges couple using a centring ring equipped with an O-ring and secured with a wing nut clamp (except for the ISO-100 flange which couples using 4 claw clamps).

The detector system, depicted in Figure 3.3, evacuates the chamber housing the probe using the rotary pump via valve 5. The evacuation process continues until the inlet pressure at Pirani gauge drops below 3 mbar to which valve 5 is closed, and valves 3 and 5 are open. As the pumps continue to evacuate the chamber, the inlet pressure drops below 0.2 mbar. A handheld nozzle connected to a helium cylinder administers gas in short bursts at points of investigation. Helium diffuses through the leaks due to the pressure differential and flows upstream to be detected by the mass spectrometer. Leak rates as low as $10^{-12}$ mbar l s$^{-1}$ can be detected. In practice, a value below $10^{-9}$ mbar l s$^{-1}$ is sufficient to ensure no ice formation develops within the probe or VTI when in operation for extended periods.

**Simulated heat load**

Heat flux from the ISO-100 flange conducts across the probe and dissipates into the helium bath leading to a warmer sample space and increased helium evaporation. Although, other forms of thermal heat loading exist (e.g. radiation) the investigation only considers conduction due to the significant heat flux involved at steady state conditions. The dDNP probe is modeled in COMSOL Multiphysics® (COMSOL Inc., Sweden) to compute the steady-state heat flux deposited into the helium bath.
Figure 3.3: Diagram of leak detection setup. A dDNP probe placed in evacuation chamber and connects to the leak detector (1) inlet flange via a corrugated pumping line. A (2) Pirani gauge measures the inlet pressure while (3-5) three valves control access to the (6) rotary pump, (7) molecular turbo pump and (8) mass spectrometer). The Handheld nozzle and helium cylinder are not visualized.

Thermal conductivity and heat capacity values for probe materials between 4–300 K are defined by [61] and included in the simulated model before computing the steady state heat load equation:

\[ Q = -\frac{kA\Delta T}{x} \]  \hspace{1cm} (3.1)

Where \( Q \) denotes the conducted heat flux in steady-state conditions, \( k \) thermal conductivity, \( A \) cross-sectional area, \( \Delta T \) temperature differential between component ends and \( x \) the distance between ends. The thermal conductivity and heat capacity of probe components are illustrated in Figure 3.4. Contributions by each component are listed in Table 3.1 and total 222.4 mW. It is worth noting, the final value is only for relative comparison since enthalpy of the cold helium gas and helium conduction are not account for, using this simplified model. The computed probe heat flux is experimentally verified in Chapter 5.
Figure 3.4: (a) Heat capacity and (b) thermal conductivity of materials used in the dDNP probe for temperatures between 4-300 K.
Table 3.1: Conductive heat flux across the dDNP probe at steady-state conditions (ΔT=296K) as computed by COMSOL Multiphysics®.

<table>
<thead>
<tr>
<th>Component</th>
<th>Material</th>
<th>Cross section (mm²)</th>
<th>Conductive heat flux (mW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample tube</td>
<td>316L stainless-steel</td>
<td>17.32</td>
<td>66.36</td>
</tr>
<tr>
<td>Coaxial transmission line (UT141-SS-C-P)</td>
<td>316L stainless-steel, copper, PTFE</td>
<td>10.07</td>
<td>140.92</td>
</tr>
<tr>
<td>Waveguide</td>
<td>304 stainless-steel (copper plated)</td>
<td>4.24</td>
<td>15.16</td>
</tr>
<tr>
<td>Waveguide</td>
<td>Copper</td>
<td>4.24</td>
<td>846.78</td>
</tr>
</tbody>
</table>

3.3 Microwave source

Since the earliest demonstrations, DNP has been limited to low magnetic fields \([10, 62]\) due to the lack of high-frequency sources with sufficient power. The use of vacuum electron sources (VES) remedied the limitation as pioneered by Griffin et al. at MIT (Cambridge, MA, USA) on a variety of high field solid-state DNP systems \([63, 64]\). The technique grew in popularity with the introduction of magic angle spinning and cryogenic sample cooling (approx. 100 K). The rise of dDNP renders the use of VES unnecessary as polarization transfer between electron, and nuclear spins occur more efficiently at 1.2 K. VES offer overwhelming power that inevitably warms the sample and helium bath \([65]\), thus deterring the overall DNP enhancement.

An alternative option is solid-state sources (SSS) that are more affordable, compact and boast better frequency stability. Unlike VES, there is no requirement for water cooling or pressurized gases \([66]\). Low power output is the main disadvantage of SSS, where the desired source characteristics for high field DNP lie at the limit of solid-state technology (Figure 3.5). However, even with considerably low powers, SSS are exclusively adopted as part of dDNP polarizer systems today.

The following section details and characterizes all SSS devices used throughout this work. A power meter (Erickson PM5, VDI, Charlottesville, VA, USA) measured the microwave power levels at all frequencies between 94 − 282 GHz (appropriate waveguide transitions equipped when needed). A spectrum analyzer (E4440A, Keysight Technologies, CA, USA) equipped with a harmonic mixer (11970W, Keysight Technologies, CA, USA or M05HWD/ M03HWD, OML, Inc. CA, USA) identifies the generated microwave frequencies.
Base oscillator and source assembly

**IMPATT diode** The widely adopted ELVA-1 microwave source (VCOM-10/94 series, ELVA-1, St Petersburg, Russia), is based on an assembly of impact ionization avalanche transit-time (IMPATT) devices [68]. The assembly (Figure 3.6a) begins with a voltage-controlled oscillator (VCO) based on an IMPATT diode. The VCO outputs a low powered signal at 7.21–7.25 GHz. The diode presents a negative resistance when in avalanche mode, which warrants its use in oscillators. A power amplifier subsequently boosts the oscillator signal between 30–50 mW before multiplying the signal with an active frequency multiplier (IAFM-10, ELVA-1, St Petersburg, Russia) to 93.75-94.25 GHz. The multiplier output incorporates a filter to reject undesired harmonics as well as an isolator to prevent reflections back into the source. A second stage amplifier boosts the signal to 200 mW which passes through a voltage controlled variable attenuator (VCVA-10 series, ELVA-1, St Petersburg, Russia) and out via a UG-387 WR-10 flange.

A covered steel plate hosts the planar source assembly and protects the delicate microwave components but renders the source bulky and heavy (Figure 3.6b – c). The steel plate also aids in stabilizing the source output due to its high specific heat capacity. The source requires 27 V for a 12 W onboard heater, amplifiers, and multiplier, while ±12 V
energize the VCO. Additionally, two independent 0-10 V control voltages tune the source frequency and attenuation level (Figure 3.6d — e).

**Figure 3.6:** (a) Source block diagram illustrates voltage controlled VCO coupled to an amplifier and multiplier to output 94 GHz. A bandpass filter, second stage amplifier and variable attenuator condition the signal. Assembled ELVA-1 VCOM-10/94/200-DA microwave source (b) front and (c) side view. Cover removed for illustration purposes. (d) Power output with attenuation voltage = 0 V across operating bandwidth. (e) The source power and frequency output while varying attenuation and tuning voltage between 0—10 V. Control voltages varied individually while the other is set to 0 V.
3.3 Microwave source

**Gunn diode**  The source installed on the polarizer employs a Gunn diode based VCO [69]. At a low applied voltage, the diode behaves like a resistor. However, the device conductance becomes negative once a threshold voltage is reached, causing a low powered oscillation between 15.61−15.69 GHz (Figure 3.7a). The VCO output couples to an active frequency multiplier (QMM94010606, Quinstar Technology Inc., CA, USA) with a multiplication factor of 6 and 1 GHz bandwidth centred at 94 GHz. From the multiplier, the output power is 4 mW at 93.65−94.15 GHz. An 18-dB amplifier follows and boosts the signal power to 200 mW. A steel plate equipped with a thermostat and heater to regulate the source temperature and thus output stability (Figure 3.7b − c). A heat sink placed above the amplifier ensures its temperature remains below 60°C. The source requires ±12 V to energize the VCO and 5 V for the active multiplier, amplifier, and heater. Additionally, two independent 0-10 V control voltages tune the source frequency and power attenuation level (3.7d − e). The source has a narrower bandwidth than the ELVA-1 source but is more compact, lighter and delivers the same power output.

**Yttrium iron garnet (YIG)**  Throughout this work, bench measurements were conducted using a microwave source employing a YIG VCO [70]. Due to their ferrite properties, a YIG sphere mounted on a ceramic rod resonates at microwave frequencies when in a magnetic field. Several loops installed around the sphere create the required magnetic field and couple energy from and the resonator. The resonator connects to the negative resistance of an amplifier to form 10 mW oscillations at 15.57−15.78 GHz (Figure 3.8a). The oscillator output couples to an active frequency multiplier (QMM94012306, Quinstar Technology Inc., USA) with a multiplication factor of 6, 23 dB gain and a 1 GHz bandwidth centred at 94 GHz. The ultimate output power is 200 mW between 93.42−94.68 GHz, delivered via a UG-387 WR-10 flange. The source is assembled on an exposed steel plate (Figure 3.8b) without any form of temperature regulation. However thermal equilibrium is achieved within 15-30 min of operation. A manual attenuator (QAL-W00000, Quinstar Technology Inc., CA, USA) controls the output power while ±10 V tune the oscillator frequency (Figure 3.8c − d). The source requires ±12 V for the VCO and 12 V for the active multiplier and amplifier.
Figure 3.7: (a) The source block diagram illustrates power and frequency controlled Gunn diode VCO coupled to an active multiplier to output 200 mW at 94 GHz. Assembled Quinstar microwave source (b) side and (c) top view. (d) Power output with attenuation voltage = 0 V across operating bandwidth. (e) The source power and frequency output while varying attenuation and tuning voltage between 0–10 V. Control voltages varied individually while the other is set to 0 V.
Figure 3.8: (a) The source block diagram illustrates frequency controlled YIG VCO coupled to an active multiplier to output 200 mW at 94 GHz. (b) Assembled Quinstar microwave source. A manual variable attenuator conditions the output power level. (c) Power output with attenuator set to 0 dB across the operating bandwidth. (d) Source frequency output while varying control voltage between -10–10 V, attenuator set to 0 dB.
**Frequency synthesizer**  All the discussed sources follow a similar architecture in which an analog base oscillator generates a signal between 7–16 GHz which is fed through multiplication and amplification stages to achieve the final desired power and frequency. Advancements in digital frequency synthesizers have made it possible to replicate the output of analog base oscillators. As such a microwave source is developed using a synthesizer (SynthHD Pro, Windfreak Technologies, FL, USA) based on an integrated VCO (ADF5356, Analog Devices, MA, USA) that could produce oscillations between 0.05-13.6 GHz. The synthesizer offers improved output stability and is controlled using a personal computer (Figure 3.9a) without the need for an I/O interface device and negative voltage supply. Output power levels are limited to 9 mW when between 11.50–12.00 GHz (Figure 3.9b). An SMA high-pass filter (VHF-8400+, Mini-circuit, NY, USA) is fitted on the synthesizer output to rejects sub-harmonic components. Oscillations couple to an active multiplier (QMM-94042608, Quinstar Technology Inc., USA) with a multiplication factor of 8, 26 dB gain and 4 GHz bandwidth centred at 94 GHz. The active multiplier is an improved iteration to predecessors in previously discussed sources, offering a broader bandwidth with a higher gain. Subsequently, the final output power is approx. 400 mW at 92–96 GHz, delivered via a UG-387 WR-10 flange.

Initially, the multiplier is mounted on a copper slab (W = 15.0±0.1 cm and L = 20±0.1 cm). The source output and temperature were monitored while momentarily energized (28°C) and again after 30 minutes (38°C) (Figure 3.9c). The multiplier output varied depending on temperature indicating a need for regulation. The source is assembled on a heat sink (SK92-100-SA, Fischer Elektronik, Germany) equipped with a thermostat and heater that regulates the multiplier temperature to 50°C (Figure 3.9e ~ f). The increased temperature leads to a lower power but stable output due to the reduction in multiplier efficiency (Figure 3.9d). The source requires 6 V to energize the frequency synthesizer, active multiplier and heater. Due to the development timeline, the source was only characterized and not deployed on a dDNP polarizer for experimental tests.

**Frequency multipliers**

It is more economical and less complicated to multiple lower frequency signals than directly generate powerful high frequencies microwaves. Frequency multipliers play an essential role in generating microwaves while providing the flexibility to alter the frequency by merely swapping a single component. When operating the polarizer at 6.7 T, a frequency doubler (200X2R4, Virginia Diodes Inc., VA, USA) appends to the 94 GHz source output. The doubler offers a 25 GHz bandwidth centred at 188 GHz with an average efficiency
Figure 3.9: (a) Labview program on a personal computer to control the output on a SynthHD frequency synthesizer. (b) The source block diagram illustrates the output of a frequency synthesizer coupled to an active multiplier to output $\sim$400 mW at 94 GHz. (c) Output vs. Input signal power from the active multiplier for an output frequency of 92, 94 and 96 GHz at 28°C, 38°C and (d) 50°C (heater regulated). The synthesizer is controlled via a personal computer (e) Top and (f) side view of the assembled synthesizer based microwave source. Cover removed for illustration purposes.
of 28.2 % between 186.83−189.38 GHz, as illustrated in Figure 3.10a. If the polarizer is operated at 10.1 T conditions, the doubler can be swapped for a tripler (T282, Virginia Diodes Inc., VA, USA) offering a 12 GHz bandwidth centred at 284 GHz with an average efficiency of 10.2 % between 280.24-283.85 GHz, as illustrated in Figure 3.10b. Both active multipliers require −36 V to bias Schottky diodes inside the devices. The limitations of this approach are two-fold: multipliers become less efficient at higher frequencies, and only discrete multiples of the fundamental frequency are achievable.

![Graph A](image1.png)

**Figure 3.10:** Efficiency of the frequency (a) doubler (T200X2R4) and (b) tripler (T282) for a 200 mW input at 94 GHz.

### 3.4 NMR spectroscopy

**Resonant circuit**

Detection of nuclear spins at any Larmor frequency is facilitated by a resonant circuit consisting of reactive tune and match (TM) elements coupled to the sample coil. The NMR circuitry in the dDNP probe consists of a parallel and series trimmer capacitors (EM25HV, Voltronics Dover Corporation, IL, USA) that remotely TM the sample coil (as the reactive elements are placed in a remote location to the sample coil). Different resonant circuit designs are further explored in Chapter 4.

**NMR spectrometer**

NMR spectra were obtained using a dedicated, full rack, high-resolution spectrometer (DirectDrive 600, Agilent Technologies, CA, USA). Pulse sequences and commands were
3.5 Experimental procedure

Sample preparation and loading

Two typical dDNP samples are studied in this work,

1. 14 M $[1^{-13}C]$pyruvic acid with 30 mM trityl (AH111501).

2. 4.5 M $[1^{-13}C]$urea dissolved in glycerol-$d_6$ and $D_2O$ (50:50 v/v) with 40 mM TEMPOL (4-hydroxy-2,2,6,6-tetramethylpiperidin-1-oxyl).

The sample ingredients are weighed in a 1.5 ml vial (Eppendorf, Hamburg, Germany) using an analytical balance (DV214C Discovery, OHAUS Corporation, NJ, USA) and thoroughly mixed using a centrifuge (MiniStar silverline, VWR International, PA, USA) and vortexer (VORTEX3, IKA-Werke, Germany). Freezing a droplet in a bath of liquid nitrogen verifies vitrification (glassing). If successful, the droplet will form a transparent clear sphere that will eventually sink in the bath. The sample is then injected into a cylindrical PTFE vial (OD = 5.0±0.2 mm, ID = 4.0±0.2 mm and $h = 35.0±0.2$ mm) and sealed by a threaded cap as demonstrated in [71]. Co-axial tubing from a fluid path [26] is attached to the cap using a UV-cured adhesive (215-C, Dymax Corp, CT, USA). The vial is immersed in liquid nitrogen to bulk freeze the sample and preserve its homogeneity. Simultaneously, 1−2 bar helium gas purges the vial via the fluid path to displace the vial’s atmosphere. The vial is successively removed from the nitrogen bath and wiped with lint-free tissue to remove frost. Helium gas purges the airlock before receiving the sample vial. The dynamic seal is drawn towards the vial to plug the airlock port, thus sealing the helium purge. The gate valve is opened allowing the vial to be manually lowered into the sample tube. The vial suspends 15−20 cm above the helium bath to pre-cool before immersion. After 10 minutes the vial is introduced into the sample space and centered in the sample coil.
Sample DNP profile

Each sample achieves maximum DNP enhancement at an optimal irradiation frequency dictated by the sample matrix and EPA. The DNP profile and subsequently optimum frequency is determined using the pulse sequence illustrated in Figure 3.11.

\[
\begin{array}{c}
\text{\(13\)C} \\
\text{e}^-
\end{array}
\]
\[
\begin{array}{c}
\text{MW_FREQ++} \\
\theta_1 \\
t_1 \\
n \longrightarrow \text{\(13\)C} \\
\theta_1 \\
t_2 \\
m \longrightarrow \text{MW_FREQ++}
\end{array}
\]

**Figure 3.11:** Pulse sequences used for measuring DNP profile. Sequence parameters \(t_1 = 20\) min, \(\theta_1 = 5^\circ\), \(t_2 = 10\) ms and \(n = 5000\). The sequence repeats \(m\) times and increases the microwave frequency on each iteration.

**14 M [\(^{1-13}\)C]pyruvic acid with 30 mM trityl** Neat [\(^{1-13}\)C]pyruvic acid doped with trityl is an efficient sample for dDNP and choice for *in vivo* MRI applications. The symmetrical DNP profile normalized to the positive maximum is illustrated in Figure 3.12a, indicating an optimal irradiation frequency of 187.96 or 188.06 GHz. The narrow ESR linewidth of trityl is depicted in Figure 3.12b, measuring 150 MHz centred at 188.01 GHz.

**Figure 3.12:** Normalized (a) DNP and (b) ESR profiles of 50 \(\mu\)L 14 M [\(^{1-13}\)C]pyruvic acid with 30 mM trityl measured at 6.7 T obtained using longitudinally detected ESR, courtesy of Andrea Capozzi, DTU.
3.5 Experimental procedure

4.5 M \([1^{-13}C]\)urea dissolved in glycerol-d\(_8\) and D\(_2\)O (50:50 v/v) with 40 mM TEMPOL

Urea dissolved in a deuterated glycerol-water mixture with TEMPOL is a well-established sample in recent cross-polarization works. The DNP profile normalized to the positive maximum is illustrated in Figure 3.13a, indicating an optimal irradiation frequency of 188.06 GHz. The broad ESR linewidth of TEMPOL measures 500 MHz as depicted in Figure 3.13b. To effectively saturate the ESR line and boost the DNP enhancement, frequency swept microwave irradiation is applied [72–74] with 50 MHz modulation at a 1 kHz rate.

![Figure 3.13: Normalized (a) DNP and (b) ESR profiles of 50 \(\mu\)L 4.5 M \([1^{-13}C]\)urea dissolved in glycerol-d\(_8\) and D\(_2\)O (50:50 v/v) with 40 mM TEMPOL obtained using longitudinally detected ESR with ELVA-1 microwave source, courtesy of Andrea Capozzi, DTU.](image)

DNP build-up

In Chapter 5, DNP-NMR verifies the performance of microwave irradiation for different waveguides and cavity configurations using the sequence depicted in Figure 3.14. Nuclear polarization is interrogated every 60 seconds for 75 minutes using a low flip angle (2.5°). Upon completing the measurement, a series of repeated pulses reduce the procured longitudinal magnetization, to thermal equilibrium. The microwave source power level is incremented before the next sequence repetition.

Pulse calibration

Performing a 90° pulse calibration using the conventional nutation method is challenging at 1.2 K due to the need for a long pulse duration (hundreds of \(\mu\)s) when using a low Q-factor resonant NMR circuit. Furthermore, a long pulse would only partially excite the broad NMR
Figure 3.14: Pulse sequences for monitoring polarization build-up for a range of microwave powers in 6.7 T magnet. Sequence parameters $t_1 = 60$ s, $\theta_1 = 2.5^\circ$, $n = 75$, $t_2 = 10$ ms and $m = 8000$. The sequence repeats $q$ times and increases the microwave power level on each iteration.

Spectrum, and use of high-powered pulse will inevitably lead to arcing inside the VTI. This is especially problematic when considering volumetrically large samples, where achieving a high magnetic field is technically challenging. Moreover, the conventional method requires several $T_1$ cycles which could lead to testing durations $>10,000$s [75]. Alternatively, the hyperpolarized sample is exploited to verify the nutation frequency ($\nu_1$) experimentally using the sequence illustrated in Figure 3.15. A series of spectra acquired with a repetition time longer than $T_2$ and much shorter than $T_1$ is fitted using:

$$M(n) = M_0(\cos \theta_1)^n$$

(3.2)

where $M_0$ denotes the initial magnetization, $\theta_1$ pulse flip angle in radians and $n$ number of pulses. Once, the flip angle is identified, the nutation frequency is calculated as $\nu_1 = \theta/2\tau$, where $\tau$ is the pulse duration.

Figure 3.15: Pulse sequences for pulse calibration. Sequence parameters $t_1 = 20-30$ min, $t_2 = 10$ ms, $n =$ number of pulses and $\theta =$ to be determined. Acquisition repetition time (T/R) to be shorter than longitudinal relaxation time ($T_1$) and longer than spin-spin relaxation time ($T_2$).
Chapter 4

The pursuit for higher RF magnetic fields in a dDNP probe

In this chapter, several coil geometries and coil sensitivity evaluation techniques are discussed. The sample coil is essential to monitor polarization. If paired with an appropriate reactive circuit the coil can accommodate cross-polarization which can improve polarizer throughput. A dDNP probe capable of DNP-CP is developed. The double resonant, local TM circuit is realized to minimize high voltages and the risk of arcing. The calibrated coil sensitivities are 2.8 and 7.7 kHz/\sqrt{W}, respectively for $^{13}$C and $^1$H. Hartman-Hahn cross polarization is achieved with $\nu_1=29$ kHz, to yield a 27% $^{13}$C polarization with a 12 min build-up time that is twice the direct $^{13}$C polarization and 4.4 times faster. Adiabatic and chirp based pulse sequences are evaluated as well. Finally arc detection methods and mitigation strategies are explored and experimentally verified.

Results and discussions in this chapter are presented in the scientific journal articles titled ‘Compact, low-cost NMR spectrometer and probe for dissolution DNP’ [76] and ‘Design of a local quasi-distributed tuning and matching circuit for dissolution DNP cross polarization’ [77].

4.1 dDNP compatible coils: transverse resonators

The primary function of NMR coils is to interface the spectrometer with the nuclear spins. Excitation pulses generate an RF field within the coil interior volume to manipulate the bulk nuclear spin magnetization. When the excitation ceases, the precessing magnetization induces a voltage proportional in magnitude to the spin polarization. dDNP probes favor the use of transverse resonators as the produced magnetic field is perpendicular to the static magnetic field. Additionally, their cylindrical shape provides convenient sample accessibility for dissolution.

For a given cylindrical resonator, the best magnetic field homogeneity is achieved when the surface current distributions across each semi-cylindrical section follow a cosinal dis-
tribution. This criterion ensures uniform spatial excitation and ultimately dictates the permitted sample volume. In practice, contiguous semi-cylindrical conductors will result in a high electric-field at the resonator center thus cause sample heating or resonator perturbation. Additionally, such a resonator structure would completely shield the sample from microwave irradiation during DNP. Therefore, the current distribution needs to be discretized along specific paths and the conductor surface reduced.

In a well designed volume resonator, current paths are symmetric respective to the $xz$ plane, anti-symmetric respective to the $xy$ plane, and are separated by an angle $\theta$ (Figure 4.1). The linearly polarized magnetic field ($B_1$) at the center of the resonator may be approx. by [78]:

$$B_1 = \frac{2\mu_0}{\pi} \frac{l}{d \sqrt{l^2 + d^2}} \int_{-\pi/2}^{\pi/2} i(\theta) \cos \theta \, d\theta$$  \hspace{1cm} (4.1)

$l$ and $d$ are, respectively, the length and diameter of the resonator. Implementing a cosinal current distribution, $i(\theta) = I \cos(\theta)$ for optimal field homogeneity, the $B_1$ amplitude is:

$$B_1 = \frac{\mu_0 I}{2} \frac{l}{d \sqrt{l^2 + d^2}}$$  \hspace{1cm} (4.2)

On the other hand, to achieve the highest $B_1$ amplitude (but poorest field homogeneity), the current distribution can be forced to $i(\theta) = 1$ when $\theta = 0, \pi$. This results in two diametrically opposing current paths, resulting in $B_1$ amplitude expressed by:

$$B_1 = \frac{2\mu_0 I}{\pi} \frac{l}{d \sqrt{l^2 + d^2}}$$  \hspace{1cm} (4.3)

Two coil designs were considered in this work, a saddle coil (Figure 4.2) and an Alderman-grant coil [79] (Figure 4.4). Both coils are volumetrically equal, provide axial sample access and offer comparable field homogeneity. The saddle coil is hand wound using 0.8 mm silver plated copper wire on a PTFE coil former (ID = $13.0 \pm 0.2$ mm, OD = $15.0 \pm 0.2$ mm and $h = 32.0 \pm 0.2$ mm). The coil former is machined with grooves to guide the wire, allowing for both parallel and series saddle coil geometries with $60^\circ$ separation between wires. Polyamide tape secures the wire to the coil former, followed by a single layer of PTFE tape.

Alternatively, the Alderman-grant coil is machined from a copper pipe (ID = $13.0 \pm 0.2$ mm, OD = $15.0 \pm 0.2$ mm, $h = 25.0 \pm 0.2$ mm and RRR > 50). The PTFE coil former is a two-parts assemble that surrounds the coil, thereby electrically isolating it from the copper
4.1 dDNP compatible coils: transverse resonators

Figure 4.1: Transverse resonator consisting of two half-cylindrical conductors. The current path indicated by red arrow positioned at angle $\theta$. Inset graph illustrates resonator as viewed from $xy$ plane and ideal cosinal current distribution for a homogeneous magnetic field [78].

cavity. The first part consists of a machined cylinder with two diameters (Section 1: ID = 11.0±0.2 mm, OD = 13.0±0.2 mm and $h = 28.5±0.2$ mm. Section 2: ID = 13.0±0.2 mm, OD = 15.0±0.2 mm and $h = 3.5±0.2$ mm) and fits in the circular groove in the lower cavity. The coil former is cooled in liquid nitrogen and slotted through the coil for a snug fit. The second part consists of a PTFE ring (ID = 13.0±0.2 mm, OD = 15.0±0.2 mm and $h = 3.5±0.2$ mm) that slides on top of the assembly to fix it to the circular groove in the cavity upper.

**Saddle coil**

A saddle coil geometry in which $\theta = 60^\circ$ is selected. This geometry yields a balanced compromise between the field homogeneity and amplitude [80] (as demonstrated in the two extreme cases, Equations 4.2 and 4.3). Optimum field homogeneity for a coil of finite length is found when the ratio $l/d$ is greater than $5/3$ [81]. Two loops either in parallel or series configurations compose a saddle coil (Figure 4.2a and Figure 4.3a). The series configuration can include multiple turns per loop. The $B_1$ amplitude at the saddle coil center, can be approx. by [82]:

$$B_1 = \frac{n2\mu_0 I}{\pi} \frac{l}{d\sqrt{d^2 + l^2}} \left[ 1 + \frac{d^2}{d^2 + l^2} \right] \cos(\theta/2)$$  \hspace{1cm} (4.4)

Where $n$ denotes the number turns in a loop. The difference in impedance (Figure 4.2c and Figure 4.3c) between a parallel and series geometry is significant. Parallel saddle
coils have a clear advantage over series saddle coils at higher frequencies and vice-versa. Following the dimensions in Figure 3.2b the parallel saddle coil yields a theoretical $B_1 = 47.6 \, \mu\text{T/}A$. The current flowing through a series saddle coil is typically double that of a parallel geometry and thus theoretical $B_1 = 95.1 \, \mu\text{T/}A$ for the dimensions in Figure 4.3b. Equation 4.4 does not account for frequency dependent current distributions along the coil conductor, which in this case, is the cause of numerical deviation. Moreover, placing the coils in the probe's microwave cavity distorts the generated magnetic field; Generally reducing the maximum $B_1$ amplitude by 25%.
Figure 4.2: CAD illustration of parallel saddle coil in (a) projected and (b) detailed view (side and cross-section). (c) Simulated impedance using copper wire. Simulated 1D magnetic field amplitude profiles along $x$, $y$ and $z$ centerlines of the sample coil in free space. Difference in curves due to frequency dependent current distributions along the coil conductor.
Figure 4.3: CAD illustration of series saddle coil in (a) projected and (b) detailed view (side and cross-section). (c) Simulated impedance using copper wire. Simulated 1D magnetic field amplitude profiles along \( x \), \( y \) and \( z \) centerlines of the sample coil in free space. Difference in curves due to frequency dependent current distributions along the coil conductor.
Alderman-Grant (AG) coil

At frequencies above 100 MHz, the wire length and coil impedance in a series saddle coil, negatively affect the coil sensitivity. Distributing the current over a surface rather than a wire alleviates the increasing coil impedance. The AG coil [79], makes use of this approach and resembles a parallel saddle coil but with thicker conductor surfaces (Figure 4.4a) in place of wires [83, 84]. The current density is highest on the edge of the coil with the current pathway being roughly equal to the coil height. Optimum field homogeneity is obtained when angle $\theta$ is between 85° and 90° [78]. To ensure the highest $B_1$ amplitude, the ratio $l/d$ should be kept above unity. Evidently, a longer coil will result in a more homogenous field but would also raise the coil resistance. The $B_1$ amplitude at the AG coil center has been empirically approx. by [78]:

$$B_1 = \frac{2\mu_0 I}{\pi} \frac{l}{d\sqrt{d^2 + l^2}} \left[ 0.744 + 0.621 \frac{d^2}{d^2 + l^2} \right]$$  \hspace{1cm} (4.5)

The $B_1$-amplitude at the center of the coil described in Figure 4.4b is yielding 41.5 $\mu$T/A. Even though the coil efficiency and impedance (Figure 4.4c) are comparable with a parallel saddle coil, an AG coil geometry provides better reproducibility and mechanical stability. Frequency dependent current distributions does affect the generated $B_1$-field across the coil (Figure 4.4d–f), although not to the extent observed in saddle coils. Placing the coil in the cavity reduces the $B_1$ amplitude by 25%.
Figure 4.4: CAD illustration of Alderman-grant coil in (a) projected and (b) detailed view (side and cross-section). (c) Simulated impedance using copper wire. Simulated 1D magnetic field amplitude profiles along $x$, $y$ and $z$ centerlines of the sample coil in free space. Difference in curves due to frequency dependent current distributions along the coil conductor.
4.2 Magnetic field amplitude estimation

A principle of reciprocity governs the coil sensitivity between transmit and receive situations [85]. This idea becomes increasingly essential when characterizing NMR circuitry and calibrating pulse flip angles.

RF bench characterization

The magnetic field in a resonator can be directly evaluated using two identically small pick-up coils (Figure 4.5), that are geometrically decoupled by partial overlap [86]. The coils have a surface area \( S \) and need to be much smaller than the resonator under test. One ‘excitation’ coil connects to a signal generator while the other ‘detection’ coil to an oscilloscope. When placed close to the resonator under test, the excitation voltage \( V_E \) produces a magnetic field, inducing a current to flow through it. The resonator induces a \( B_1 \) field and thus voltage \( V_D \) across the pick-up coil terminals, which is captured by the oscilloscope. The coil sensitivity at the tuned frequency \( (\omega_0) \) can be determined by [87]:

\[
B_1/\sqrt{P} = \frac{\sqrt{Z_0(V_D/V_T)}}{\omega_0 S} \tag{4.6}
\]

For Equation 4.6 to be accurate, the pick-up coils should not significantly load the resonator. In other words, the gain \( (V_D/V_T) \) should be limited to -30 dB.

Alternatively, a single tuned pick-up coil, critically coupled to the resonator can be used. A capacitor tunes the coil to \( \omega_0 \) while a series resistor \( (R) \) raises the total input impedance to \( Z_0 \). Since the single coil both excites and detects, a time-interleaving mechanism is needed (e.g., circulator or directional coupler). In this case the resonator sensitivity is determined by [88]:

\[
B_1/\sqrt{P} = \frac{V_D/V_T}{\omega_0 S} \sqrt{\frac{2(R+Z_0)}{2}} \tag{4.7}
\]

The Q-factor is the widely adopted figure of merit to indicate the efficiency of any resonator. In electrical systems, this refers to the ratio of resistance to impedance present in a circuit. Thus, the unloaded Q-factor of a tuned resonator is defined as:
\[ Q = \frac{\omega_0 L}{R} \]  

(4.8)

where R and L denote the intrinsic coil resistance and inductance. It is easiest to identify these ohmic parameters and thus Q-factor using a VNA coupled to a matched resonator. However, in that case, the resonator is loaded, and the circuit Q-factor reduces to half the value defined by Equation 4.8. The Q-factor is proportional to the resonator sensitivity as described by the following relation:

\[ \eta \sqrt{Q} \propto \frac{B_1}{\sqrt{P}} \]  

(4.9)

where \( \eta \) is the filling factor of a sample with respect to the resonator volume. The unloaded Q-factor is obtained by loosely coupling a pick-up coil pair to the resonator and measure the full width at half maximum (FWHM) using a VNA. The unloaded Q-factor value is found by computing:

\[ Q = \frac{\omega_0}{\Delta \omega} \]  

(4.10)

Spatial mapping of sensitivity measurements is challenging using pick-up loops. For this, the perturb sphere method provides a solution. The method makes use of a metallic sphere, a pick-up coil pair weakly coupled to the resonator and a VNA [89]. To begin, the pickup loops and VNA identify the resonant frequency. Meanwhile, a small sphere (suspending by a thread or dielectric rod) is introduced inside the resonator. The sphere perturbs the resonator impedance, ultimately changing its resonance frequency. Subsequently, the sensitivity of the coil in the sphere location can be determined [90, 91]:

\[ \frac{B_1}{\sqrt{P}} = \frac{1}{2} \sqrt{\left( \frac{\mu_0}{\Delta \omega \pi r^3} \right) \left( \frac{\delta \omega}{\omega_0^2} \right)} \]  

(4.11)

Where \( r \) denotes sphere radius and \( \delta \omega \) is the total shift in resonant frequency. This techniques is particularly advantageous for small resonators (coils or cavities), where the pick-up coils cannot enter without causing significant perturbation.

**RF characterization in the cryostat**

Reactive TM elements coupled to the sample coil govern the resonant and detection frequency. NMR probes often host multiple resonant circuits supplemented by externally tuneable elements to allow a broad range of frequencies. In a dDNP probe, the variable reactive element reliability significantly degrades due to the low temperature. Remote TM
schemes offer the closest experience to NMR probes, where users can investigate multiple nuclei at different frequencies by manipulating TM element reactance outside the VTI. In contrast, local TM schemes require probe withdrawal from the cryogenic environment to modify the detection frequency. Widely used ceramic capacitors are prone to thermal fracturing and failure due to temperature cycling between cryogenic and room temperatures. Nonetheless, local TM schemes offer significantly higher sensitivity than remote TM schemes, as reported in [92–95].

Due to the location of the resonant circuit inside the cryostat, interacting with the sample coil using pick-up loops or a perturbing sphere is no longer applicable. Instead, the loaded Q-factor can be used to determine coil sensitivity. This approach is not valid when measuring via a remote TM scheme due to the mismatch between the transmission line and sample coil. The standing wave significantly degrades the Q-factor, which dominates the total circuit losses. Moreover, inductive and resistive contributions per unit length from the transmission line eventually result in a constant Q-factor (Figure 4.6). Theoretical and measured Q-factor values show good agreement, in retrospect more data samples are required to verify longer transmission line lengths.

![Diagram of Normalised Q-factor vs Transmission line length](image)

**Figure 4.6:** Calculated Q-factor for local (−) and remote (—) TM schemes (circuit design inset). Q-factor measurements (○) obtained using a variable transmission line, AG coil and a trimmer capacitors.
In this case, the remote TM circuit sensitivity can be determined using transmission line analysis. The following section demonstrates the approach used to calibrate the dDNP probe illustrated in Chapter 3. The probe employs an AG sample coil connected to a 780 mm semi-rigid coaxial cable (UT141SS-C-P, JYEBAO Co., Taiwan). The computed sensitivity is verified experimentally using DNP-NMR. A circuit model of the remotely TM sample coil as present in the polarizer is outlined in Figure 4.7.

Figure 4.7: Circuit model of the resonant circuit employing remote TM scheme. The sample coil and UT141-SS-C-P coaxial cable are inside the cryostat and couple to an RG316/U cable at room temperature via hermetic SMA connector. Two capacitors TM the observed impedance to the HPA impedance.

To ensure the transformed coil impedance \( Z_B \) remains inductive, a flexible coax cable (RG316/U) of length \( l_2 = 100 \text{ mm} \) or \( l_2 = 640 \text{ mm} \) is used when investigating \(^1\text{H} \) (285.55 MHz) or \(^{13}\text{C} \) (71.8 MHz) nuclei, respectively. Using transmission line theory \([67]\), the input impedance is defined by:

\[
Z_B = R_B + jX_B = Z_0 \cdot \left( \frac{Z_A + Z_0 \tanh(l_1(\alpha_1 + j\beta_1) + l_2(\alpha_2 + j\beta_2))}{Z_0 + Z_A \tanh(l_1(\alpha_1 + j\beta_1) + l_2(\alpha_2 + j\beta_2))} \right) \tag{4.12}
\]

where \( \alpha \) denotes attenuation constant, \( \beta \) propagation constant and subscript index refers to the respective transmission line. Two high-Q trimmer capacitors (EM25HV, Knowles Voltronics, Norwich, UK) TM the load impedance. The tuning \( (C_t) \) and matching \( (C_m) \) element values are found by solving the matching conditions \([67]\):

\[
B = \frac{X_B \pm \sqrt{R_B} \sqrt{R_B^2 - R_B Z_0 + X_B^2}}{R_B^2 + X_B^2} \tag{4.13}
\]

\[
C_t = \frac{B}{\omega} \tag{4.14}
\]
4.2 Magnetic field amplitude estimation

\[ X = \frac{1}{\omega C_t} + \frac{X_B Z_0}{R_B} - \frac{Z_0}{R_B B} \]  \hspace{1cm} (4.15)

\[ C_m = \frac{1}{\omega X} \]  \hspace{1cm} (4.16)

To satisfy the conditions using capacitive elements, Equations 4.13 and 4.15 are only valid when \( B \) and \( X \) are positive, therefore an appropriate sign is to be chosen in equation 4.15. Subsequently, the input impedance of the parallel LC resonant circuit is defined as:

\[ Z_C = \frac{1}{j\omega C_t} + \frac{1}{Z_B} \]  \hspace{1cm} (4.17)

and can be matched to the HPA impedance \((R_g)\) such that:

\[ Z_{in} = \frac{-j}{\omega C_m} + Z_C = R_g = 50\Omega \]  \hspace{1cm} (4.18)

Voltage and current distributions across the circuit are determined using circuit theory to identify the current flowing through the coil and nutation frequency for a given excitation power. First, the voltage across the HPA terminals and the current flowing to the NMR circuitry are defined:

\[ V_g = \sqrt{2P_{in}Z_{in}} \]  \hspace{1cm} (4.19)

\[ i_g = \frac{V_g}{Z_{in}} \]  \hspace{1cm} (4.20)

where \( P_{in} \) denotes the power accepted by the circuit. Second, voltage and current distributions across the parallel LC resonant circuit are found by:

\[ V_C = \frac{V_g Z_C}{Z_C + jX} \]  \hspace{1cm} (4.21)

\[ i_C = \frac{V_C}{Z_C} \]  \hspace{1cm} (4.22)

Third, the amplitude voltage of an excitation pulse coupled through both transmission lines is expressed as:

\[ V_0^+ = \frac{V_C}{(1 + \Gamma_b) \exp (l_1(\alpha_1 + j\beta_1) + l_2(\alpha_2 + j\beta_2))} \]  \hspace{1cm} (4.23)

where \( \Gamma_b = (Z_B - Z_0)/(Z_B + Z_0) \).
Finally, the sample coil voltage and current can be determined:

\[ V_A = V_0^+(1 + \Gamma_A) \]  
\[ i_A = \frac{V_A}{Z_A} \]

where \( \Gamma_A = \frac{Z_A - Z_0}{Z_A + Z_0} \). In the interest of verifying the results using DNP-NMR, the nutation frequency \( (\nu_1) \) will be used instead of \( B_1 \) is directly proportional to the coil current:

\[ \nu_1 = \frac{1}{2} B_1 i_A \gamma \]

The estimated nutation frequency per square root power for a transmission line with an attenuation \( \alpha \) and length up to 1000 mm is illustrated in Figure 4.8. Maximum nutation frequency is achieved when the transmission line length is 0 mm (i.e. local TM). The nutation reduces to half with the addition of a 100 mm transmission line section and with 90% when extending the line to 250 mm. The total transmission line length used in the dDNP probe amounts to 1420 mm or 880 mm for \(^{13}\)C and \(^1\)H, respectively.
4.3 Cross-polarization DNP

Nuclear spins with long $T_1$ relaxation (e.g. $^{13}$C, $^{15}$N, etc.) are greatly sought after in studies involving dDNP. Unfortunately, the DNP process becomes prohibitively long to achieve the best possible polarization [29]. In samples with nitroxide radicals or a dilute low-$\gamma$ nuclei concentration. Cross-polarization [96] accelerates polarization of low-$\gamma$ nuclear spins by transferring magnetization from high-$\gamma$ nuclear spins, as outlined by Figure 4.9. Both spin magnetizations are translated with a 90° pulse and spin-locked for a contact duration $\tau$. It is imperative for both spin systems to experience the same effective field strength in order to satisfy the Hartmann–Hahn condition [96], $\gamma_{1H} \nu_{1H} = \gamma_{13C} \nu_{13C}$, given a spin system with $^{13}$C and $^1$H spins. This approach is especially effective since DNP proton polarization is rapid and intense. If the condition is satisfied, CP-DNP is expected to yield an enhancement up to $\gamma_{1H}/\gamma_{13C}$ in $^{13}$C spins polarization, at a reduced build-up time, close to the build-up time of the high-$\gamma$ nuclear spin.

**Figure 4.8**: Normalized nutation frequency as a function of line attenuation $\alpha$ per square root power against transmission line length. Values based on de-embedded measured sample coil impedance. Inset graph illustrates nutation frequency for varying pulse powers using the dDNP probe circuit. Experimentally verified $\nu_1$ indicated by ■ and □.
A typical $^1$H linewidth in solid-state is in the order of 50–100 kHz while $^{13}$C is between 10–20 kHz (depending on deuteration degree of sample). Meaning to achieve a $90^\circ$ pulse that will excite the entire linewidth, pulse durations of 2.5–5 $\mu$s and 12.5–25 $\mu$s are required for $^1$H and $^{13}$C, respectively. However, the short pulse durations render satisfying the Hartmann–Hahn condition not possible with the available amplifier power. Extending the pulse duration (while demanding less power) at the cost of less efficient magnetization transfer is warranted but leads to a higher likelihood of arcing in the low-pressure helium atmosphere.

Fortunately, the hard $90^\circ$ pulses can be substituted for less power stringent adiabatic and chirp pulses [97]. Achieving these high RF pulses is technically challenging due to the imposed coil geometry required for sample dissolution and the inherent low breakdown voltage of the helium in the VTI. Moreover, the issue is exasperated by the need of a homogeneous excitation field across the sample volume. Performing CP-DNP requires meticulous pulse optimization to manage the excitation energy, sample optimization to reduce the low-gamma spins linewidth and an accommodating resonant circuit which could resonate at two frequencies without forming an arc. The next sections will explore the realization of such a resonant circuit capable of performing CP-DNP.

### 4.4 Double resonance schemes

#### Remote TM

Remote TM schemes have the advantage of adopting from a library of existing multi-resonant NMR circuit designs [98–100]. Some designs are more practical than others, due to the number of elements needed and voltage distributions across circuit elements during excitation. The implemented remote TM circuit (Figure 4.10) is based on [101] and couples to a single semi-rigid coaxial cable (UT141SS-C-P, JYEBAO, Taiwan) to access the coil from the top flange.
4.4 Double resonance schemes

Figure 4.10: Remote TM scheme for double resonance NMR circuit. Sample coil (L) is accessed via a single 50 Ω coaxial cable. Two channels couple to the coaxial cable to tune (C2, C4) and match (C1, C3) the coil to their respective frequencies. An LC trap (L2, C5) isolates the two channels.

A pair of trimmer capacitors (Knowles Voltronics, Norwich, UK) couple to the transmission line to TM each channel at the desired resonant frequency. An LC stopband trap tuned to the lower channel provides >20 dB of isolation between the two channels. The circuit is simple to construct but suffers greatly in sensitivity, as listed in Table 4.1. Attempts to use smaller coils yield higher sensitive due to their greater filling factor and lower resistance. Furthermore, lower loss coaxial cables marginally improve the resonant circuit sensitivity, but result in a higher VTI base temperature as demonstrated with a flexible coaxial cable (RG316/U, JYEBAO, Taiwan). Due to the insensitivity of the NMR circuit, no noticeable shift in resonance frequency occurs when loading the sample into the coil. The remote TM circuit sensitivity is too low to adequately perform efficient cross polarization. Ultimately, one needs to sacrifice either the large sample volume (>1 ml) or the capability of performing dissolutions.

Local TM

It is less technically challenging to perform CP-DNP on dissolution compatible, large samples with local TM schemes. This is evident by the list of successfully documented low-temperature CP-DNP experiments (Table 4.2). Circuit designs adopting orthogonal concentric coils [102, 103] or a dual-resonant coil [104, 105] rely on two coaxial cables to access to each respective frequency channel. Lumped elements are distributed on or near the coil structure to achieve the highest sensitivity. Channel isolation is achieved by geometry in the case of orthogonal coils or by frequency traps in the case of a double resonant coil. Furthermore, all designs employ ceramic NP0 capacitors which are suitable to operate in cryogenic environments.
Two designs were explored to perform CP-DNP using a local TM scheme. The first implemented circuit design (Figure 4.11) relies on two LC traps to provide $>30$ dB isolation between the two channels. Inductors were hand wound using 0.8 mm copper wire alongside 0.110” × 0.110” NP0 ceramic capacitors (1111C, Passive Plus, Inc, NY, USA). Each trap presents a stopband and passband for its respective channel. Components were hosted on a PCB positioned above the cavity and coupled to an AG coil (ID=13 mm, $l=25$ mm) by a 20 mm low-loss semi-rigid cable (UT-141C-TP, JYEBAO, Taiwan). Two semi-rigid coaxial cables (UT141SS-C-P, JYEBAO, Taiwan) connect to the PCB from the top flange and provide access to each channel. When cooled to 1.2 K, the double resonant circuit yields a Q-factor of 150 and 222 for the $^{13}$C and $^1$H channels, respectively.

The circuit suffered from two significant drawbacks that rendered CP-DNP impossible. Firstly, the number of elements involved made it challenging to satisfy the channel conditions of tuning, matching, or isolation simultaneously at 1.2 K. Change in capacitance value was not systematic across the different capacitor values when cooled. Additionally, the deviation in capacitance value was not reproducible outside the VTI in liquid nitrogen, thus rendering testing a slow and costly. Secondly, the circuit topology resulted in high voltages between the capacitor electrodes, which in turn caused arcing (inductors also suffer from arcing but can be constructed with distant terminals). Higher rated capacitors can help mitigate arcing but are physically large, costly and not readily available (made on demand with several weeks lead time).

<table>
<thead>
<tr>
<th>Coil geometry</th>
<th>$\nu_{13C}/\sqrt{P}$ (kHz$/\sqrt{W}$)</th>
<th>$\nu_{1H}/\sqrt{P}$ (kHz$/\sqrt{W}$)</th>
<th>$Q(f_0=^{13}\text{C})$</th>
<th>$Q(f_0=^{1}\text{H})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parallel saddle</td>
<td>0.14</td>
<td>0.42</td>
<td>56.8</td>
<td>80.4</td>
</tr>
<tr>
<td>(ID=14 mm, $H=21$ mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series saddle</td>
<td>0.22</td>
<td>0.36</td>
<td>46.8</td>
<td>67.6</td>
</tr>
<tr>
<td>(ID=14 mm, $H=21$ mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AG</td>
<td>0.15</td>
<td>0.39</td>
<td>59.6</td>
<td>77.2</td>
</tr>
<tr>
<td>(ID= 13 mm, $H=25$ mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AG†</td>
<td>0.16</td>
<td>0.67</td>
<td>58</td>
<td>83.4</td>
</tr>
<tr>
<td>(ID= 9 mm, $H=25$ mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.1: Remote TM resonant circuit sensitivity for different coil geometries. All coils accessed via UT141SS-C-P semi-rigid stainless-steel coaxial cable. Use of RG316/U flexible coaxial cable instead. Resonant frequencies $f_0(^{13}\text{C}) = 71.8$ MHz and $f_0(^{1}\text{H}) = 285.55$ MHz. Nutation frequency determined experimentally.
Table 4.2: State-of-art low-temperature CP-DNP experiments. Missing information indicated by a dash or subsisted for relevant description. $(†)$ Sample volume not specified, but can accommodate a maximum 100 $\mu$L sample volume. $\frac{\epsilon_{\text{CP-DNP}}}{\epsilon_{\text{DNP}}}$ is the ratio of polarization achieved using direct DNP of spins and using CP-DNP. Similarly, $\frac{\tau_{\text{CP-DNP}}}{\tau_{\text{DNP}}}$ is the ratio between the build-up time constants of direct DNP and with CP-DNP. Polarization value $P_{\text{max}}$ reported in solid-state.

<table>
<thead>
<tr>
<th>Coil geometry</th>
<th>Matching scheme</th>
<th>$B_0$ field (T)</th>
<th>$\nu_{13C}/\sqrt{P}$ (kHz/$\sqrt{W}$)</th>
<th>$\nu_{1H}/\sqrt{P}$ (kHz/$\sqrt{W}$)</th>
<th>Pol($^{13}$C) (%)</th>
<th>$\frac{\epsilon_{\text{CP-DNP}}}{\epsilon_{\text{DNP}}}$</th>
<th>$\frac{\tau_{\text{CP-DNP}}}{\tau_{\text{DNP}}}$ (s)</th>
<th>Sample</th>
<th>Sample volume</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solenoid</td>
<td>Local</td>
<td>3.35</td>
<td>14.7</td>
<td>11.7</td>
<td>23</td>
<td>2.4</td>
<td>890/170</td>
<td>1M $[^{1}$-$^{13}$C] sodium acetate D$_2$O/ethanol (67:33 v/v) 30 mM TEMPO</td>
<td>$^{1}$100 $\mu$L</td>
<td>[105]</td>
</tr>
<tr>
<td></td>
<td>Remote</td>
<td>3.35</td>
<td>30 kHz, $Q=69$</td>
<td>30 kHz $Q=112$</td>
<td>24</td>
<td>2.2</td>
<td>1014/580</td>
<td>4.5 M $[^{1}$-$^{13}$C] urea glycerol-d$_3$/D2O (1:1 v/v) 30 mM TEMPOL</td>
<td>25 $\mu$L</td>
<td>[52]</td>
</tr>
<tr>
<td>Series saddle</td>
<td>Local</td>
<td>6.7</td>
<td>3.9</td>
<td>3</td>
<td>45</td>
<td>1.7</td>
<td>325/810</td>
<td>3 M $[^{1}$-$^{13}$C] sodium acetate D$_2$O/ethanol (67:33 v/v) 50 mM TEMPO</td>
<td>50 $\mu$L</td>
<td>[104]</td>
</tr>
<tr>
<td>AG resonator</td>
<td>Remote</td>
<td>3.35</td>
<td>6</td>
<td>6.1</td>
<td>-</td>
<td>$&gt;2$</td>
<td>-</td>
<td>4.5 M $[^{1}$-$^{13}$C] urea glycerol/D2O (1:1 v/v) 50 mM TEMPOL</td>
<td>100 $\mu$L</td>
<td>[106]</td>
</tr>
<tr>
<td>Solenoid</td>
<td>Local</td>
<td>6.7</td>
<td>2.7</td>
<td>3.33</td>
<td>20</td>
<td>1.7</td>
<td>-/2021</td>
<td>7 M $[^{6}$Li] lithium chloride ethanol-d$_6$/D$_2$O/H$_2$O (40:40:20 v:v) 50 mM TEMPO</td>
<td>40 $\mu$L</td>
<td>[30]</td>
</tr>
<tr>
<td>Concentric series</td>
<td>Local</td>
<td>6.7</td>
<td>3.9</td>
<td>3</td>
<td>64</td>
<td>6.4</td>
<td>1014/168</td>
<td>3 M $[^{1}$-$^{13}$C] sodium acetate D2O/ethanol (67:33 v/v) 50 mM TEMPO</td>
<td>50 $\mu$L</td>
<td>[103]</td>
</tr>
<tr>
<td>saddles</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tbody>
</table>
Figure 4.11: First local TM circuit design for double resonance NMR circuit. Sample coil (L) is accessed via a short 50 Ω coaxial cable (20 mm). Two channels couple to the coaxial cable to tune \((C_2, C_4)\) and match \((C_1, C_3)\) the coil to their respective frequencies. Two traps \((L_2, C_5, L_3\) and \(C_6, C_7\) and \(L_8\)) isolate the two channels by forming a stopband at the opposing channel frequency and a bandpass at their respective frequency.

The second implemented circuit design addressed these drawbacks [77]. Fewer elements realize the design, featuring several inductors that allow broader fine tuning. Unlike, capacitors values that vary in discrete steps, inductors are freely adjustable by modifying the spacing between turns. Inside the cavity, three 0.110” × 0.110” capacitors and a single turn inductor are soldered across the AG coil terminal. The first capacitor \((C_1)\) is selected to resonant with the AG coil at the higher frequency, while the second capacitor \((C_2)\) connected in parallel resonates at the lower frequency. An LC trap placed in series with the second capacitor blocks current flow at the higher frequency, thereby yielding a double resonant coil. A 25 mm flexible coaxial cable (RG316/U, JYEBAO, Taiwan) couples the coil to an external PCB. Two frequency selective L-networks (filters) transform the tuned circuit impedance to 50 Ω. The low-pass filter \((C_4\) and \(L_2\)) transform the higher frequency channel impedance while the high-pass filter \((C_5\) and \(L_3\)) transforms the low-frequency channel. Element values should be considered, as to not inadvertently form a resonance at the channel frequencies. Once again the inductors are hand wound, but larger 0.380” × 0.380” capacitors are used to mitigate arcing. To achieve higher sensitivity, the sample coil inner diameter is reduced by 3 mm (ID = 10 mm) while a single flexible coaxial cable (RG316/U, JYEBAO, Taiwan) replaced the two semi-rigid cables that provided access to the circuit. A diplexer couples to the cable via the top flange and allows isolated use of each channel. Overall the circuit achieved a sensitivity of \(v_{13c}/\sqrt{P} = 2.8 \text{ kHz}/\sqrt{W}\) and \(v_{1H}/\sqrt{P} = 7.7 \text{ kHz}/\sqrt{W}\).
Four CP-DNP sequences were tested using a 50 µL 4.5 M [1-13C]urea dissolved in glycerol-d₈, D₂O and H₂O (5:2:3 v/v) with 50 mM TEMPOL:

1. Hartman-Hann sequence (HHCP) as illustrated in Figure 4.9.

2. Modified Hartman-Hann sequence (HHCP-Chirp) with adiabatic chirp pulse replacing a hard 90° pulse.

3. The laboratory frame de- and remagnetization (LAFDR) sequence [107, 108], relies on chirp pulses to satisfy the CP condition.

4. The adiabatic remagnetization in the rotating frame (ADRF-ARRF) sequence is akin to HHCP-Chirp but the contact pulse is interleaved between the ¹H and ¹³C channels [109].

Experimental CP-DNP results are listed in Table 4.3. Both HHCP and LAFDR sequences preform equally, suggesting the $B_1$-field strength is the limiting factor for HHCP. Another indication of pronounced $B_1$-field limitation is observed when comparing HHCP and HHCP-chirp. The chirp pulse is more efficient at cross-polarization transfer. The improvement observed between hard and adiabatic 90° pulses possibly indicate $B_1$ inhomogeneities over the sample volume.
Table 4.3: Comparison of solid-state $^{13}$C polarization achieved by different CP-DNP sequences. $\nu_1 = 29$ kHz for HHCP sequences, $\nu_1 = 8$ kHz for LAFDR and ADRF-ARRF. Chirp pulses are 250 $\mu$s long and a sweep bandwidth of 100 kHz. $\epsilon_{\text{CP-DNP}} / \epsilon_{\text{DNP}}$ is the ratio of polarization achieved using direct DNP of spins and using CP-DNP. $\tau_{\text{CP-DNP}}$ is the build-up time constants of polarization due to CP-DNP.

<table>
<thead>
<tr>
<th>Sequence</th>
<th>$\text{Pol}_{\text{max}}(^{13}\text{C})$ (%)</th>
<th>$\epsilon_{\text{CP-DNP}} / \epsilon_{\text{DNP}}$</th>
<th>$\tau_{\text{CP-DNP}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HHCP</td>
<td>19</td>
<td>1.4</td>
<td>480</td>
</tr>
<tr>
<td>HHCP-Chrip</td>
<td>27</td>
<td>1.9</td>
<td>720</td>
</tr>
<tr>
<td>LAFDR without overlap</td>
<td>24</td>
<td>1.7</td>
<td>780</td>
</tr>
<tr>
<td>LAFDR with overlap</td>
<td>26</td>
<td>1.9</td>
<td>720</td>
</tr>
<tr>
<td>ADRF-ARRF</td>
<td>13</td>
<td>0.9</td>
<td>540</td>
</tr>
</tbody>
</table>

4.5 Practical challenges

Arcing in low-pressure atmosphere

Thus far sensitivity has been the driving metric for circuit design. However, CP sequences generally require sustained excitation pulses. Given the high Q-factor of the proposed resonator, large voltages between element terminals are inevitable and meticulous care is required to mitigate arcing. What is often referred to as “arching” is, in fact, the last step of a dielectric breakdown process. Compared to other dielectrics, a perfect vacuum theoretically has the highest breakdown voltage. However, in reality a partial vacuum environment exists in the VTI. Gaseous helium present in the VTI has a low breakdown voltage due to it being less dense than air and requires less energy to ionize. Paschen’s law determines this voltage for a gas dielectric [110], Figure 4.13 illustrates the breakdown voltage in low-temperature helium gas at typical dDNP pressures. Note, that these curves assume a uniform static field. In practice, the field is non-uniform, suggesting the true breakdown voltage is slightly lower [111].

Before arcing, the strong electric field liberates an electron that collides with a neutral helium molecule and creates a positive ion. This event leads to a chain reaction, producing an avalanche of free electrons and many positive ions which impart a slight conductivity to the gaseous helium atmosphere (Figure 4.14). If the electric field sustains, a glow appears between the electrodes indicating continued ionization. Next, the current density rises between the two electrodes, heating the helium gas and reducing its density. This leads to a rapid increase in atmospheric conductivity, voltage collapse and the formation of an arc.
Due to the small pressure gradient across the VTI, ionized helium molecules will remain within an electric field region until they tumble away due to rising freshly boiled helium. Meaning, the ionization process accumulates within the gas volume even after an arc forms. For this reason, future arcs occur with less excitation power after an initial arc event.

![Figure 4.13: Pashchen curves determining the breakdown voltage in gaseous helium for varying electrode spacing. The legend indicates the VTI pressure according to the temperature of the helium bath as expressed by the international temperature scale of 1990 (ITS-90). Graph adapted from [110].](image)

**Detection of arcing**

Depending on the excitation power, arcs in the VTI are audible from outside the cryostat (typically producing a ‘click’). When an arcs forms, the sample coil becomes detuned and mismatched. The reflected power at the excitation port provides a more accurate sign of arcing. A single channel local TM circuit tuned to 285.55 MHz (single channel circuit from Figure 4.11, without any LC traps) and a directional coupler are used to investigate this phenomenon in the VTI (Figure 4.15). Gaseous helium surrounded the TM circuit PCB while liquid helium submerged the sample coil.
Figure 4.14: Breakdown voltage vs. discharge current along the electric field between two electrodes. Inset diagrams illustrate mechanisms leading to arcing. Adapted from [110].

Figure 4.15: Experimental setup to detect arcing by observing the reflected power caused by a detuned/mismatched resonant circuit. The testing frequency was set to 285.55 MHz, corresponding to $^1$H at 6.7 T conditions.
A 4 µs pulse excites the resonant circuit with varying power from 1 W to 97 W. The needle valve was kept partially open while the VTI pressure was 1.2 mbar. A repetition time of 2 min allowed for freshly boiled helium gas to rise through the VTI. Observing Figure 4.16b, it is evident that pulse powers 1–5 W do not trigger an arcing event, while a 17 W pulse does within 1 µs of excitation. Powers greater than 17 W produced an audible click within the cryostat and produced a distinct reflected waveform trail (Figure 4.16b). Non-arcing pulses feature the characteristic resonant circuit ring down, which is proportional in duration to the circuit Q-factor. In contrast, when an arcing event occurs, the waveform ends abruptly. Sometimes a ring down is present but will be distorted or non-continuous. As a comparison, the reflected power from a non-arcing probe in air (273 K) at 1 atm is illustrated in Figure 4.16c-d.

Electrode pairs prone to causing an arc can be visually inspected through a transparent vacuum chamber constructed from plexiglass (Figure 4.17a). The chamber may be evacuated to reach an atmospheric pressure below 10 mbar or purged with helium gas and sealed. The resonant circuit is then pulsed with increasing power levels until an arc event occurs (Figure 4.17b-c). The following approach is convenient and economical in detecting and troubleshooting arc prone areas in a resonant circuit design.

**Mitigation of arcing**

At this point, lowering the voltage across circuit electrodes stands as a nearly unavoidable solution to mitigate arcing. However, barring changes to the resonant circuit; the surrounding dielectric can be modified to sustain electric-fields strengths without the persisting arc event. One possible approach entails flooding the VTI with liquid helium to submerge both the sample coil and the extruding TM circuit. The breakdown voltage in liquid helium is higher than in gas \([37,39,40]\). The exact difference is debatable upon several physical dielectric parameters such as the liquid mixture purity and temperature but also the testing apparatus and the electrode shape, size and surface finish. Figure 4.18 illustrates the region in which measured liquid helium breakdown is expected to occur as stipulated by multiple studies in the literature \([113–115]\).

A set of experiments were conducted using the setup illustrated in Figure 4.15 for pulse powers between 1 – 97 W (2 min repetition time, 2.2 µs pulse) while the VTI pressure is maintained at 1.2 mbar. The reflected waveforms in Figure 4.19a, suggests a slight improvement in arc mitigation, as breakdown still occurs at 97 W (similar to compared to gaseous helium dielectric). Nonetheless, there is an improvement, as illustrated in Figure
Figure 4.16: (a) Reflected power for different excitation pulse powers with a TM circuit in gaseous helium (1.2 K helium bath). Arcing occurs for pulse powers >17 W. (b) Zoomed inset of reflected power indicating ring down trial of the resonant circuit. (c) Reflected power for different excitation pulse powers in room temperature 1 atm air. (d) Zoomed inset of reflected power.
4.19b. An arc occurred in gaseous helium 1 μs into a 17 W pulse, while in liquid helium a 20 μs, 50 W pulse can be sustained without any signs of breakdown.

Another approach considered in this work involves applying an external substance between the arc prone electrodes. The substance serves to displace helium molecules away from the intense region of the electric field. The applied substance would undoubtedly have a dielectric value higher than air and consequently will cause reactive element impedance to change. Two substances were tested, grease (Krytox™ GPL-227, DuPont, DE, USA) and a two compound epoxy (Araldite® AV 138M-1 & Hardener HV 998, Huntsman Advanced Materials, Switzerland). The grease is PTFE based and applies directly from a tube nozzle. It is not adhesive and wipes off easily with tissue paper. Approx. 100 mm$^3$ of grease was
applied on circuit electrodes. The grease is brittle at low temperatures and needs to be mechanically reinforced by polyaimide tape.

On the other hand, epoxy is an adhesive that forms a strong resin when cured. Applying the epoxy requires preparing a temporary mould around the TM PCB circuit. For this purpose, Polyamide tape secured to the PCB underside and around the edge should suffice. The poured pre-mixed epoxy forms a ~1cm epoxy layer above the PCB surface. Unlike grease, the epoxy adheres to the PCB and cannot be removed with ease.

The modified TM circuits were tested in both gaseous and liquid helium dielectrics (1.2 K helium bath). The TM circuit experienced a greater shift in resonance with epoxy than the grease, indicating the epoxy resin has a high dielectric constant. The grease covered TM circuit showed promising results mitigating arc formation in liquid helium (Figure 4.21). Pulse powers were incremented after each excitation with a 2 min repetition time. Due to no arcing at maximum power (97 W), the process was continued until an arc event occurred on the third iteration.

**Figure 4.18:** Region in which any measured breakdown field strength may occur (shaded). The high limit (dark) is extrapolated from the Paschen curve while the low limit (light) is adapted to represent a breakdown in bubbles. Graph adapted from [114].
Figure 4.19: (a) Reflected power for different excitation pulse powers with TM circuit in liquid helium (1.2 K). Arcing occurs during 97 W pulse power. (b) Intermediate power 52 W can be sustained without arcing.
In gaseous helium, the TM circuit did not trigger an arc when excited with 400 \( \mu \)s long pulses with power levels up to 97 W. Subsequently, longer 1 ms pulses were investigated; to which the first arc occurred at 26 W (Figure 4.21a). Lowering the power to 20 W resolves the problem, allowing for pulse extension up to 1.7 ms (Figure 4.21b). The epoxy covered circuit did not yield much success. The TM circuit experienced increased arcing in liquid helium, even at low powers with short durations (10 \( \mu \)s, 5-17 W). Consequently, further testing was suspended, allocating remaining resources to the Krytox™ covered TM circuit.

Figure 4.20: (a) Reflected power for different excitation pulse powers from a TM circuit covered with Krytox™ grease in liquid helium (1.2 K). Arcing occurs during third 1.5 ms, 97 W pulse. Inset figures zoom in on leading and trailing edges of the reflected waveform. Resonant circuit ringdown can be distinctly observed.
Figure 4.21: (a) Reflected power for 26 W excitation pulse powers from a TM circuit covered with Krytox™ grease in gaseous helium (1.2 K helium bath). Arcing occurs approx. 900 µs into pulse duration. Inset figures zoom in on leading and trailing edges of the reflected waveform. Resonant circuit ringdown appears distorted as a result of the arc event. (b) Reflected power for 19.8 W excitation pulse powers from a TM circuit covered with Krytox™ grease in gaseous helium (1.2 K helium bath). Inset figures zoom in on leading and trailing edges of the reflected waveform. Resonant circuit ringdown can be distinctly observed.
Chapter 5

Influence of microwave delivery on the DNP process

This chapter presents two strategies for increasing the microwave density across a sample volume during irradiation. The contribution herein facilitates DNP at higher field strengths (up to 10.1 T), where power is increasingly scarce at higher frequencies. The two microwave strategies were verified using two samples employing a trityl or TEMPOL radicals in DNP-NMR experiments. The first strategy approx. doubled the delivered microwave power to the sample. While the second resulted in approx. 2.3 dB increase in equivalent microwave power.

Results and discussions are partially presented in the scientific journal article titled ‘Optimized microwave delivery in low-temperature DNP’ [116].

5.1 Introduction

Several sample properties dedicate the optimal microwave intensity to achieve full electron transition saturation, e.g. radical concentration and inhomogeneous line broadening. Transmission losses in a waveguide become more severe as frequency increases [67], but a brute force increase in power is not the solution. Moreover, especially in the case of dry magnets where the cooling efficiency is limited, excessive microwave power will result in sample heating, thus lowering the DNP enhancement [65]. Therefore, efficient transmission while maintaining a reasonably low source power is essential when working at high field. Two goals need to be fulfilled to achieve this aim between 94 – 282 GHz. First, minimize transmission loss while maximizing thermal isolation between the microwave source and sample. Second, maximize the microwave field density across the sample volume.
5.2 Waveguide Selection

Geometry

The polarizer dimensions and magnet homogeneity dictate the waveguide length needed to couple the source to the sample space. The waveguide conductivity and aperture directly influence the observed transmission losses and mode of propagation. The ideal waveguide would have the smallest cross-sectional area (to minimize thermal conduction) and lowest attenuation. For instance, the attenuation due to conductive losses in widely adopted rectangular waveguides is defined by [67]:

\[
\alpha_c [\text{dB/m}] = 20 \log_{10}(e) \frac{R_s}{a^3 b \beta k n} (2b \pi^2 + a^3 k^2) \tag{5.1}
\]

where \(b\) and \(a\) denote the height and width of the waveguide, intrinsic impedance of the waveguide \(\eta = \sqrt{\mu_0 \mu_r / \varepsilon_0 \varepsilon_r}\), surface resistance \(R_s = \sqrt{\omega \mu_0 / 2 \sigma}\), wavenumber \(k = \omega \sqrt{\mu_0 \mu_r \varepsilon_0 \varepsilon_r}\) and propagation constant \(\beta = \sqrt{k^2 - [(m \pi / a)^2 + (n \pi / b)^2]}\) for propagation mode \(\text{TM}_{nm}\) or \(\text{TE}_{nm}\). Similarly, in circular waveguides conductive losses is expressed as [67]:

\[
\alpha_c [\text{dB/m}] = 20 \log_{10}(e) \frac{R_s}{r k \eta \beta} \left[ \frac{(p_{nm}^n)^2}{r^2} + \frac{k^2}{p_{nm}^n - 1} \right] \tag{5.2}
\]

where \(r\) denotes the radius of the waveguide, propagation constant \(\beta = \sqrt{k^2 - (p_{nm}^n / r)^2}\) and the root Bessel function \(p_{nm}^n\) corresponds to propagation mode \(\text{TM}_{nm}\) as listed in Table 5.1. The term \(p_{nm}^n\) is swapped for the root derivative of Bessel function \(p_{nm}^n\) for propagation mode \(\text{TE}_{nm}\) as listed in Table 5.2.

<table>
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<tr>
<th>(n)</th>
<th>(p_{n1})</th>
<th>(p_{n2})</th>
<th>(p_{n3})</th>
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<td>2.405</td>
<td>5.520</td>
<td>8.654</td>
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<tr>
<td>2</td>
<td>5.135</td>
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<table>
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<th>(p_{n2}^{'})</th>
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<tbody>
<tr>
<td>0</td>
<td>3.832</td>
<td>7.016</td>
<td>10.174</td>
</tr>
<tr>
<td>1</td>
<td>1.841</td>
<td>5.331</td>
<td>8.536</td>
</tr>
<tr>
<td>2</td>
<td>3.054</td>
<td>6.706</td>
<td>9.970</td>
</tr>
</tbody>
</table>
Corrugated waveguides offer an elegant solution to reduce conductive losses [117] and have been successfully adopted into dDNP probes [55, 118]. Use of the propagation mode HE_{11} confines the transmission power density to the waveguide centre, thereby minimizing conductive losses from the walls. Conductive losses in a circular corrugated waveguide are defined as [119]:

$$\alpha_c [\text{dB/m}] = 20 \log_{10}(e) \frac{Rs}{2n} \frac{p_{nm}^2}{k^2 r^3} \left( \frac{(1 - \frac{t}{2})^2 \sin^2(kd) + \frac{d}{p} + \frac{1}{kp} \sin(kd) \cos(kd)}{(1 - \frac{t}{2})^2 \sin^2(kd)} \right)$$

(5.3)

where \( p_{nm} = 2.405 \) denotes the root of a Bessel function, parameters \( r, t, p \) and \( d \) correspond to the corrugated waveguide geometry illustrated Figure 5.1. Unfortunately, this option is not favorable when compared to a smooth bore waveguide due to the following reasons:

1. Beyond the designated bandwidth corrugated waveguides seize to offer the lowest attenuation.
2. Even though manufacturing techniques have evolved recently [119, 120], development costs are still high.
3. Frost or dew formation between corrugations may hinder the waveguide reliability.

Only rectangular and circular waveguides are considered in this study. Equations 5.1 and 5.2 establish two findings; firstly, an inverse relationship exists between the waveguide attenuation and perimeter. As a consequence, overmoded waveguides promote low-loss

![Figure 5.1: Cross-sectional drawing of a circular corrugated waveguide section with inner radius \( r \), corrugation width \( t \), period \( p \) and depth \( d \).](image-url)
transmission. Secondly, circular waveguides offer a better ratio between attenuation and perimeter than rectangular waveguides as illustrated in Figure 5.2. When choosing the waveguide size, the upper perimeter limit was established to be where the attenuation rate reduces less than the heat load rate increases, rendering further expansion thermally costly. The lower perimeter limit would be established as the perimeter of a single-mode WR-10 waveguide.

As such, a seamless smooth wall 304 stainless-steel tube with a diameter $4.16 \pm 0.2$ mm forms the waveguide walls. The fundamental propagation mode is $\text{TE}_{11}$ ($p_{11} = 1.841$) with a cut-off frequency of 42.26 GHz, other mode cut-off frequencies are listed in Tables 5.3 and 5.4. Mode converters can be utilized to exploit propagation modes with reduced attenuation (e.g. $\text{TE}_{01}$) [121, 122]. Attenuation associated with the first four propagation modes is illustrated in Figure 5.3. However, manufacturing mode converters is increasingly challenging at higher millimeter frequencies and was not explored in this work.

**Table 5.3:** Cut-off frequencies of $\text{TM}_{nn}$ excitation modes for a circular waveguide ($r = 2.08$) mm.

<table>
<thead>
<tr>
<th>$n$</th>
<th>$\text{TM}_{n1}$</th>
<th>$\text{TM}_{n2}$</th>
<th>$\text{TM}_{n3}$</th>
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</thead>
<tbody>
<tr>
<td>0</td>
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<td>126.71 GHz</td>
<td>198.65 GHz</td>
</tr>
<tr>
<td>1</td>
<td>87.96 GHz</td>
<td>161.05 GHz</td>
<td>233.54 GHz</td>
</tr>
<tr>
<td>2</td>
<td>117.87 GHz</td>
<td>193.21 GHz</td>
<td>266.74 GHz</td>
</tr>
</tbody>
</table>

**Figure 5.2:** Theoretical attenuation vs cross-section perimeter of (a) rectangular ($\text{TE}_{11}$) and (b) circular ($\text{TE}_{10}$) stainless-steel waveguide ($\sigma = 1.45 \times 10^6$ S/m) at (a) 94, (b) 188 and (c) 282 GHz.
Table 5.4: Cut-off frequencies of TE\textsubscript{nm} excitation modes for a circular waveguide (r = 2.08) mm.

<table>
<thead>
<tr>
<th>n</th>
<th>TE\textsubscript{n1}</th>
<th>TE\textsubscript{n2}</th>
<th>TE\textsubscript{n3}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>87.96 GHz</td>
<td>126.71 GHz</td>
<td>198.65 GHz</td>
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<tr>
<td>1</td>
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</tr>
<tr>
<td>2</td>
<td>117.87 GHz</td>
<td>193.21 GHz</td>
<td>266.74 GHz</td>
</tr>
</tbody>
</table>

Figure 5.3: Conductive loss attenuation vs. frequency for modes TE\textsubscript{11}, TM\textsubscript{01}, TE\textsubscript{21} and TE\textsubscript{01} in a circular (r = 2.08 mm) stainless-steel (\(\sigma = 1.45 \times 10^6\) S/m) waveguide.

Material properties

Stainless-steel is a poor conductor both thermally (16 W/mK) and electrically (\(\sigma_{SS} = 1.45 \times 10^6\) S/m). A solution to address this setback is to internally electroplate the waveguide with copper or gold, thereby mitigating conductive losses while maintaining thermal isolation [123]. Other solutions involve using a copper waveguide in combination with a bandgap structure [124] that creates a thermal discontinuity invisible to microwaves. Unfortunately, the structure has a limited bandwidth and suffers from flange misalignment or cocking. Another more straightforward solution adopts a waveguide assembly containing a waveguide section made from a poor thermally conducting material, as implemented in [35]. Ultimately, electroplating provided most attractive, as it offered the lowest attenuation using a single waveguide structure.
5.3 Reduction of ohmic losses via electroplating

Electroplating procedure

Electroplating the inner walls of the tube with at least a single skin depth of copper yields a composite waveguide with the thermal properties of stainless-steel and electrical conductivity of copper ($\sigma_{\text{Cu}} = 5.6 \times 10^6 \text{ S/m}$). Before electroplating, the waveguide is treated using a metal polish (Autosol®, Dursol-Fabrik Otto Durst, Germany) and a soft brush to mechanically reduce surface oxide impurities [125]. A spring-loaded fixture (Figure 5.4c) hosts the waveguide and provides a cathode wire tension through the tube (Figure 5.4a). Fluid flows through the waveguide with the aid of a peristaltic pump ( LongerPump BT300-2J, Hebei, P.R. China) specified to displace up to 900 mL/min while rotating at 300 RPM. Two silicone tubes connect on either end of the fixture and lie in the chemical bath to allow for fluid ingress and egress (Figure 5.4b). A picture of the fixture during operation is displayed in Figure 5.4d.

![Figure 5.4: Diagram of (a) electrical and (b) plumbing connections on the plating fixture. (c) CAD drawing illustrating 1. tension spring, 2. copper wire 3. tension plate, 4. waveguide, 5. perforated bath let 6. fixture walls. (d) Suspended electroplating fixture above a copper cyanide bath. Electrode polarity and fluid flow direction indicated on the image.](image-url)
The 8 step electroplating process is detailed at the end of the section (Table 5.6) and consists of 5 different actions:

1. **Cathodic cleaning**: The liberation of gases from the cathode scrubs the inner waveguide wall, displacing grease and excess polish.

2. **Neutralization**: Water pumped through the waveguide to rinse any remnant solvents from the former bath.

3. **Acid treatment**: Removal of alkaline residuals or tenacious oxide films. The acid treatment also allows for surface roughening which promotes stronger electrodeposited adherence.

4. **Nickel plating**: The stainless-steel walls are pre-plated with Wood’s nickel to form a host layer for the final copper plate.

5. **Copper plating**: The alkaline copper cyanide bath deposits 0.3 µm of copper per A/dm² a minute. Current flow is limited to 300 mA as low amperage is favoured to reduce surface roughness [126]. The internal waveguide area is 1.02 dm², requiring a minimum plate time of 150 s to deposit a single skin depth at 94 GHz (Table 5.5). Plating time is extended to 30 min, equivalent of depositing approx 12 skin depths of copper on the inner waveguide walls; to account for plate oxidation or abrasion during post-plate treatment. Once electroplated the waveguide is treated with Autosol® Metal Polish applied with a soft brush to reduce surface roughness. Subsequently, the waveguide is rinsed with ethanol and dried with helium gas.

| Table 5.5: Skin depth (\(\delta = \sqrt{2/\omega\mu_0\mu_r\sigma}\)) of microwaves in stainless-steel and copper waveguides. |
|---|---|---|
| 94 GHz | 188 GHz | 282 GHz |
| Stainless-steel | 1363.0 nm | 964.0 nm | 787.1 nm |
| Copper | 215.5 nm | 152.4 nm | 124.4 nm |
Table 5.6: 8 step process to electroplate 820 mm stainless-steel ($r = 2.08$ mm) waveguide.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>NaOH ($aq$)</td>
<td>66.5 g/L</td>
<td>H$_2$O ($l$)</td>
<td>25°C</td>
<td>CuCN ($aq$)</td>
<td>57 g/L</td>
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<tr>
<td>Na$_2$SiO$_3$ ($aq$)</td>
<td>25.5 g/L</td>
<td>Bath temperature</td>
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<td>NaCN$_2$ ($aq$)</td>
<td>94 g/L</td>
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<tr>
<td>Bath temperature</td>
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<td>25°C</td>
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<td>Voltage</td>
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<td>Current</td>
<td>7.5 A</td>
<td>Voltage</td>
<td>1.10 V</td>
<td>Voltage</td>
<td>1.25 V</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Current</td>
<td>1.5 A</td>
<td>Current</td>
<td>300 mA</td>
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<td></td>
</tr>
</tbody>
</table>
5.3 Reduction of ohmic losses via electroplating

Verification via bench measurements

The copper plating is verified on the bench using the setup depicted in Figure 5.5. Two WR10, WR05 or WR03 rectangular to circular transitions (attenuation of 0.23±0.02, 0.27±0.03 and 0.49±0.04 dB each corresponding to 94, 188 and 282 GHz, respectively) couple the waveguide to the source (or multiplier) and power meter (Erickson PM5, Virginia Diodes Inc., VA, USA). A quick connect (GuideLock®, Quantum Microwave, MA, USA) assists in coupling the waveguide’s modified UG387 flange to the transition flange to mitigate cocking or misalignment. The attenuation of five waveguides before and after electroplating is illustrated in Figure 5.6. The mean observed reduction in attenuation was 2.55±1.03, 2.54±0.48 and 3.38±0.22 dB at 94, 188 and 282 GHz, respectively. Ultimately, the waveguide installed in the dDNP probe reduced attenuation by 3.25, 3.17 and 3.77 dB across the bandwidth.

The higher electric conductivity of copper, lower cost and efficient plating conditions promoted its use over gold (σ_{Au}=4.1x10^7) as a plating metal. Often gold is favoured for plating in electrical or chemical applications due to its superior resistance to corrosion. As such, waveguide attenuation and plate degradation were monitored across a period of 12 months after plating. Waveguide attenuation throughout the duration experienced no change, and the copper layer remained smooth and shiny (although no longer bright pink) while stored at room temperature in approx. 25 – 30% humidity. Furthermore, the installed waveguide performance remained consistent for at least 6 months of DNP-NMR testing, while experiencing thermal cycling and water condensation (on the outside) caused by probe withdrawal from the VTI. Waveguide bench measurements yield approx. 0.5 dB higher attenuation than theoretically calculated. This is due to misalignment in the measuring apparatus as well as resilient surface roughness.

Figure 5.5: Block diagram of waveguide bench measurement setup. Microwave source based on YIG oscillator couples to doubler or tripler to operate at 188 or 282 GHz, respectively. Transitions converts the propagation mode and couple to the waveguide to the source and power meter.
Influence of microwave delivery on the DNP process

**Figure 5.6:** Theoretical microwave attenuation in stainless-steel (−) and copper (−−) circular waveguides (TE11, r = 2.08 mm, ρ′11 = 1.841, σSS = 1.45 × 10^6 S/m and σCu = 5.8 × 10^7 S/m) including bench measured stainless-steel and copper plated waveguides. Attenuation of copper plated waveguide used in further experimentation indicated by ■.

### 5.4 Refined microwave scattering in an overmoded cavity

The sample measures several wavelengths in dimension and is indirectly irradiated inside the cavity. Attempting to achieve a single mode resonance at the frequency of interest is unfeasible. However, engineering the conditions to support a standing wave is realizable. A cylindrical cavity design with 4 brass rods extruding from the top and bottom has been demonstrated in [52, 127]. The structure supports a standing wave at the 25 µL sample location. The microwaves are delivered from the sample side via the waveguide and a 45° chamfer. Although comparison with and without the rods was not investigated, simulated B-field distribution illustrates a standing wave across the sample volume, with an intensity comparable with that from inside the waveguide.

Another method of creating a standing wave is with a Fabry-Perot resonator. Prior improvements observed in MAS probes [128, 129] has led to the development of a similar design in a dDNP cavity but for a 100 µL sample [130]. A brass 45° chamfer reflects microwaves towards an NMR coil and sample cup. A concave brass chamfer placed behind the sam-
5.4 Refined microwave scattering in an overmoded cavity

A chamfer reflects incident microwaves to the sample. Similarly, a reciprocal concave chamfer is placed behind the brass 45° chamfer to focus reflections onto the sample. Simulated H-field distributions show a standing wave across the sample volume with a field intensity approx. twice that observed inside the waveguide. Once fabricated and experimentally verified using DNP-NMR, the Fabry-Perot resonator reduced the samples build up time constant by approx. 50% suggesting a definitive increase in H-field intensity.

Based on improvements achieved by the previous examples, the dDNP probe cavity features a chamfer and reflector, designed using the EM simulation software, CST Microwave Studio (Dassault Systèmes, France). The mesh cell size resolution is set to \( \lambda/12 \) and \( \lambda/24 \) within the chamfer, reflector, and sample regions to improve simulation accuracy. The simulation was performed using a time domain solver at a single frequency for microwave H-field components (188 GHz) and RF B\(_1\)-field components (71.8 MHz). All fields are captured across the coil center (cut planes \( x = 0 \) and \( z = 18 \)).

**Microwave chamfer**

To avoid perturbing the sample coil homogeneity, the waveguide outlet is restricted from extruding into the cavity. As a result, microwaves scatter upon entry of the cavity leading to a reduced field intensity in the sample region. Fortunately, the sample is encompassed by the Alderman-Grant coil that can be exploited to confine the microwaves in a smaller volume than the cavity. To do so, a chamfer reflects incident microwaves into the 87° coil opening. EM simulations determined an optimum angle of 75° is required to achieve the desired goal. The chamfer was machined from brass and soldered onto the upper cavity flange. It measures 11.7±0.1 mm high and extrudes by 5.0±0.1 mm towards the sample coil (Figure 5.7a–b).

**Segmented reflector**

Incident microwaves propagate through the coil opening and sample volume. Some of the microwave power reflects due to change in material properties between the helium bath and sample but the majority travel towards the opposing coil opening and back into the cavity. Reflecting the waves at the second coil opening would confine microwaves within the coil volume and further increase the field intensity. Placing a conductive reflector near the coil will perturb its homogeneity, however, segmentation mitigates this distortion. The cut-off wavelength for a rectangular aperture (segment) is found by \( \lambda_c = 2a \), where \( a \) = longest aperture dimension. The reflector is fabricated on a 0.127 mm Rogers RO3003
laminate (Rogers Corporation, AZ, USA) with a dielectric constant $\varepsilon_r = 3.00$ and single 0.35 $\mu$m copper cladding.

A honeycomb geometry etched on the laminate minimizes the formation of large eddy currents. The hexagonal geometry provides an interlocking pattern without sharp edges, that typically lead to higher localized current densities. The reflector is installed between the coil former and coil, with its dimensions depicted in Figure 5.7c. The segmented conductor covers the coil opening.

The Q-factor of a locally tuned Alderman-Grant coil is measured on the bench while employing a variety of reflector geometries at 180 MHz. Results listed in Table 5.7 support the need for segmentation as well as the effectiveness of the honeycomb pattern.

Table 5.7: Measured Q-factor of locally-tuned Alderman-Grant coil at 180 MHz while employing several reflector types.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Q</th>
</tr>
</thead>
<tbody>
<tr>
<td>No reflector</td>
<td>355</td>
</tr>
<tr>
<td>Segmented reflector</td>
<td>342</td>
</tr>
<tr>
<td>Uniform reflector (unsegmented)</td>
<td>126</td>
</tr>
<tr>
<td>Blank reflector (dielectric)</td>
<td>352</td>
</tr>
</tbody>
</table>
Simulated microwave and RF field distributions

The sample volume in the EM simulation was expanded to 1 cm³ (spherical volume) to adapt the solution to larger samples sizes. Electric sample properties are adopted from [131], where the authors report $\varepsilon_r = 3.5 \pm 0.1$ and $\tan \delta = 0.005 \pm 0.005$ at 140 GHz for a 1 M $^{13}$C-urea in a volumetric ratio 6:3:1 d$_8$-glycerol, D$_2$O and H$_2$O with 10 mM TOTAPOL at 77 K. These values are further supported by [132] where the dielectric properties of glycerol, propylene glycol, ethylene glycol and dimethyl sulphoxide are investigated between 193-293 K at 2.02 GHz. It can be concluded that $\varepsilon_r = 2 - 4$, independent of frequency at temperatures <193 K.

Simulated time-averaged H-field distributions across the cavity isocentre are shown in Figure 5.8. The field intensity is normalized to a maximum intensity located in the waveguide. The chamfer directs the microwaves to the sample via the Alderman-Grant opening. It could be noted, less than -20 dB of the incident microwave power scatters to the cavity walls or around the coil opening. The higher permittivity of the PTFE coil former and sample sphere causes resulting higher microwave field intensities inside their respective volumes. Addition of the chamfer and reflector raises the average H-field integrated across the spherical sample volume by a factor of 2.85 (corresponding to a 9.1 dB increase in source power). H-field distributions employing other cavity configurations and reflector types are illustrated in Appendix A.1.

Simulated $B_1$-fields across the sample coil are depicted in Figure 5.9. The region encompassing a 95% DSV homogeneity shrinks from approx. 10 mm to 8 mm when employing a segmented reflector. The chamfer location and geometry does not perturb the coil homogeneity. Additional $B_1$-field distributions employing other cavity configurations and reflector types are illustrated in Appendix A.2.
Figure 5.8: Simulated time averaged H-field at 188 GHz. Field normalized to maximum field intensity inside the waveguide. Upper row figures refer to the cross-section at $x = 0$, with the bottom row at $z = 18$. (a) & (b) illustration of augmented cavity, (b) & (d) time averaged H-field in a cavity, (e) & (f) time averaged H-field in an augmented cavity. Arrow indicating the direction of propagation of reflected waves.
Figure 5.9: Simulated $B_1$-field at 71.8 MHz across coil isocentre for cavity (a) without and (b) with augmentation. (c) 1D $B_1$-field distribution across the cut plane, dotted line signifies 95% field homogeneity.
5.5 Verification of microwave delivery via DNP-NMR

Microwave delivery is investigated via DNP-NMR using stainless-steel (both with and without an augmented cavity) and copper plated waveguides (with augmented cavity). $^{13}$C nuclear polarization is measured every 60 s for 75 min using a low flip angle pulse ($2.5^\circ$). Experiments are repeated at least three times, for source power levels from 5-55 mW in 10 mW increments. Additional measurements at 1 and 2.5 mW are acquired when verifying the copper plated waveguide. Sample space temperature and cryostat pressure values are regulated to $1.20\pm 0.01 \text{ K}$ and $0.8\pm 0.05 \text{ mbar}$ at the start of every experiment. The irradiation process is evaluated using 2 unique samples:

1. 50 $\mu$L solution of 14 M $^{[1-13]}\text{C}$pyruvic acid with 30 mM trityl (AH111501).

2. 100 $\mu$L solution of 4.5 M $^{[1-13]}\text{C}$urea dissolved in glycerol-d$_8$ and D$_2$O (50:50 v/v) with 40 mM TEMPOL.

$^{13}$C polarization and build-up time constant for 50 $\mu$L 14 M $^{[1-13]}\text{C}$pyruvic acid with 30 mM trityl are illustrated in Figure 5.10 at varying powers levels. All DNP probe configurations achieved approx. 65% maximum polarization, requiring at least 2.5 mW with a copper waveguide, 5 mW using a stainless-steel waveguide with an augmented cavity and 15 mW when exclusively employing a stainless-steel waveguide. Increasing microwave power beyond 25 mW causes up to 35% relative degradation in nuclear polarization when using a copper plated waveguide.

Similarly, up to 10% reduction is observed when using a stainless-steel waveguide with an augmented cavity for microwave powers exceeding 45 mW. Although, no observable degradation occurs when exclusively using a stainless-steel waveguide. The build-up time reduces with increasing power levels following an inverse relationship. At power levels with reported polarization loss, build-up time constants reduce linearly due to heating caused by microwave irradiation.

Neat $^{[1-13]}\text{C}$pyruvic acid doped with a trityl radical is a well-established, efficient sample for dDNP at the traditional 3.35 T field strength, as well at higher fields 4.6–7 T [29, 31, 133, 134]. This behavior is primarily due to trityl’s narrow ESR line spectrum compared to nitroxyl radicals (e.g. TEMPOL). The enhancement profile in Figure 5.10a shows that low powers only partially saturate the electron transition leading to reduced nuclear polarization [40]. Nonetheless, all microwave configurations eventually result in maximum achievable polarization but at slightly increased power level. The higher microwave field density across the sample volume allows for full saturation and higher polarization. Beyond this point, higher power levels contribute more towards heating the sample. The
effect is most prevalent when irradiating with maximum power (55 mW) using a copper plated waveguide, in which the sample space temperature and VTI pressure promptly rise by $0.12 \pm 0.01$ K and $0.55 \pm 0.05$ mbar to $1.32 \pm 0.01$ K and $1.35 \pm 0.05$ mbar, respectively. In such a regime, relaxation times are shortened causing less efficient DNP and lower nuclear polarization. Moreover, heating the sample also yields faster build-up times due to accelerated relaxation processes at a higher temperature (see Figure 5.10b). Observing the enhancement profile of all microwave configurations, it is evident that optimum irradiation power is inversely proportional to the microwave field density across the sample.

DNP measurements for 100 $\mu$L 4.5 M $[1-^{13}$C] urea in glycerol-d$_8$ and D$_2$O (50:50 v/v) with 40 mM TEMPOL are illustrated in Figure 5.11 for varying power levels. All microwave configurations achieve approx. 28 ± 5% maximum polarization at different power levels. In this case, 5 mW with a copper waveguide and 10 mW using a stainless-steel waveguide regardless of cavity augmentation. Increasing microwave power causes up to 5% reduction in nuclear polarization when using a copper plated waveguide. Build-up time constants decrease following a power law with respect to irradiated power levels. Inclusion of an augmented cavity leads to approx. 30% decrease in build-up time while the use of a copper plated waveguide results in approx. 45%.

TEMPOL’s ESR line width is approx. 5–6 times wider than trityl. Low power levels partially saturate the electron transitions resulting in sub-optimal polarization as illustrated in Figure 5.11a. Increased power levels remedy this limitation for all microwave configurations. However, the effect of heating at higher power levels is suppressed for this sample. At maximum power using a copper plated waveguide, 15% of maximum polarization is lost, a notable contrast to the 50% observed in the former sample. Build-up time constants in 5.11b converge and plateau for increased power levels, thus indicating less sensitivity to heating by microwave absorption (resonant by the electron spins in the sample and non-resonant in the metallic structures).

Overall this behavior is attributed to the two competing mechanisms of heating and electron Zeeman transition saturation. Increasing the power level causes greater saturation that in turn promotes spectral diffusion across the ESR line. Raising the temperature due to heating accelerates spin-lattice relaxation making saturation more difficult. All DNP experiments in this study featured continuous microwave irradiation at a constant power level. The main advantage of more delivered power is the ability to vary power levels in favour of higher build-up rates, thereby accelerating the polarization process.

The copper plated waveguide reduced resistive attenuation by 3.2 dB at 188 GHz. In turn, the average H-field across the sample volume is expected to increases by a factor
Figure 5.10: (a) Polarization and (b) build-up time constants for 50 µL 14 M [1-13C] pyruvic acid with 30 mM trityl (AH111501) irradiated using a copper plated waveguide, stainless-steel waveguide, and stainless-steel waveguide with chamfer and reflector.
Figure 5.11: (a) Polarization and (b) build-up time constants for 100 µL 4.5 M [1-13C] urea dissolved in d8-glycerol and D2O (50:50 v/v) with 40 mM TEMPO irradiated using a copper plated waveguide, stainless-steel waveguide, and stainless-steel waveguide with chamfer and reflector.
of approx. $\sqrt{2}$ which is in good agreement with the $\sim 45\%$ decrease in build-up time. As for the augmented cavity, EM simulations estimated a 2.85 factor increase in field density, which is the equivalent of boosting source power by 9.1 dB. However, the measured $\sim 30\%$ reduction in build-up time, instead suggests a 2.3 dB equivalent boost in source power. Difference between values can be attributed to unaccounted variation between the two cavity models, real and simulated. Physical changes due to component misalignment can result in a greater field density across the sample volume without cavity augmentation or lower field density than estimated with augmentation.

5.6 Optimized microwave irradiation

It is evident from Figures 5.10 and 5.11 that there is no microwave power limitations at 6.7 T, especially for an efficient sample such as neat pyruvic acid with trityl. In all conducted experiments microwave irradiation is continuous, however gain can be attained by considering an intermittent or variable power irradiation scheme. Illustrated in Figure 5.12a is the polarization build up for 100 $\mu$L 4.5 M $[1^{13}\text{C}]$urea dissolved in glycerol-d$_8$ and D$_2$O (50:50 v/v) with 40 mM TEMPOL, with varying power levels between 1-55 mW. The power levels can be varied to expedite nuclear polarization at the start of the process with high power levels, followed by a period of reduced power to achieve the highest possible polarization. An optimum power for a given time can be determined by optimizing a series of mono-exponential build-up curves, as depicted in Figure 5.12b. The technique has not been thoroughly explored and will be considered for future works, especially with the means to achieve higher microwave power densities across the sample volume (400 mW, 94 GHz microwave source, plated waveguide and augmented cavity).
5.7 Heat load estimation

Conducted heat flux across the dDNP probe is quantified by identifying helium consumption from the magnet vessel with and without microwave irradiation for an extended duration of time. Given the two measurements and known power from microwave irradiation, conducted heat flux by the dDNP probe can be determined. Experimentally, 5.15±0.5 L of liquid helium is consumed to cool the sample space to 1.4 K in a span of 24 h. For the same duration and average microwave irradiation of 27.1 mW via a copper plated waveguide 5.65±0.5 L are consumed. Given all irradiated microwave energy is converted into heat, the following ratio presents the total volume of boiled helium,

\[(P + Q)t / V \quad (5.4)\]

where \( V \) denotes consumed helium volume, \( t \) is experiment duration and \( P \) microwave power. Substituting measured data in Equation 5.4 yields,

\[(27.1 \text{ [mW]} + Q \text{ [mW]}) \quad (5.5)\]

\[86400[s]/5.85 \pm 0.5 [l] \quad (5.6)\]

\[(0 + Q \text{ [mW]}) \times 86400 [s]/5.15 \pm 0.5 [l] \quad (5.7)\]
Equating Equations 5.5 and 5.6 identifies the heat flux conducted by the dDNP probe,

\[(27.1 \times 10^{-3} + Q) 86400 = (0 + Q) 98413\]  

\[Q = 195 \pm 20\ \text{mW} \]  

The experimentally equated heat load value is in good agreement to the theoretical value of 222.4 mW. Good agreement is obtained between the calculated and experimentally verified heat load values. Indeed, the computed thermal model could have incorporated other forms of heat transfer such as cooling from rising helium gas but not without significant numerical complexity. The demonstrated method is valuable for thermal budgeting during dDNP probe design, even when utilizing a simplified model.
Chapter 6

Low-cost DNP-NMR spectrometer

In this chapter, a compact two channel benchtop spectrometer is developed, suitable for use up to 450 MHz. This, in part, aids the deployment of a polarizer system without the need of a traditional full-rack spectrometer. Sensitivity tests indicate the bench spectrometer achieves 90% and 50% the SNR value of that from a dedicated full rack spectrometer for $^1$H and $^{13}$C spectra measured at 6.7 T.

Results and discussions are partially presented in the scientific journal article titled ‘Compact, low-cost NMR spectrometer and probe for dissolution DNP’ [76].

6.1 State of the art

Monitoring polarization build-up is crucial for verifying DNP efficiency. Polarizers are often equipped with a low-cost bench NMR spectrometer or rack based a RF module, as hyperpolarised solid-state samples have an enhanced SNR and broad spectral linewidths. Nevertheless, their limited capabilities (e.g. low frequency, single channel, etc.) do not allow for more advanced NMR pulse sequences in the solid-state (e.g. cross polarization) nor monitor high gamma nuclei (e.g. $^1$H) at higher magnetic fields ($\geq 3.35$ T). Traditionally, dedicated full-rack spectrometers fulfill the need for high-resolution spectroscopy in high-field NMR magnets or MRI scanners. Their improved capabilities handle rapidly decaying hyperpolarized liquid-state signals and narrow line spectra with ease. Use of a dedicated spectrometer would be an ineffective solution to our initial problem due to cost and space. Moreover, some manufacturer features (e.g., automatic TM control, NMR tube spin control, temperature regulation) are not required by a dDNP polarizer. Consequently, the quest to develop a low-cost compact NMR spectrometer for high-field spectroscopy begins.

Two driving trends dictated the development of NMR spectrometers in recent years. Firstly, the brute-force pursuit for greater NMR sensitivity and increasingly higher field magnets [135] has led to the development of high-frequency dedicated rack spectrometers. NMR operators certainly enjoy the advantages associated with high-field spectroscopy. However, initial spatial and financial investments in deploying such magnets marginalize spectrome-
Low-cost DNP-NMR spectrometer costs, thereby making their adoption a matter of convenience (usually a single manufacturer supplies, installs, and maintains the magnet and spectrometer). Secondly, the need for offsite experimentation has resulted in compact but low-frequency benchtop spectrometers, due to a paired permanent magnet [136].

Spectrometer manufacturers and developers

The two diverging trends have slowed development of compact spectrometers capable of serving high-field NMR applications at frequencies of hundreds of MHz. Fortunately, the interest in dDNP and the aging of NMR detection equipment has revitalized the development of compact spectrometers, suitable for high-fields. Although choices remain scarce, prominent candidates are discussed below in order of release date to the public:

**Kea**² (Magritek, Wellington, New Zealand): First developed by Robin Dykstra as part of his Ph.D. studies at Massey University in 2006 and commercialized by Magritek Ltd (New Zealand) as ‘Kea’ [137]. The compact Kea² benchtop spectrometer (36×23×15 cm) followed shortly after and offers one receiver and two transmitter channels operating up to 100, or 400 MHz with the extended range model (discontinued in 2018). Spectrometer subsystems are modularized and assembled into a small rack which constitutes the chassis of the instrument. A proprietary software package called Prospa controls the spectrometer via a USB interface.

**OPENCORE NMR 2** (Kazuyuki Takeda, Japan): Homemade spectrometer developed at Kyoto University in 2007 bearing the name OPENCORE NMR [138, 139]. An electronically improved iteration was introduced in 2016, OPENCORE NMR 2. Spectrometer development has been an open hardware project since its inception, meaning all circuit design files are readily available to the public for free to replicate. The spectrometer offers three transmitter and one receiver channels operating up to 400 MHz. Higher operating frequencies can be achieved by modifying the transmitter mixer and sampling procedure [139]. An open source software called opencoreNMR controls the spectrometer via a USB interface. The OPENCORE NMR 2 spectrometer has a proven record as a compact spectrometer for a 3.35 T polarizer system [52] and is widely adopted in its country of origin Japan for a myriad of applications [140–142].

**Scout** (Tecmag Inc, TX, USA): Commercial benchtop spectrometer released in 2011. Its compact form factor (33×18×33 cm) offers one receiver and one transmitter (expandable to two) channels operating up to 300 MHz. A proprietary software package called TNMR controls the spectrometer via a USB interface. The receiver boasts a specified recovery time of < 1 μs, granting operators superior capabilities for solid-state spectroscopy.
Pulse (RS\textsuperscript{2}D, Mundolsheim, France): Latest commercial compact spectrometer (46x50x52 cm) introduced in 2018 and designed to replace legacy high-resolution spectrometers. The spectrometer offers two transmitter and two receiver channels operating between 200–600 MHz and controlled via a proprietary software package called SPINit. Modular subsystems interface together to form the final product.

**Spectrometer architecture**

All spectrometers adopt a comparable architecture, typically consisting of a host computer interfaced with an onboard digital signal processor (DSP) and/or field programmable gate array (FPGA) logic, representing the system core. The core is responsible for synchronizing and controlling subsystems as well as data acquisition and processing; this includes generating all necessary signals and processing and storing acquired NMR data.

A digital transceiver interfaces the exclusively digital core with the analogue RF front end and consists of a transmitter and receiver. Both subsystems rely on the principles of heterodyning to up or down convert signals with the use of mixers and multipliers. Although there are several ways of designing a transceiver, modern compact spectrometers utilize an FPGA and external direct digital synthesizers (DDS) to execute many of the required tasks.

In the transmitter (Figure 6.1), the DDS generates two in-phase signals at frequencies $f \pm x$ and $x$ (where $x<f$ and $f$ is the desired frequency). The product of mixing the signals are two frequencies $f$ and $f \pm 2x$. Subsequently, a low pass filter (LPF) rejects the $f \pm 2x$ image, and the desired signal is pulse-shaped using an amplitude modulator (AM). It may seem redundant to generate two frequency neighboring signals to $f$ than directly generating the one desired. However, mixing allows the transmitter to generate a range of frequencies and phases when multiplexing several DSS outputs. Furthermore, higher frequencies can be achieved than capable with a single DDS when cascading mixers [143].

![Diagram of transmitter architecture](image)

**Figure 6.1:** General transmitter architecture in a digital transceiver consisting of at least two DDS, mixer, filter and amplitude modulator.
The receiver (Figure 6.2) processes the NMR signal at frequency $f$ and ultimately outputs a set of digitized baseband quadrature signals. The received RF signal mixes with a frequency $f + x$ to obtain a down-converted signal at frequency $x$. A high-speed analogue-to-digital converter (ADC) digitizes the signal and couples the output into a quadrature demodulator to obtain baseband in-phase and quadrature signal components. An LPF reduces the baseband bandwidth by rejecting higher frequency components. The baseband bandwidth can be further reduced by decreasing the ADC sample rate for down-converted $x$ frequency signal.

![Diagram](image)

**Figure 6.2:** General receiver architecture in a digital transceiver. The receiver begins with a local oscillator and mixer to down-convert incoming RF signals. A high-speed ADC converts the signal and couples into a quadrature demodulator for in-phase and quadrature component separation. An anti-aliasing low pass filter reduces channel bandwidth.

The digital transceiver is only capable of generating and processing signals within a narrow amplitude range. The RF front end (Figure 6.3) remedies this limitation and consists of an RF high power amplifier (HPA) and a low noise amplifier (LNA), to condition the signal levels between the probe and transceiver. A transmit/receive (T/R) switch diplexes between the two respective channels using active PIN diodes, anti-parallel diodes and/or a $\lambda/4$ transmission lines (depending on transmitter pulse power and tolerable receiver deadtime). Unlike the system core or digital transceiver, the RF front end is application specific and significantly constrains a spectrometer’s operational bandwidth.
6.2 Requirements

Follows is a list of performance criteria based on current spectrometers capabilities:

1. Operational bandwidth is sufficient for multiple $B_0$ field strengths up to 10.1 T.
2. Two independent channels present.
3. Advanced NMR pulse sequences enabled (e.g. adiabatic and arbitrary shaped pulses).
4. High power handling for low duty cycle pulsing.
5. Capable of handling solid-state samples (i.e. short receiver deadtime <2 $\mu$s).
6. Compact form factor (benchtop).
7. Low receiver noise figure and sufficient gain to achieve competitive SNR to dedicated spectrometers.

Currently, all candidate spectrometers partially satisfy the performance criteria list. The faster and easier way to achieve the desired spectrometer is to supplement an existing product to meet performance criteria. Ultimately, the Kea² spectrometer is selected due to its affordable modular solution and well-documented architecture. A duplexer module designed for high-field solid-state spectroscopy was developed and integrated into the spectrometer.
6.3 Kea² spectrometer

Specifications

The Kea² spectrometer is pre-equipped by the manufacturer with a DSP and digital transceiver. Standard Eurocard sized PCBs host module electronics and connect via a common spectrometer backplane. An external HPA (TwinPulse 400, Tomco Technologies, Australia) enables high power pulsing and offers two output channels, up to 100 W for 200–650 MHz and up to 300 W for 5–300 MHz. Both transmitter channels can produce 14-bit sinusoidal waveforms up to 400 MHz with a maximum output power of 0 dBm into a 50 Ω load. However, the onboard synthesizer electronics can produce higher frequencies but at lower signal purity. The digital receiver channel comprises a 100 MS/s, 16-bit ADC with a 100-dB dynamic range.

Transmitter characterization

A digital oscilloscope (RTO 1044, Rhode & Schwarz, Germany) connected to the transceiver characterizes the RF output. A 20 µs pulse terminates into a 50 Ω port while observing the power spectrum facilitated by the oscilloscope FFT function. The output frequency and power are swept using the Prospa and recorded in Figure 6.4. The transmitter satisfies the requested output level within a 1 dB variation up to 400 MHz. Higher frequencies are attainable but result in lower power levels and a higher number of spurious peaks surrounding the frequency of interest. Spurs occur as a product of mixing during heterodyning as demonstrated by the captured data in Table 6.1.
Figure 6.4: Measured Kea² transceiver output for varying requested power and frequency.

Table 6.1: Measured spurious peaks (≥-50 dBc) frequency and magnitude for 0 dBm requested power output.

<table>
<thead>
<tr>
<th>Output frequency (MHz)</th>
<th>Spur frequency (MHz)</th>
<th>Spur magnitude (dBc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>100</td>
<td>-41.0</td>
</tr>
<tr>
<td>100</td>
<td>200</td>
<td>-41.6</td>
</tr>
<tr>
<td>150</td>
<td>300</td>
<td>-36.2</td>
</tr>
<tr>
<td>200</td>
<td>400</td>
<td>-33.1</td>
</tr>
<tr>
<td>250</td>
<td>150</td>
<td>-50.6</td>
</tr>
<tr>
<td></td>
<td>350</td>
<td>-50.0</td>
</tr>
<tr>
<td>300</td>
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<td>-33.9</td>
</tr>
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<td>400</td>
<td>-27.8</td>
</tr>
<tr>
<td>350</td>
<td>250</td>
<td>-36.6</td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>-16.9</td>
</tr>
<tr>
<td>400</td>
<td>200</td>
<td>-19.5</td>
</tr>
</tbody>
</table>
The HPA output was also characterized with the addition of a 50 dB attenuator at the oscilloscope port to prevent overloading during pulsing. Measured power levels illustrated in Figure 6.5 indicate that both amplifier channels meet manufacturer specifications. Furthermore, HPA gain at 285.55 MHz on channel A and 71.8 MHz on channel B is illustrated in Figure 6.6. The HPA experiences compression at an input power of -6 and -3 dBm on channels A and B, respectively.

![Graph of HPA output across frequency bandwidth](image)

**Figure 6.5**: HPA (TwinPulse 400) output across frequency bandwidth for 50 dBm channel A (200–650 MHz) and 55 dBm channel B (5–300 MHz).

### Design of duplexer module

The developed duplexer consists of three independent components: the switch driver, T/R switch and LNA as illustrated in Figure 6.7. The final module measures 3 rack units (13.3 cm) by 21 height pitch units (10.7 cm).

**T/R switch driver**  The switch driver is responsible for sourcing the current required for the fast switching T/R mechanism and applying the required bias voltages as commanded by the DSP. A TTL signal from the DSP couples via the backplane and buffers by a 74HC240 inverting driver (U2) as illustrated in Figure 6.8. A -15 V rail provides the reverse bias voltage, while an LM340MP-5.0 (U1) regulates the 8 V rail to provide a 5 V forward bias voltage.
Figure 6.6: HPA (TwinPulse 400) gain to input power for 50 dBm channel A (200–650 MHz) and 55 dBm channel B (5-300 MHz). Channel A tested at 285.55 MHz while channel B tested at 71.8 MHz.

Voltage. In pulse mode, the P-channel MOSFET (Q1) source-drain conductivity is high when a low-level voltage is present at its gate, causing the bias node voltage to rise to 5 V. In acquisition mode, a high-level voltage from U2 buffers through the common-base transistor amplifier (Q3) and distributes across R6. A positive gate-source voltage causes N-channel MOSFET (Q2) source-drain conductivity to rise, causing the bias node voltage to fall to -15 V.

T/R switch PIN diodes D1, D2 and D3 (MA4P504-1072T, MACOM Technology Solutions, MA, USA) illustrated in Figure 6.9, facilitate switching between pulse and acquisition modes. An exchangeable λ/4 cable couples the probe port to the LNA to improve isolation during pulse mode. A 5 V forward bias voltage applied when pulsing causes all diodes to conduct, thereby isolating the LNA from the power amplifier and couples to the probe port. PIN diode conduction seizes during acquisition mode due to a -15 V reverse bias voltage. Consequently, coupling the probe port to the LNA input while isolating the power amplifier. The 39 Ω resistors limit bias currents coupled to the switch via 1.3 µH RF choke.
Figure 6.7: (a) Illustration of an integrated duplexer in Kea² spectrometer. The duplexer consists of two printed circuit boards (T/R switch and a switch driver circuit). (b) The T/R switch is enclosed by two aluminum shields to mitigate electromagnetic interference.

(RFC) inductors. In pulse mode all PIN diodes are forward biased and source 64 mA each, resulting in a series impedance of 0.5 Ω.

Transient diode voltages switching from acquisition and pulse mode are illustrated in Figure 6.10, as captured by an oscilloscope with a high impedance port. Transitioning from acquisition to pulse mode takes 690 ns, which is the time needed for the diode voltage to reach steady state forward bias conditions. The PIN diode I-regions are filled with charge proportional to the diode carrier lifetime. The reverse bias voltage expels this charge rapidly causing the resistance of the I-region to increase. The diode voltage overshoots by 0.6 V for 100 ns due to the rapid increase in current flow. Furthermore, PIN diodes are forward biased 2 µs before pulsing on the benchtop spectrometer.

Transitioning into acquisition mode, the reverse bias voltage expels charge carriers from the PIN diodes. The storage time takes 550 ns and causes a significant drop in diodes voltage. Afterwards, the voltage exponentially reduces further until steady state reverse bias is reached and the diodes cease to conduct. Overall, the total time required to switch into acquisition time is ~2400 ns.
Figure 6.8: Schematic of the T/R switch driver. U2 buffers TTL from the backplane to switching transistors Q1 & Q2 (via Q3). Capacitors C1-C12 are bypass capacitors. Resistors R4 & R6 ensure appropriate transistors biasing. The bias node voltage couples to T/R switch via RG316 coaxial cable. R1 and R5 prevent MOSFET oscillation.

Figure 6.9: Schematic of the T/R switch. Diodes D1-D3 in combination with a $\lambda/4$ cable provide isolation between the LNA input J6 and HPA J1. The source bias current is determined by resistors R2 & R3 and fed via RFC L1-L4. Anti-parallel diodes D4 reduce LNA saturation. C1, C3-5 are by-pass capacitors, while C2 and C6 are decoupling capacitors.
As the resistance rises the reverse current is limited, causing charge gradient diffusion to be the driving mechanism of depletion rather than the reverse bias voltage. For this reason, the PIN diode voltage requires approx. 3.5 times longer to reach steady state reverse bias. However, the duplexer enters acquisition mode much sooner as the PIN diode impedance rises to tens of Ohms once storage time has elapsed, which occurs in a fifth of the total settling time.

![Figure 6.10](image)

**Figure 6.10:** Transient bias voltage measured at node $V_{\text{bias}}$ as depicted by inset circuit. TTL signal initiates change between 5V and $-15\,\text{V}$. (a) Switching between acquisition to pulse takes 690 ns to reach steady-state voltage. (b) Switching between pulse to acquisition mode takes $\sim 2400\,\text{ns}$ of which $\sim 550\,\text{ns}$ are storage time (PIN diode discharging due to bias voltage as oppose to charge gradient diffusion).

Steady-state T/R switch scattering parameters are measured using a vector network analyzer (E5062A, Keysight Technologies, CA, USA). The insertion loss between the HPA and probe is $<0.66\,\text{dB}$, while isolation between the HPA and LNA is $>36\,\text{dB}$ as recorded in Figure 6.11. In acquisition mode, insertion loss between the probe and LNA is limited to $<0.87\,\text{dB}$. RFC inductors contribute much of the observed insertion loss between the HPA and probe for frequencies below 50 MHz. Pulses couples from the HPA to NMR circuit without concerns of damaging or saturating the LNA due to low insertion loss and high isolation between the HPA and LNA. Further isolation between the HPA and LNA is attainable by reducing parasitic inductance from the diode packaging. Insertion losses at lower frequencies decrease, by employing larger RFC inductors. Additional crossed diodes assist in reducing LNA saturation during pulsing. However, parasitic capacitance in the diode packaging increases insertion loss between the probe and LNA input at higher frequencies.
Figure 6.11: Scattering parameters between the HPA, LNA and probe (as depicted in inset circuit). Isolation between the HPA and LNA \((S_{31})\) as well as insertion loss between the HPA and probe \((S_{21})\) were measured during pulse mode \((V_{\text{bias}} = +5\text{V})\). Insertion loss between the probe and LNA \((S_{32})\) was measured during acquisition mode. The transmission line was replaced accordingly to resemble \(\lambda/4\) at the measured frequency (length was kept as short as practically possible).

**Low noise amplifier**  The duplexer employs an LNA (AU-2A-150, L3 Narda-MITEQ, NY, USA) that offers an average gain of 34.5 dB with a typical noise figure of 1.4 dB up to 500 MHz, as measured with a spectrum analyzer (E4440A, Keysight Technologies, CA, USA) employing a calibrated noise source (346B, Keysight Technologies, CA, USA). 15 V from the Kea\(^2\) backplane energizes the LNA which could handle a maximum continuous wave input of 13 dBm. Three pairs of crossed diodes (SMP1340-075LF, Skyworks Solutions, MA, USA) placed at the LNA input mitigate saturation and reduce receiver dead time.

**Spectrometer benchmark**

The Kea\(^2\) benchtop spectrometer performance is benchmarked against a dedicated high-resolution spectrometer (Direct Drive 600, Varian Inc, CA, USA) by acquiring \(^1\text{H}\) and \(^{13}\text{C}\) spectra on a hyperpolarized sample at 6.7 T and comparing the overall SNR. The sample used for this investigation is 100 \(\mu\text{L}\) 4.5 M \([1-{^{13}\text{C}}]\text{urea dissolved in 5:4:1 glycerol-}{_d}_8:\text{D}_2\text{O:}\text{H}_2\text{O (v:v)}\) 40 mM TEMPOL. Both spectrometers employ comparable RF frontends with the only exception being the duplexers. A spectrum analyzer (E4440A, Keysight Technologies,
CA, USA) employing a calibrated noise source (346B, Keysight Technologies, CA, USA) measured the duplexer gain and noise figure (Figure 6.12). The Direct Drive duplexer operates up to 300 MHz, hence the sharp reduction in gain at higher frequencies. Typically, an additional channel is available to handle higher frequencies. The benchtop duplexer provides a lower noise figure primarily due to the inherit LNA specifications. 

The receiver noise floors are characterized at 290 K for both spectrometers. As spectrometers only representing magnitude in arbitrary units (not the desired dBm for this measurement) a signal generator (SMC100A, Rhode & Schwarz, Germany) outputting a continuous wave at 285.55 and 71.8 MHz references spectral power values. Each measurement consists of 4096 data points captured across a 2 MHz bandwidth for two configurations. First, with the signal generator coupled to the receiver and second with the receiver input terminated with a 50 Ω load. The measurement concluded a noise floor of -108 dBm/Hz and -140 dBm/Hz for the Kea² and Direct Drive spectrometers, respectively.

![Figure 6.12: LNA (a) gain and (b) noise figure measurements in Kea² and high-resolution spectrometer. Both amplifiers isolated from hosting circuit and tested on the bench.](image)

The sample vial was cooled in a helium bath to 1.2 K and irradiated with microwaves for 10 minutes. Next two ¹H spectra are acquired using both the Kea² and DD spectrometers. The process is repeated for the acquisition of two ¹³C spectra after allowing 30 minutes of microwave irradiation. 2.4° and 1.3° excitation pulses were employed for acquiring ¹H and ¹³C spectra, respectively. Spectra consist of 4096 samples with a spectral width of 1 MHz on the benchtop and 1.25 MHz on the DD (receiver gain set to 0 dB). A line broadening of 3 kHz was applied to the captured spectra in post-processing.
Acquired hyperpolarized $^1$H and $^{13}$C spectra are shown in Figure 6.13, respectively. The ratio between the amplitude of the peak and the root-mean-square of a signal-free area from the spectrum defined SNR value. The Kea$^2$ records an SNR value of 1170 for $^1$H and 88 for $^{13}$C spectra, while the dedicated spectrometer obtained 1276 and 132 for the nuclei. Both spectrometers acquired spectra that have been oversampled and quantized via a 16-bit ADC, with both duplexers hosting PIN diodes with similar lifetimes biased with similar source currents and bias voltages. Albeit, the Direct Drive spectrometer achieved 10% and 50% higher SNR when measuring $^1$H and $^{13}$C spectra, respectively. Reasons for this difference stem from the inherent lower receiver noise floor of the dedicated spectrometer. The Kea$^2$ SNR can be improved with a second stage amplifier; however, the high receiver noise floor would limit the available dynamic range.
Chapter 7

Conclusion and future works

In this thesis, two double resonant dDNP probes are developed for solid-state DNP experiments and CP-DNP experiments. Microwave intensity across the sample volumes is doubled without increasing the static thermal load on the sample space nor compromising the RF coil homogeneity. Finally, a compact two-channel benchtop spectrometer is realized, suitable for high-field solid and liquid-state NMR spectroscopy.

Instrumentation

In Chapter 3, the realization of the DNP polarizer system and principles of its experimental operation were described. A dDNP probe has been realized, facilitating the ability to perform double resonance solid-state DNP experiments with dissolution capabilities. The design is optimized for minimum static heat load, thus allowing a sustained low sample space temperature and consequently higher DNP enhancement. The refined probe design complexity leads to lowered manufacturing and material costs. For the work herein, the design caters for a ∼900 mm long VTI with a base temperature of 1.2 K but may be adapted to any VTI length or base temperature; case in point, the variable field, cryogen-free, polarizer with its 400 mm long VTI. The theoretical conductive heat load is verified by a series of helium evaporation experiments, thereby permitting further thermal optimizations if required. Two 800 mm long probes were manufactured and operated reliably for dDNP purposes.

SSS are becoming more efficient due to improved semi-conductors. Here-in characterized and dissected are four SSS assemblies, including two multipliers to provide microwave irradiation at 94, 188 and 282 GHz (corresponding to $B_0 = 3.35, 6.7$ and 10.1T). Swapping or removing the multiplier swiftly permits changing the frequency. The need for temperature regulation is key to reproducibility and is incorporated into the design and latest source assembly featuring a 4 GHz tuning range around 94 GHz and 400 mW output. The base oscillator benefits from being a digital synthesizer which can adopt different modulation schemes and controlled directly from a personal computer.
Conclusion and future works

The pursuit for higher RF magnetic fields in a dDNP probe

In Chapter 4, a method for determining the sensitivity of a coil is outlined and verified with reasonable accuracy using a closed form approach and extends for both remote and local TM schemes. Techniques to identify the Q-factor of a resonant circuit are also discussed. Experimental and calculated measurements indicate FWHM of resonance is a non-coherent indicator of Q-factor when employing a remote TM scheme.

A dDNP probe capable of CP-DNP is developed. The double resonant, local TM is realized to minimize high voltages and the risk of arcing. The calibrated coil sensitivities are 2.8 and 7.7 kHz/√W, respectively for $^{13}$C and $^1$H. HHCP is achieved at $\nu_1=29$ kHz, yielding a 27% $^{13}$C polarization with a 12 min build-up time. That is twice the direct $^{13}$C polarization and 4.4 times faster.

Arc detection techniques are demonstrated, including the realization of a plexiglass vacuum chamber to allow visual arc detection and via reflected power as observed by an oscilloscope. Herein presented are multiple reflect power profiles relating to varying pulse lengths, power, and the surrounding environment. The probability of arcing is significantly reduced with the application of a PTFE based grease on high voltage circuit locations.

Influence of microwave delivery on the DNP process

In Chapter 5, it is demonstrated that a circular waveguide provides the best ratio between transmission attenuation and surface area (leading to thermal conduction). The microwave field intensity across the sample volume is increased via two different strategies. Instruments and methods for reliably electroplating stainless-steel waveguides are formulated and tested. Plated specimens reduced transmission losses by half and did not degrade in performance up to 12 months after plating. Moreover, the use of a plated waveguide did not compromise the low VTI base temperature. A mirror and segmented reflector inside the cavity, are designed, simulated, and tested to increase the field density across the sample without perturbing the RF coil homogeneity.

The two microwave configurations were verified using two samples employing a trityl and TEMPOL radical in DNP experiments. Use of a copper plated waveguide approx. doubled the delivered microwave power to the sample. While the inclusion of an augmented cavity resulted in approx. 2.3 dB increase in equivalent microwave power.
Two channel benchtop spectrometers for DNP-NMR

The pursuit of an autonomous polarizer hinge, in part, on the availability of an onboard spectrometer to monitor polarization build-up. In Chapter 6, a duplexer is developed to integrate into a benchtop spectrometer and extend its operational bandwidth up to 450 MHz. The bench spectrometer achieved 90% and 50% the SNR value of that from a dedicated full rack spectrometer for $^1$H and $^{13}$C spectra, respectively, measured at 6.7 T. The spectrometer could accommodate both solid and liquid-state spectroscopy including advanced pulse sequences for a significantly reduced cost and space.

Future works

Explored in this section are ideas and concepts that could expand the application of contributions discussed in this thesis.

Currently the primary limitation of simultaneously polarizing multiple samples in the cryogen-free polarizer is ‘cooling power’, (albeit, the current VTI bore is also very limited and will require major probe modifications to accommodate an extra sample). Pursuing a solution to this problem will yield great reward in an emerging trend towards cryogen-free polarizer systems.

The developed duplexer can be miniaturized by employing a surface mount LNA instead of a packaged component. Similarly, the $\lambda/4$ cable may be substituted for an LC lumped model, situated on-board the duplexer. By replacing lumped capacitors with varactor diodes, the lumped transmission line length can be electronically tuned by adjusting the biasing varactor voltage. The Kea$^2$ is equipped to accommodate an integrated 100 W amplifier, which could replace the external 19” rack HPA used in this thesis. Moreover, if the spectrometer is used exclusively for monitoring polarization (similar to the SPINlab polarizer), then a simple $< 15$ dB gain amplifier will suffice instead.

There is capacity to expedite the DNP process by considering intermittent or variable power irradiation schemes, especially with the discussed means of increasing the microwave density across the sample volume (400 mW, 94 GHz source, plated waveguide and augmented cavity). Another interesting prospect is to utilize the increase power levels for more advanced schemes like the integrated solid effect [144] nuclear orientation by electron spin locking [145].

Realizing a efficient CP-DNP lies in balancing between samples size, the choice of sequence and the ability to perform dissolution. Naturally, the latter is non-negotiable for this work leading to the evident problem of arcing in the low pressure helium atmosphere. One way
of mitigating arcing is by exploring methods of encapsulating the circuit with an insulating dielectric. The material can be molded to in the geometry of the circuit for a close fit. Furthermore the VTI atmosphere can be doped with sulfur hexafluoride which is known to be a proven arc quenching substance.
Appendix A

EM simulations

A.1 Average H-field distributions at 188 GHz across overmoded cavity with different configurations

EM simulations computed in CST Microwave Studio 2018 (Dassault Systèmes, France) using the time domain solver. The mesh cell size resolution is set to $\lambda/12$ and to $\lambda/24$ within the chamfer, reflector, and sample regions to improve simulation accuracy. The total mesh number approaches $\approx 60,000,000$ mesh cells and is computed in approx. 4–6 hours. A field monitor set to 188 GHz captures H-field components. An auto regressive filter is applied to avoid oscillations and artifacts in S-parameter measurements. The waveguide excitation port is configured to support propagation mode $TE_{11}$. Field distributions are then imported into MATLAB 2017 (MathWorks, MA, USA) for post processing.
Figure A.1: Simulated time averaged H-field at 188 GHz. H-field normalized to maximum field intensity in waveguide. Upper row cross-section at x=0 with bottom row at z=18. (a) & (b) Cavity without any modifications. (c) & (d) Cavity with chamfer. (e) & (f) Cavity with chamfer and uniform reflector. (g) & (h) Cavity with chamfer and segmented reflector. (i) & (j) Cavity with chamfer and blank reflector.
A.2 \textit{B}_1\text{-field distributions at 71.8 MHz across sample coil with different cavity configurations}

EM simulations computed in CST Microwave Studio 2018 (Dassault Systèmes, France) using the Time domain solver. The mesh cell size resolution is set to $\lambda/20$ and to $\lambda/25$ within the chamfer, reflector, and sample regions to improve simulation accuracy. The total mesh number approaches $\approx 200,000$ mesh cells and is computed in approx. 10–20 minutes. A field monitor set to 71.8 MHz captures the H-field components. Moreover, the field amplitude is normalized to 1 A flowing through the lumped element excitation port. Field distributions are consequently imported into MATLAB 2017 (MathWorks, MA, USA) for post processing.
Figure A.2: Simulated B-field at 71.8 MHz. Upper row cross-section at x = 0, with bottom row at z = 18. (a) & (b) Cavity without any modifications. (c) & (d) Cavity with chamfer. (e) & (f) Cavity with chamfer and uniform reflector. (g) & (h) Cavity with chamfer and segmented reflector. (i) & (j) Cavity with chamfer and blank reflector.
References


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