

ADVANCEMENTS IN MULTINUCLEAR MULTICHANNEL NMR AND MRI

A Dissertation

by

STEPHEN EDWIN OGIER

Submitted to the Office of Graduate and Professional Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

Chair of Committee,	Steven M. Wright
Committee Members,	Mary P. McDougall
	Christian Hilty
	Samuel Palermo
Head of Department,	Miroslav M. Begovic

December 2019

Major Subject: Electrical Engineering

Copyright 2019 Stephen Edwin Ogier

ABSTRACT

The introduction of receive arrays revolutionized ^1H MRI and *in vivo* NMR by increasing SNR and enabling accelerated imaging. All MRI scanners manufactured today are equipped to receive signals from ^1H array coils, but few support multi-channel reception for other nuclei. The extension of receive arrays to non- ^1H nuclei has proven difficult because of the lack of broadband array receivers. These nuclei often have low sensitivity and stand to benefit greatly from the increase in SNR arrays provide.

This dissertation presents a variety of technologies that have been developed to enable the development and use of X-nuclear and multi-nuclear arrays. Frequency conversion receiver front-ends provide a straightforward and cost-effective approach for adapting standard ^1H multi-channel array receivers for use with other nuclei. Two generations of frequency translation receiver front-ends have been developed that use active mixers to convert the received signal from a non- ^1H array to the ^1H frequency for reception by the host system receiver. This first-generation system has been demonstrated on 4.7T and 7T systems without any decrease in SNR as compared to the stock systems, and has been shown to be capable of accommodating ^1H decoupling. The second-generation receiver was developed to add the capability to simultaneously convert signals received from multiple nuclei as well as to streamline the setup and use of the translation system. Frequency translation has been shown to be able to convert ^1H -only multi-channel receivers for use with other nuclei with minimal degradation of SNR.

In addition, a standalone broadband system capable of simultaneous multi-nuclear imaging and spectroscopy at 1T and 4.7T has been developed. This system can either operate completely independently or interface with existing systems. The broadband system has been demonstrated with simultaneous imaging and spectroscopy of three nuclei.

This work allows existing multi-channel MRI receivers to be adapted to receive signals from nuclei other than hydrogen, allowing for the use of receive arrays for in vivo multi-nuclear NMR.

DEDICATION

“Let the favor of the Lord our God be upon us,
and establish the work of our hands upon us;
yes, establish the work of our hands!”

Psalm 90:17

ACKNOWLEDGEMENTS

I would first like to thank my committee chair, Dr. Wright, for his support and wisdom over the past several years. Without his experienced advice, none of this would have ever worked. Additionally, I wish to thank Dr. McDougall for her relentless enthusiasm and encouragement.

I am forever indebted to Dr. John Bosshard and Dr. Neal Hollingsworth, who have helped me to become a good engineer, and more importantly provided good council and stimulating conversation during the highs and lows of research.

Thanks to Matthew Wilcox for being the other half of the translation project and accompanying me on many, many trips to Dallas.

I would like to thank our collaborators at University of Texas-Southwestern Medical center, specifically Dr. Sergey Cheshkov, Dr. Ivan E. Dimitrov, and Dr. Craig Malloy for their generosity with magnet time and trusting me with their 7T system.

I would also like to thank my parents for their support and encouragement and for never questioning why I decided to get a PhD.

Finally, I'd like to thank my wife, Kathrine, for her incredible patience and unwavering support.

CONTRIBUTORS AND FUNDING SOURCES

Contributors

This work was supervised by a dissertation committee consisting of Dr. Steven Wright [advisor] and Dr. Samuel Palermo of the Department of Electrical and Computer Engineering, Dr. Mary McDougall of the Department of Biomedical Engineering, and Dr. Christian Hilty of the Department of Chemistry.

I would like to acknowledge the assistance of Sandeep Ganji of Philips Healthcare in loading and reformatting the 7 T spectroscopic data.

I was assisted in development of the multinuclear frequency translation system in Chapter 4 by Dr. Neal Hollingsworth.

Dr. John Bosshard was instrumental in the development of the broadband system described in Chapter 5, and substantial contributions were also made by Dr. Neal Hollingsworth, Scott Blaczyk, and Brian Bass. The triple-tuned coil was developed principally by Hongli Dong, and the triple-nucleus receiver front-end was developed by Dr. Chung-Huan “Tim” Huang.

All other work conducted for the dissertation was completed by the student independently.

Funding Sources

Graduate study was supported by a Graduate Merit Fellowship from Texas A&M University.

This work was also made possible in part by the National Institutes of Health under Grant Number R21HL120064 and the Cancer Prevention Research Institute of Texas under Grant Number RP150456. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the sponsors.

NOMENCLATURE

^1H	Hydrogen, Protium isotope, commonly referred to as Proton
^2H	Hydrogen, Deuterium isotope, commonly referred to as Deuterium
^{13}C	Carbon-13
^{15}N	Nitrogen-15
^{23}Na	Sodium-23
^{31}P	Phosphorus-31
B_0	Static Magnetic Field
B_1	Transmit RF Magnetic Field
B_2	Decoupling RF Magnetic Field
CSV	Comma-Separated Value
DDS	Direct Digital Synthesis
DNP	Dynamic Nuclear Polarization
FID	Free Induction Decay
FOV	Field-of-View
FPGA	Field-Programmable Gate Array
FTW	Frequency Tuning Word
I ² C	Inter-Integrated Circuit
IF	Intermediate Frequency
LNA	Low Noise Amplifier
FTU	Frequency Translation Unit

LO	Local Oscillator
MRSL	Magnetic Resonance Systems Lab
MRI	Magnetic Resonance Imaging
NMR	Nuclear Magnetic Resonance
PHIP	Parahydrogen-Induced Polarization
PLL	Phase-Locked Loop
ppm	Parts-per-Million
RF	Radiofrequency
RFPA	Radiofrequency Power Amplifier
RMS	Root Mean Square
SABRE	Signal Amplification by Reversible Exchange
SAW	Surface Acoustic Wave
SDR	Software Defined Radio
SFDR	Spurious-Free Dynamic Range
SNR	Signal-to-Noise Ratio
SPDT	Single-Pole Double-Throw
SPI	Serial Peripheral Interface
TCXO	Temperature-Controlled Crystal Oscillator
TTL	Transistor-Transistor Logic
VGA	Variable-Gain Amplifier

TABLE OF CONTENTS

	Page
ABSTRACT	ii
DEDICATION	iv
ACKNOWLEDGEMENTS	v
CONTRIBUTORS AND FUNDING SOURCES.....	vi
NOMENCLATURE.....	viii
TABLE OF CONTENTS	x
LIST OF FIGURES.....	xiv
LIST OF TABLES	xvii
1. INTRODUCTION.....	1
1.1. Nuclear Magnetic Resonance Spectroscopy	1
1.2. Parallel MRI.....	2
1.3. Dissertation Organization.....	4
1.4. Dissertation Style	5
2. BACKGROUND AND MOTIVATION	6
2.1. Nuclear Magnetic Resonance.....	6
2.1.1. Fundamentals of NMR	6
2.1.2. Hyperpolarization.....	8
2.1.3. ¹ H Decoupling	10
2.1.4. NMR Imaging.....	11
2.2. Radiofrequency Mixers	11
2.2.1. Theoretical Basis	11
2.2.2. Spurious Signals	12
2.2.3. Phase in RF Mixers	12
2.2.4. Passive and Active Mixers	13
2.2.5. Importance of Phase Coherence	14
2.3. Direct Digital Synthesis	15
2.4. Magnetic Resonance Systems	16

E-1. phasing.m.....	136
E-2. lb.m.....	136
E-3. snr.m.....	137

LIST OF FIGURES

	Page
Figure 2.1: Doubly-balanced diode mixer.....	13
Figure 2.2: Block diagram of a basic DDS synthesizer.	15
Figure 2.3: Overview of a MRI system.....	16
Figure 3.1: Two approaches to frequency translation.	28
Figure 3.2: Equipment room frequency translation rack.....	32
Figure 3.3: 16-channel frequency translation system.....	32
Figure 3.4: Four-channel frequency translation board. RF and LO inputs are on the bottom edge, and IF outputs are on the top edge.....	35
Figure 3.5: Spectral diagram of mixing ^1H -decoupled signal off-resonance.	39
Figure 3.6: Translator performance for ^1H decoupled ^{13}C at 4.7T.....	45
Figure 3.7: Translator performance comparison for ^{13}C at 7 T.....	46
Figure 3.8: Spectra from individual ^{13}C array elements at 7 T.	47
Figure 3.9: Comparison of data received by volume coil with data from 16-element receive arrays.	48
Figure 3.10: Demonstration of channel-to-channel isolation at 7T.	49
Figure 4.1: Multinuclear translation system block diagram.....	57
Figure 4.2: Manual Translator Control GUI. Settings shown are a typical configuration for 16 ^{13}C channels at 4.7T.	59
Figure 4.3: Control unit, containing, from top to bottom, empty slot for transmit translation unit, translator control unit, and power supply unit.	62
Figure 4.4: Interior of control unit.....	63
Figure 4.5: Exterior of multinuclear frequency translation unit.....	68
Figure 4.6: Interior of multinuclear frequency translation unit.....	68

Figure 4.7: Block diagram of 4-channel translation board.....	73
Figure 4.8: 4-Channel Frequency Translation board for Multinuclear Translation System.....	74
Figure 4.9: Spreadsheet calculator for optimizing DDS clock frequency.....	78
Figure 4.10: Test inputs to multinuclear translation system.	82
Figure 4.11: Test outputs of multinuclear translation system.	83
Figure 4.12: Reference isopropanol spectra.....	85
Figure 4.13: Translated isopropanol spectra.	86
Figure 4.14: SNR versus number of averages for stock Varian system and Varian system with Multinuclear Translation System inserted.....	87
Figure 4.15: SNR versus number of averages for stock Varian system and Varian system with Multinuclear Translation System with the original version's LO source.....	88
Figure 5.1: Block diagram of broadband system.	92
Figure 5.2: Front of full broadband system.	94
Figure 5.3: Interior of broadband system small signal unit.....	95
Figure 5.4: Gradient single-ended to differential converter.....	98
Figure 5.5: Gradient RMS conversion circuit.	99
Figure 5.6: Power amplifier unit.	100
Figure 5.7: Power supply unit.	102
Figure 5.8: Triple-tuned single-port coil designed for ^1H , ^{23}Na , and ^2H	103
Figure 5.9: Block diagram of flexible triplexer.....	104
Figure 5.10: Triplexing front-end and broadband T/R switch.	105
Figure 5.11: How offsetting simultaneous RF pulses can reduce the error in tip angle by reducing maximum instantaneous power.....	107

Figure 5.12: Comparison of ^{23}Na pulse calibration series acquired with only a ^{23}Na pulse (A) and simultaneous ^{23}Na and ^2H pulses (B-D).....	109
Figure 5.13: Cross-sectional diagram of phantom used for simultaneous imaging of ^1H , ^{23}Na , and ^2H	110
Figure 5.14: Simultaneous ^1H , ^{23}Na , and ^2H images acquired with the lab-developed triplexer, a lowpass filter, and singly-acquired reference images taken on the Varian imager.	112
Figure 5.15: Cross-sectional diagram of phantom used for simultaneous imaging of ^1H , ^{13}C , and ^{15}N	113
Figure 5.16: Comparison of ^1H , ^{13}C , and ^{15}N acquired on broadband system to Varian reference.....	114
Figure B-1: Overview Schematic	129
Figure B-2: PIN diode and LED driver circuits.	130

LIST OF TABLES

	Page
Table 2.1: Polarizations for common nuclei at assorted B_0 field strengths.....	7
Table 3.1: Local Oscillator Frequencies for ^{13}C	26
Table 3.2: Translator Performance.....	43
Table 4.1: Pin Diode Driver switching performance	76
Table 4.2: Multinuclear Translator Performance	80
Table 5.1: SNR comparison of images in Figure 5.14.	112

The amount of power needed to excite the spins is enormous in comparison to the signal the spins produce, which rarely exceeds 1 μV . The massive discrepancy in signal level between the transmitted and received signals drives a great deal of NMR and MRI system design, as the sensitive receive electronics must be protected against the powerful transmit RF pulses.

2.1.1.3. Chemical Shift

One of the fundamental methods by which NMR spectroscopy is able to provide insight into the structure of molecules is through chemical shift. Chemical shift, measured in parts-per-million and commonly denoted by δ , is the difference in frequency between different nuclei in a molecule caused by non-uniformity in electron density. Differences in electron density cause different nuclei to experience slightly different static magnetic fields, which causes them to have slightly different precession frequencies.

The range of common chemical shifts varies between different nuclei. Most ^1H resonances fall within an approximately 10 ppm range, whereas the full ^{13}C chemical shift range covers approximately 220 ppm.

2.1.2. Hyperpolarization

Hyperpolarization refers to a group of techniques that allow the polarization of a sample of spins to be increased greatly beyond what thermal equilibrium polarization would be at that temperature [23].

Multiple nuclei can be hyperpolarized simultaneously, but after polarization, they undergo T_1 relaxation, so it is imperative that the nuclei are imaged/interrogated rapidly and simultaneously.

