Av. Carl Friedrich Gauss, 3
08860 – Castelldefels, Barcelona
SPAIN

24 May 2022

Referee report on the doctoral thesis:
"Ultra-Low and Truly Zero-Field Nuclear Magnetic Resonance" by Piotr Put

The dissertation concerns, as the title indicates, nuclear magnetic resonance (NMR) at very low magnetic field strengths, including near-zero field conditions in which the effect of magnetic fields on the material of interest is negligible. This is an exotic regime for NMR, which under normal practice is performed at high magnetic fields. Indeed, great expense is often required to achieve fields that are used in the normal NMR modalities, and one of the motivations for the current work is to find alternatives that are lower cost, smaller, and more portable. In this exotic, near-zero-field regime, NMR experiments look very different from high-field NMR experiments, both as regards the spin physics within the molecules under study, and as regards the experimental systems used to study them. The first part of the dissertation provides a kind of guided tour of this exotic realm of zero- and ultra-low field (ZULF) NMR, with detailed exposition on the several physical effects that determine nuclear spin dynamics in liquid systems (both at high and low fields), the physics underlying the two main atomic magnetometer technologies used to detect ZULF NMR signals, nuclear hyperpolarization methods, and the expected spectra arising in thermally-polarized and hyperpolarized media. The second part of the dissertation describes experimental methods developed during the thesis, including the invention of a new variant of magnetometry by nonlinear magneto-optical rotation, gas-phase systems for generation of parahydrogen and its use for hyperpolarization of liquid samples, ZULF NMR setups with two magnetometer types, and a portable ZULF NMR setup. The third portion of the dissertation reports ZULF NMR spectra and their analysis, using the above described methods and instrumentation, for several new scenarios, including ZULF NMR spectra of organophophorous compounds, small biomolecules, and ^{13}C methanol used as a comagnetometer to search for spin-gravity coupling.

The dissertation is impressive, both for the breadth of the background material presented, and for the amount of laboratory work accomplished during the thesis. The thesis is dense and at times challenging to read, but in the end it is comprehensible, well-referenced, and follows a logical progression that facilitates an accumulation of knowledge when read from beginning to end. I think it will be a valuable reference for future students and others wanting to enter this relatively young and rapidly evolving research area.

The first chapter describes physical preliminaries, such as the density matrix formalism, rotation operators, and visual representation of spin density matrices. The discussions are brief and focused on the aspects that are used later in the dissertation. One would not be able to learn these quantum mechanical concepts and methods from this chapter alone, but presumably a serious reader of this dissertation has already studied these topics previously, so the real role of the chapter is to define notations and avoid misunderstandings. An exceptions is the density matrix visualization material, which, like the rest of the chapter, is a review of very well-established material, but is not so universally known. Regarding this visualization material, **I would ask the author to clarify the statement "The surface contains as much information about the state as the density matrix."** My impression is that, to a knowledgeable human at least, the density matrix, written out with a few digits of precision, conveys more information, more precisely than does the AMPS, as seen for example in Fig. 3.8 or Fig. 3.9. In contrast, the AMPS representation is more intuitive.

The second chapter describes the spin dynamics of nuclei in NMR scenarios, including the density matrix description and its relation to the Bloch equations, the spin Hamiltonian

including dipolar, quadrupolar, and electron-mediated couplings, and various limits and approximation regimes of this Hamiltonian, including the role of motional averaging and "truncation" of terms in the Hamiltonian due to the presence of a strong field. The role of the magnetic field is discussed in general and various regimes of field strength are defined. A brief motivation for and history of ZULF NMR closes the chapter. This chapter is necessary within the dissertation to introduce many key concepts and definitions, and is also presented in a style suitable for a textbook, making it a very good introduction to the different regimes and the simplifications and approximations that are appropriate in them. There is one part that I believe is either incorrect, or perhaps not presented with enough explanation: The physical basis for J-coupling is explained on page 23, and identifies four mechanisms by which two nuclei can indirectly interact through their mutual interactions with a molecule's electrons. The "second order diamagnetic interaction" (Eq. 2.56) appears to depend on the position of both nucleus 1 and nucleus 2, as one might expect for a coupling between two nuclei. But the "paramagnetic spin-orbit coupling" (Eq. 2.55) and the "spin-dipole interaction" and "Fermi contact interaction" appear to depend only on the position of one of the nuclei (the vector $r_{1,j}$ appears, but not $r_{2,j}$). **Please explain this. How do the PSO, SD and FC interactions give rise to an interaction of the form $I_1 \cdot J_{12} \cdot I_2$ (Eq. 2.52)?**

Chapter 3 describes various experimental techniques, with a focus on the spin physics they induce. The topics presented include thermal polarization using electromagnets or permanent magnets, parahydrogen production using cryogenic cooling and paramagnetic surfaces, and various methods of parahydrogen-induced polarization (PHIP), including hydrogenic PHIP, SABRE, and SABRE-relay methods. The chapter then continues to describe the physics of optically pumped magnetometers, including dc and ac magnetometry by NMOR, and SERF magnetometry. A ZULF-NMR setup including two home-built NMOR magnetometers is described, and representative signals are exhibited. The chapter concludes with a discussion of zero-field NMR signal mechanisms, in light of the previously described polarization methods. This chapter is very ambitious, in that it aims to cover a great deal of material, both providing theory and history/references, as well as describing some of the experimental work within the thesis. The chapter is successful, I believe, in providing an overview and introduction, but is not sufficiently detailed to be useful as a reference. Some important topics are discussed rather superficially and, as a result, the physical picture conveyed is not clear. For example: Considering SABRE, and SABRE-relay, for example, it is not clear how the spin polarization arises, whether this is in the catalyst or in the target molecule. For example, the description

> When we consider a system of two protons from a parahydrogen molecule (labelled A and A') and target nuclei (B), LAC can be used to transfer system from the singlet state $|S_0, \alpha\rangle$ to the specific triplet state $|T_{+1}, \beta\rangle$, where the state of parahydrogen is shown in singlet-triplet basis, while the state of target nuclei [sic] is indicated by spin up α and spin down β Zeeman states.

Indicates how the target could experience a spin-exchange with one of the parahydrogen protons. But why is the reverse process, from $|S_0, \beta\rangle$ to the specific triplet state $|T_{-1}, \alpha\rangle$ not equally likely to occur, so that the initially unpolarized target molecule is still unpolarized after the LAC? **The SABRE mechanism should be explained in more detail.**

As regards the experimental systems description in Chapter 3, these are also not described in full detail, but this is reasonable as the systems are described in the following chapter and the listed publications. Toward the end of the chapter, on p. 81, I was surprised to see in Eq. 3.75, a Hamiltonian that does not appear correct. In particular, the r.h.s. of that equation would

appear to have units of energy times time. **Please explain Eq. 3.75 and how the effect of a dc field pulse is calculated**, e.g., to arrive at Eq. 3.76.

The description of ZULF NMR signals in terms of J-couplings and spin degeneracies is clear and helpful, especially as regards understanding the frequencies and splittings seen in the ZULF NMR spectra presented later in the thesis. In contrast, there is little insight given to the strength of the lines. On p. 86, one finds

> The relative amplitudes of subsequent NMR can be also analytically calculated for XA_n spin systems. The transition probability between two states $|m>$ and $|n>$ is given as: Eq. 3.92.

This suggests that the relative amplitudes of the peaks are proportional to the transition dipole matrix elements, without reference to the density matrix. **Please explain what determines the strengths of the peaks, and the role of the state (or density matrix) in determining the peak amplitudes.**

Chapter 4 describes experimental systems and methods for ZULF NMR, including shielding, magnetometers, polarization magnets and transport schemes, controls, data acquisition and software. The chapter is informative and provides a clear picture of the methods used, and some of the frustrations encountered, such as failure of heating wires. The chapter does not provide enough information to for a following student or other researcher to reproduce some of the systems and methods described. For example, the sensitivity of a SERF magnetometer of the sort described in this chapter is a complicated function of the temperature (and thus alkali vapor density), buffer gas pressure, beam power, beam diameter, field modulation frequency, field modulation amplitude, and other factors. Most of these numbers are not given in the chapter, and neither is the achieved sensitivity.

Chapter 5 presents results on J spectroscopy of phosphorous compounds, and on ZULF NMR spectroscopy using continuous SABRE hyperpolarization of ^{15}N-pyridine.

Chapter 6 presents results on ZULF NMR of small biomolecules, including labelled fumarate, glucose, and urea.

The results in chapters 5 and 6 are published (two articles per chapter). These chapters are notably easier to read than the preceding chapters.

Chapter 7 presents an as-yet-unpublished study on the use of ZULF NMR techniques for comagnetometry based on liquid ^{13}C methanol. The work follows closely an earlier study using a different molecule, namely

> Wu, T., Blanchard, J. W., Kimball, D. F. J., Jiang, M., and Budker, D. (2018). Nuclear spin comagnetometer based on a liquid of identical molecules. Physical Review Letters, 121(2):023202.

The presentation of the motivations, methods, and analysis of the comagnetometer physics is systematic and clear. The comagnetometer is sensitive to hypothetical spin-gravity couplings, which manifest in the splitting of ZULF NMR spectral lines. Ratios of splittings are identified that are insensitive to magnetic field fluctuations, while being sensitive to spin-gravity couplings. The work arrives to the conclusion that the statistical sensitivity of the 13C methanol comagnetometer is somewhat better than the existing limits on spin-gravity coupling to the proton, from

Kimball, D. F. J., Dudley, J., Li, Y., Patel, D., and Valdez, J. (2017). Constraints on long-range spin-gravity and monopole-dipole couplings of the proton. Physical Review D, 96(7):075004.

One minor comment: **On p. 141, Figure 7.1, part b, there appears to be a non-degenerate F=1 level, and a threefold degenerate F=0 level. I believe the labels have been switched.**

In section 7.4.1, "Spin-gravity coupling effect on nuclear spin": The model for the spin-gravity coupling effect allows for a different coupling to the proton and to the neutron, even though these have the same spin. **Are there reasons to believe (in extensions of general relativity, or in quantum gravity, for example), that gravity would couple differently to protons and to neutrons?** If the couplings are in fact the same, $\chi_n = \chi_p$, the expression for δv_2^{SG} (Eq. 7.15) becomes independent of g, but δv_1^{SG} (Eq. 7.14) still depends on g. **Can you explain this difference?**

On p. 148, the comagnetometer's statistical sensitivity is compared against the result reported in Kimball et al. (2017). But that reported result is limited by systematic uncertainties, with statistical uncertainties making a relatively small contribution. It seems likely, then, that the comagnetometer's performance will be determined by its systematic uncertainties. The dissertation notes that the systematic effects due to magnetic field gradients are expected to be greatly reduced in the liquid-state comagnetometer (as in Wu et al. (2018)). **Please explain what other systematic effects are expected to be important.**

Regarding the readability of the dissertation: the spelling is remarkably accurate. Considering the notorious difficulty of English spelling, this is an accomplishment, although in this computer-assisted era it is not possible to distinguish the contribution of the author from the contribution of his software. In contrast, the grammar is far from perfect, with many errors, especially as regards the use of articles, e.g., "a" and "the." We can hope that in the future, software will also solve these difficulties for us. I will separately supply an annotated version of the manuscript that indicates many such errors (but by no means all of them!). I do not know if it is possible at this stage to fix these before the dissertation is printed.

I note also that the candidate has published a good portion of this thesis in peer-reviewed research journals. Both the number and quality of the publishable results from the thesis is high, and there is no doubt that the candidate has achieved the high level of scientific maturity expected of a PhD.

In conclusion, the dissertation presents 1) a broad, coherent, and useful introduction to the topic of ZULF NMR, 2) a detailed description of novel experimental equipment and techniques, and 3) original research results on several topics of current interest. The extensive knowledge acquired by the candidate during the PhD thesis is clear from this dissertation, and the work represents an important addition to the field. **In this context, the thesis meets all the formal and customary requirements for a PhD dissertation, and I request the admission of Mr. Piotry Put to further stages of the PhD defense.**

Morgan W. Mitchell

ICREA Research Professor at ICFO
Av. Carl Friedrich Gauss, 3
08860 Castelldefels
Barcelona - SPAIN
morgan.mitchell@icfo.es