STUDIES ON LONG-LIVED STATES AND COHERENCES IN NMR

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by

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Dedicated to my

Family and

Supervisor

Certificate

I certify that the thesis entitled ***Studies on Long-Lived States and Coherences in NMR*** submitted by **Mr. Rituraj Mishra** to Indian Institute of Technology Delhi for the award of **Doctor of Philosophy** is a record of bona fide research work done by him. He has worked under my guidance and supervision and has fulfilled the requirements for the submission of this thesis which to my knowledge has reached the requisite standard. The result presented in this thesis have not been submitted in part or full to any other University or Institute for the award of any degree or diploma.

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(Rituraj Mishra)

Abstract

Since the invention of the NMR, it has proved its potential in the field of biomedical, medical, chemical, material, physical, and even other sciences. Applications of this potent technique range from structure determination of large and small molecules, molecular dynamics, chemical kinetics, quantum computing to MRI (Magnetic Resonance Imaging). One of the reasons for such a wide array of applications is rooted in the higher lifetime of the excited state which is limited by longitudinal relaxation ($\sim T_1$) and transverse relaxation ($\sim T_2$). Endeavors of further enhancement or extension of the life-time travelled a long way through Transverse Relaxation Optimized Spectroscopy (TROSY), which relies on relative cancellation of relaxation due to dipolar tensors and chemical shift anisotropy tensors, to recently developed Long-Lived States (LLS) and Long-Lived Coherences (LLC). Out of these two lifetime enhancing techniques, the main part of the thesis is dedicated to the removal of restrictions in LLC and its applications. Apart from LLC, spin dynamics during Spin Lock Induced Crossing (SLIC) is also analyzed. The thesis is composed of five chapters.

In the introductory chapter, the Hamiltonians, operators, superoperators and product operator formalism are discussed. An introduction to various bases, i.e., product operator basis (PB), singlet-triplet basis (STB) and the single transition operator basis (STOB) is provided. Further, the fundamental theory and basic pulse sequences to create LLS and LLC are discussed in detail. Redfield theory of relaxation is described for most dominant relaxation mechanism, dipolar, in a liquid state. The application of Redfield theory to find out the effect of dipolar relaxation on LLS and LLC, in superoperator basis, is thoroughly presented.

Chapter 2 presents a thorough study on the Spin-Lock Induced Crossing (SLIC) sequence, a sequence to create LLS in nearly equivalent two-spin system. This chapter provides a vector picture explanation in product-operator basis (POB) and single transition operator basis (STOB). Further in this chapter, the functional form of the operators are determined by Fourier transforming the time domain simulated data. This functional variation modifies the earlier fitting equation of DeVience to find out chemical shift difference between two nearly equivalent protons. The Liouville-von Neumann equation is solved to find the dependence on the initial condition of operators generated during the spin locking interval. A two-parameter optimization technique is also a part of this chapter.

After this foray into LLS, the rest of the thesis is aimed at LLC in three-spin systems and multiple two-spin systems.

Chapter 3 is divided into two parts, i.e., A and B. Part A is about the application of basic LLC sequence to find out relative signs of coupling constants. A three-spin system LLC spectrum result in three peaks at a combination of three coupling constants. The mathematical formulation of these combinations is derived for determining the relative sign of the coupling constants and unobservable coupling constant. The process is exemplified with three-spin systems, such as 2-furoic acid, ethyl vinyl ether, phenylalanine, acrylonitrile and 2, 3-dibromo propionic acid. Part B provides an alternative sequence, composed of soft pulses, to filter out the systems with different relative signs of the coupling constants. The sequence is successfully tested on furfural, ethyl vinyl ether, and phenylalanine.

The extension of the LLC to a pair of two-spins in a three-spin system is the prime focus of chapter 4. The two-spin dipolar relaxation theory of LLC is extended to three-spin

systems, and the theoretical relaxation lifetime of LLC is calculated for furfural and ethyl vinyl ether. Experiments, which utilizes soft pulses to excite and lock the desired coherence, are designed for the confirmation of the theory. The experimental LLC lifetime for two three-spin compounds, i.e., ethyl vinyl ether and furfural, is determined and compared with the theoretical one. The chapter ends up with possible reasons of mismatch between the theoretical and experimental values.

The final chapter extends the LLC to multiple two-spin systems. The main restriction to the extension is to lock the coherence at the average of the chemical shift of the two peaks (on-resonance locking), which is not possible in a system with multiple two-spins. Hence, the effect of off-resonance locking (locking away from the average of the two peaks) is studied theoretically and experimentally on 2, 3 dibromothiophine (DBT), which suggests a composite low-power locking instead of continuous wave (cw) locking. The density operator $\sum_{i=1}^{3} I_{1x}^{i} - I_{2x}^{i}$, i = 1 to 3 was generated in the mixture (citric acid, DBT and 2, 3, 6-trichlorbenzaldehyde (TCB)) with selective inversion IBURP-2 pulses, and LLCs were successfully created in all pairs of the mixture. The sequence is termed as Broad Band LLC (BBLLC.) The use of BBLLC is also demonstrated as a filter for two-spin systems in a mixture of four ($AA'XX'$) and two-spin systems (furan + TCB + citric acid), and in a compound, 1, 3-di-p-tolyl-propenone, having two four-spin systems and one two-spin system.

सारांश

नाभिकीय चुंबकीय अनुनाद (एन० एम० आर०) स्पेक्ट्रोस्कोपी ने अपनेआविष्कार के बाद से ही, अपनी क्षमता को विभिन्न वैज्ञानिक क्षेत्रों जैसे जैव-चिकित्सा, चिकित्सा, रसायन, भौतिक विज्ञान इत्यादि में सिद्ध किया है। इस शक्तिशाली तकनीक के अनुप्रयोग बड़े और छोटे अणुओं की संरचना निर्धारण, आणविक गतिशीलता, रासायनिक बलगतिकी, क्वांटम कंप्यूटिंग से लेकर एमआरआई (चुंबकीय अनुनाद प्रतिबिम्बन) तक फैले हुए हैं। एन० एम० आर० के इतने विस्तृत अनुप्रयोगों का एक कारण इसकी उत्तेजित अवस्था के उच्च जीवनकाल में निहित है, जो कि अनुदैर्ध्य छूट जीवन काल ($\sim T_1$) और अनुप्रस्थ छूट जीवन काल ($\sim T_2$) द्वारा सीमित है। इन जीवन- कालों को पुनः विस्तृत करने के प्रयासों ने ट्रांसवर्स रिलेक्सेशन ऑप्टिमाइज़्ड स्पेक्ट्रोस्कोपी (ट्रॉक्सी), जो कि द्विध्रुवी प्रदिशों और रासायनिक सृति विषमदैशिता के सापेक्ष निरस्त्रीकरण पर निर्भर करता है, से लेकर हाल ही में विकसित लॉन्ग-लिवेड स्टेट्स (एलएलएस) और लॉन्ग-लिवेड कोहरेंस (एलएलसी) तक एक लंबा सफर तय किया है। इन दो जीवनकाल बढ़ाने वाली तकनीकों में से, प्रबन्ध का मुख्य हिस्सा एलएलसी और इसके प्रतिबंधों को हटाने के लिए समर्पित है। स्पिन लॉक इंडेड क्रॉसिंग (एसएलआईसी) के दौरान स्पिन प्रावैगिक का विश्लेषण भी इस प्रबन्ध का एक हिस्सा है । यह प्रबन्ध पाँच अध्यायों से मिलकर बना है।

परिचयात्मक अध्याय में, हैमिल्टनियन, ऑपरेटर, सुपरऑपरेटर और उत्पाद ऑपरेटर औपचारिकता पर चर्चा की गयी है। इसके साथ विभिन्न आधारों, अर्थात् उत्पाद ऑपरेटर आधार (PB), सिंगलेट-ट्रिपलेट आधार (STB) और एकल संक्रमण ऑपरेटर आधार (STOB), का परिचय भी इस अध्याय में दिया गया है। इसके अलावा, एलएलएस और एलएलसी बनाने के लिए मौलिक सिद्धांतों और मूलभूत स्पन्द अनुक्रमों पर विस्तार से चर्चा की गई है। द्रव-अवस्था में सबसे प्रमुख द्विध्रुवीय रिलेक्सेशन तंत्र के लिए रेडफील्ड रिलेक्सेशन सिद्धांत का भी वर्णन इस अध्याय में किया गया है। सुपरऑपरेटर आधार में एलएलएस और एलएलसी पर द्विध्रुवीय रिलेक्सेशन के प्रभावों का पता लगाने के लिए रेडफील्ड सिद्धांत के आवेदन को विस्तारपूर्वक प्रस्तुत करना भी इस अध्याय का उद्देश्य है ।

अध्याय 2 स्पिन-लॉक प्रेरित क्रॉसिंग (एसएलआईसी) अनुक्रम पर एक संपूर्ण अध्ययन प्रस्तुत करता है। यह अनुक्रम लगभग बराबर दो-स्पिन प्रणाली में एलएलएस बनाने के लिए उपयोग किया जाता है। यह अध्याय उत्पाद-ऑपरेटर

आधार (POB) और एकल संक्रमण ऑपरेटर आधार (STOB) में एक वेक्टर चित्र स्पष्टीकरण प्रदान करता है। इस अध्याय में आगे, ऑपरेटरों के फलन रूप को समय क्षेत्र कृत्रिम आंकड़ों के फूरियर रूपांतरण द्वारा निर्धारित किया गया है। यह क्रियात्मक रूप, डी-विएन्स के पहले के फिटिंग समीकरण, जो कि दो समान समतुल्य प्रोटॉ नों के बीच रासायनिक सृति के अंतर का पता लगाने के लिए उपयोग की जाती है, को संशोधित करती है। स्पिन लॉकिंग अंतराल के दौरान उत्पन्न ऑपरेटरों की प्रारंभिक स्थिति पर निर्भरता खोजने के लिए लिउविल-वॉन न्यूमैन समीकरण का हल किया गया है। एक दो-पैरामीटर अनुकूलन तकनीक भी इस अध्याय का एक हिस्सा है।

एलएलएस में इस प्रारंभिक प्रयत्न के बाद, बाकी थीसिस तीन-स्पिन सिस्टम और कई दो-स्पिन सिस्टम में एलएलसी के निर्माण में उद्देशित है।

अध्याय 3 को दो भागों, अर्थात्, ए और बी भाग में विभाजित किया गया है। भाग ए युग्मन स्थिरांक के सापेक्ष संकेतों का पता लगाने के लिए मूलभूत एलएलसी अनुक्रम के आवेदन के विषय में है। एक तीन-स्पिन एलएलसी स्पेक्ट्रम तीन युग्मन स्थिरांकों के संयोजन पर तीन श्रृंग प्रदान करता है। युग्मन स्थिरांक के सापेक्ष संकेतों और अस्पष्ट युग्मन स्थिरांक के निर्धारण के लिए इन संयोजनों का गणितीय सूत्रीकरण किया गया है। इस प्रक्रिया को तीन-स्पिन प्रणालियों, जैसे कि 2- फ़्यूरोइक एसिड, एथिल विनाइल ईथर, फेनिलएलनिन, एक्रिलोनिट्राइल और 2, 3- डाई ब्रोमो प्रोपियोनिक एसिड, के साथ उद्धृत किया गया है, । भाग बी विभिन्न सापेक्ष संकेतों वाले तीन-स्पिन यौगिकों में विभेद के लिए मृदु स्पन्दों से बना एक वैकल्पिक अनुक्रम प्रदान करता है। इस अनुक्रम को फरफ़्यूरल, एथिल विनाइल ईथर और फेनिलएलनिन पर सफलतापूर्वक परीक्षण किया गया है।

अध्याय 4 एलएलसी का विस्तार तीन-स्पिन प्रणाली में दो-स्पिनों के एक युग्म में करने पर केंद्रित है। एलएलसी के दो-स्पिन द्विध्रुवीय रिलेक्सेशन सिद्धांत को तीन-स्पिन प्रणालियों तक विस्तारित किया गया है, और एलएलसी के सैद्धांतिक रिलेक्सेशन जीवनकाल की गणना फरफ़्यूरल और एथिल विनाइल ईथर के लिए की गयी है। सिद्धांत की पुष्टि के लिए ऐसे प्रयोग योजित किए गए हैं, जो वांछित कोहेरेन्सेस को उत्तेजित एवं अभिबद्ध करने के लिए मृदु स्पन्दों का उपयोग करते है। दो तीन-स्पिन यौगिकों, अर्थात्, एथिल विनाइल ईथर और फरफ़्यूरल का

प्रयोगात्मक एलएलसी जीवनकाल का निर्धारण किया गया है एवं इसकी सैद्धांतिक जीवनकाल के साथ तुलना भी इस अध्याय में प्रस्तुत की गयी है। अध्याय सैद्धांतिक और प्रयोगात्मक परिणामों की भिन्नता के संभावित कारणों के स्पष्टीकरण के साथ समाप्त होता है।

अंतिम अध्याय एलएलसी को एक से अधिक दो-स्पिन सिस्टम तक बढ़ाने पर आधारित है। दो श्रृंगों का उनकी औसत रासायनिक सृति पर अभिबध्दिकरण (लॉकिंग) , एलएलसी को एक से अधिक दो-स्पिन सिस्टम में बनाने में मुख्य प्रतिबंध लगाता है। अतः, ऑफ-रेजोनेंस अभिबध्दिकरण (लॉकिंग) (दो श्रृंगों के औसत से दूर अभिबध्दिकरण) के प्रभाव का सैद्धांतिक और प्रयोगात्मक रूप से अध्ययन 2, 3 डाई-ब्रोमोथियोफिन (डीबीटी) पर किया गया है, जिससे यह निष्कर्ष निकलता है कि कॉन्टिन्युअस तरंग स्पन्द की जगह पर कम्पोसिट स्पन्द का उपयोग किया जाना चाहिए। चयनात्मक व्युत्क्रम IBURP-2 स्पन्दों की सहायता से घनत्व ऑपरेटर, $\sum_{i=1}^{3} I_{1x}^{i} - I_{2x}^{i}$, i = 1 to 3, i = 1 से 3 एक मिश्रण (सिट्रिक एसिड, डीबीटी और 2, 3, 6-ट्राइक्लोरोबेन्जल्डिहाइड (टीसीबी)) में तैयार किया गया, और मिश्रण के सभी युग्मों में सफलतापूर्वक का निर्माण किया गया। इस अनुक्रम को ब्रॉड बैंड एलएलसी (बीबीएलएलसी) का नाम दिया गया है। बीबीएलएलसी का उपयोग एक मिश्रण (फ्यूरान+ टीसीबी+ डीबीटी), जो कि चार ($AA'XX'$) और दो-स्पिन सिस्टम से मिलकर बना है, एवं एक यौगिक (1, 3-di-p-tolyl-प्रोपेनोन) में दो-स्पिन सिस्टम के फिल्टर के रूप में भी दिखाया गया है।

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