Micro-Striplines and Micro-Slot NMR Probes

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Striplines are commonly used to transport signals in microwave and radio frequency circuits. They are easily implemented on printed circuit boards. Over the past two decades, wave guides with planar geometry have found increasing use as inductive detectors in miniaturised nuclear magnetic resonance systems. In this article, we give a brief overview of the theory of striplines and resonators built from them, and we review the literature on their use in NMR spectroscopy.

I. INTRODUCTION

Nuclear magnetic resonance refers to the interaction of a system of nuclear spins exposed to a static magnetic field with an oscillatory field, usually in the radio frequency range (anywhere from 1 kHz to several GHz)[1]. In the overwhelming majority of cases, the changes in the spin state that result from this interaction are read out through a voltage induced by the spin precession into a surrounding conductor. Even though alternative readout approaches have been demonstrated, and have their advantages in certain cases, this type of inductive detection has proven to be both robust and easy to implement. Indeed, while the earliest demonstrations of nuclear magnetic resonance, pioneered by Rabi,[2] relied on the deflection atomic beams in inhomogeneous fields according to the spin state, NMR did not take off as a widely used tool until the invention of the direct induction method, independently discovered by Bloch[3] and by Purcell, Torrey, and Pound[4] in 1946.

Among other advantages, inductive detection allows the use of the same structure for both excitation and detection of the nuclear spin precession. Particularly in the context of the Fourier spectroscopy method,[5] this has become very useful. It is relatively easy to expose a sample to an oscillatory magnetic field by surrounding it with a suitable conductor, through which an alternating current is sent at the appropriate frequency. The precessing spins induce a measurable voltage in the same conductor. Of course, there are technical problems to be solved that arise due to the high power that is needed in some cases for excitation, while the induced voltages are very small and require exquisitely sensitive receivers. It is not uncommon for excitation RF power to approach several kW, whereas the power available for spin detection is typically of the order of only a few pW.

The earliest inductive NMR systems have almost exclusively relied on solenoid coils as excitation/ detection systems. As the applications of NMR have diversified, and new technologies have become available, other geometries have been explored. In particular, the advent of superconducting magnets with cylindrical bores has led to the development of saddle coils and related resonator geometries. Magnetic resonance imaging, in particular for medical applications, brought the need to accommodate much larger samples, which was met by the development of birdcage resonators. Hence, most of the current NMR detectors follow a roughly cylindrical form factor. There are some applications, though, which require a more planar geometry. In particular, the study of thin films, membranes, and interfaces is complicated in cylindrical detector systems. Special, flattened solenoid probes have been developed for the study of membrane proteins under solid-state NMR conditions[6]. As the magnetic fields, and, correspondingly, the Larmor frequencies used in MRI scanners have increased, uniform penetration of the radio frequency magnetic fields into the tissue has become more and more difficult. Since biological systems contain ionic solutions, non-conservative electric fields arising in the detector system need to be shielded from getting in contact with the tissue. The dielectric losses incurred from interaction between these electric fields and the tissue degrade the sensitivity of the detection, but they also lead to excessive power deposition in the tissue during excitation. As a solution, surface coils for localised MR imaging of human subjects based on circular or quadratically laid out strip lines have been proposed.[7] NMR spectroscopy is an extremely versatile tool. Nuclear spins turn out to be excellent spies. They are well insulated from the noisy electronic degrees of freedom to allow for long spin coherence life times, which is the basis of sharp spectral lines. At the same time, the nuclear Larmor frequency turns out to depend in subtle ways on the electronic environment. In combination, these two features make it possible to both accurately measure the nuclear Larmor frequency, and to interpret it in terms of the molecular environment that surrounds the nucleus.

Compared to many other spectroscopic techniques, NMR suffers from a major drawback: its relative insensitivity. While UV/VIS techniques, in particular fluorescence, can detect signals from single molecules with relative ease, NMR typically requires of the order of 10^{15} spins to resonate within a narrow bandwidth (1 Hz or so) in order for the signal to be measurable. To some extent, this can be alleviated by long measurement times. Since the signal/noise ratio only grows with the square root of the measurement time, sensitivity still limits the application of NMR in practice. The design of NMR detectors that offer optimal sensitivity has therefore been a long-standing research topic in magnetic resonance. Sensitivity is determined by the signal/noise ratio that can be obtained within a specified amount of time from a defined number of spins. Inductive detectors based on resistive metals invariably produce thermal noise. Under optimal conditions, where all non-intrinsic sources of noise have been eliminated by shielding, the black-body radiation of the resonator structure itself leads to a noise voltage spectral density which is essentially independent of frequency, and scales proportionally to the square root of the ohmic resistance of the detector. The relationship between the NMR spin precession and the induced voltage signal has been discussed by Hoult and Richards in terms of the correspondence principle.[8] The induced signal strength from a single spin depends on the normalised magnetic field (generated by the detector per unit current) at the location of the spin. Hence, efficient detectors need to be designed such that the magnetic field they generate per unit current is maximal. This conflicts with the requirement of low resistance, which is important to keep the noise voltage small, and an optimal compromise must be found in practice between the two. It has been well known for about two decades that the mass sensitivity (i.e., the signal/noise ratio per spin) of inductive detectors is roughly inversely proportional to the detector size. This can be rationalised by examining the normalised magnetic field and the radio frequency resistance of a particular detector geometry as a function of its overall dimensions. For example, the magnetic field generated by a single circular loop of diameter d made of a wire of thickness h is given approximately by $H/I = 1/(\pi d)$. If the geometry is scaled by a factor α, the H/I value therefore scales as α^{-1}. At typical NMR frequencies, the skin depth in Cu amounts only to a few μm. Therefore, as both the wire diameter and the loop diameter are scaled by the same factor α, the resistance of the structure remains roughly constant, as long as the wire diameter remains larger than the skin depth. As a result the signal to noise ratio is expected to scale roughly as $1/\alpha$. A similar argument can be made for solenoid coils. In practice, the observed scaling is weaker. Still, NMR detectors based on micro coils (i.e., with dimensions of tens to hundreds of μm) have been shown to provide very high mass sensitivities. This has formed the basis of hyphenated techniques, where upstream chromatographic separation is combined with downstream detection by an NMR system equipped with a micro detector.[9] Microfluidics is a rapidly expanding field of science and technology. The underlying idea is borrowed from micro electronics: to integrate complex functionality in a mostly two-dimensional layout, making use of efficient lithographic fabrication technologies. This lab-on-a-chip (LoC) approach has proven especially fruitful in enabling total analysis systems, which integrate sample preparation, chromatographic separation, and detection on single chip platform.[10] Since lithographic techniques allow the accurate reproduction of complex and very highly resolved features, microfluidic systems can be designed to mimic highly complex environments with great control and accuracy. This enables the culture of biological systems under artificial and highly controlled conditions, while closely mimicking the natural environment. This has become an invaluable tool for the study of differentiated cells, their development, and the interplay between different cell types. **REFS needed!!** NMR spectroscopy is uniquely suited to observe metabolic processes in live systems. It therefore has great potential as an observation tool in microfluidic culture assays. However, in spite of significant efforts, its use in the context of microfluidic devices is not yet widespread. There are a number of reasons for this. On the one hand, the planar geometry of microfluidic devices is not easily combined with common NMR detectors, which are typically designed for a cylindrical sample. Another limitation is the poor sensitivity of NMR, which is exacerbated by the small sample amounts typically available in microfluidic systems. As will become apparent in the following, micro stripline detectors are of particular interest in this context, since they inherently follow a planar geometry, and they can offer extremely high mass sensitivity. The first NMR probes based on a strip line geometry have been proposed in the context of magnetic resonance imaging. Their use for NMR spectroscopy at the microscope was first proposed by Maguire et al[11] in 2004. They integrated a stripline containing a small slot into a radio frequency resonator. The slot leads to current crowding, and consequently to a very large H/I value locally. This geometry provides excellent mass sensitivity, but the achieved spectral resolution was still relatively poor. A few years later, van Bentum and Kentgens and coworkers proposed a stripline detector based on a symmetric geometry with ground planes on either side of the strip line. By tapering the transition in the width of the strip line broadening of the resonance lines due to magnetic susceptibility artefacts could be largely reduced,[12] leading to excellent performance in terms of resolution. While these probes were operated in a flow mode, with fixed capillaries acting as sample holders, this geometry has recently been modified by Finch et al. to a transmission line probe based on two identical planar conductors, which can accommodate an exchangeable microfluidic chip. Looking into the future, strip line based detector geometries offer significant potential for further advances in miniaturisation. Their fabrication using lithographic techniques is straightforward, in contrast to intrinsically three-dimensional geometries such as solenoids, and there is no reason why they could not be successfully applied to detectors an order of magnitude or more smaller than the ones that have been demonstrated so far. Another exciting possibility is the use of stripline detectors in travelling wave mode, rather than as resonators carrying standing waves. Travelling wave NMR, which been demonstrated in the context of magnetic resonance imaging and (macroscopic) NMR spectroscopy, could have signifiant advantages at the micro scale, since it allows the spatial separation of the sample and the detection circuitry. The remainder of this chapter is organised as follows: first, some theoretical aspects of strip lines and strip-line based resonators are examined in section 2. Section 3 provides a chronological overview of the development of micro-NMR strip line and micro strip based detectors, and finally, section 4 discusses some of the recently demonstrated applications.

II. THEORY

III. STRIPLINE NMR

[1] A. Abragam, *The Principles of Nuclear Magnetism.* Oxford University Press, 1961.
[2] I. Rabi, J. Zacharias, S. Millman, and P. Kusch, "A new method of measuring nuclear magnetic moment," *Physical Review*, vol. 53, no. 4, pp. 318–318, 1938.
[3] F. Bloch, "Nuclear Induction," *Phys. Rev.*, vol. 70, no. 7-8, pp. 460–474, Oct. 1946.
[4] E. M. Purcell, H. C. Torrey, and R. V. Pound, "Resonance Absorption by Nuclear Magnetic Moments in a Solid," *Phys. Rev.*, vol. 69, no. 1-2, pp. 37–38, Jan. 1946.
[5] R. R. Ernst and W. A. Anderson, "Application of Fourier Transform Spectroscopy to Magnetic Resonance," *Review of Scientific Instruments*, vol. 37, no. 1, pp. 93–102, Jan. 1966.
[6] B. Bechinger and S. J. Opella, "Flat-coil probe for NMR spectroscopy of oriented membrane samples," *Journal of Magnetic Resonance (1969)*, vol. 95, no. 3, pp. 585–588, Dec. 1991.
[7] X. Zhang, K. Ugurbil, and W. Chen, "Microstrip RF surface coil design for extremely high-field MRI and spectroscopy," *Magn. Reson. Med.*, vol. 46, no. 3, pp. 443–450, Sep. 2001.
[8] D. Hoult and R. Richards, "Critical Factors in the Design of Sensitive High Resolution Nuclear Magnetic Resonance Spectrometers," *Proceedings of the Royal Society of London. Series A, Mathematical and Physical Sciences*, vol. 344, no. 1638, pp. 311–340, 1975.
[9] A. Webb, "Nuclear magnetic resonance coupled microseparations," *Magn Reson Chem*, vol. 43, pp. 688–696, 2005.
[10] A. Manz, N. Graber, and H. WIDMER, "Miniaturized Total Chemical-Analysis Systems - a Novel Concept for Chemical Sensing," *Sensor Actuat B-Chem*, vol. 1, pp. 244–248, 1990.
[11] Y. Maguire, N. Gershenfeld, and I. L. Chuang, "Slitted and stubbed microstrips for high sensitivity, near-field electromagnetic detection of small samples and fields," Patent US7 560 927B2, Jul., 2009.
[12] J. Bart, J. W. G. Janssen, P. J. M. van Bentum, A. P. M. Kentgens, and J. G. E. Gardeniers, "Optimization of stripline-based microfluidic chips for high-resolution NMR," *J. Magn. Reson*, vol. 201, no. 2, pp. 175–185, 2009.