

Features of nuclear magnetic resonance signals registration in weak magnetic fields for express - control of biological solutions and liquid medium by nuclear magnetic spectroscopy method.

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Abstract. This paper presents a method of nuclear magnetic spectroscopy in weak magnetic fields, as well as the peculiarities that arise when experimental studies conducting of biological fluids and liquid medium. The proposed method allows to measure of the condensed matter relaxation constants in weak magnetic fields by the method of nuclear magnetic resonance for express control of their condition at the place of study. The accuracy smaller than 1%. The results of experimental studies of various fluids and their mixtures are presented.

Keywords: Nuclear magnetic resonance, nuclear magnetic spectrometer, a biological solution, liquid medium, the magnetic field, times the longitudinal T_1 and transverse T_2 relaxation, the signal-to-noise ratio.

1. Introduction

The one of conditions for obtaining reliable results in the condensed matter research is the availability of reliable information about the state of the medium (for example, the presence of impurities, possible structural changes that have occurred for various reasons, etc.). This is especially important in the case of using the medium after a long period of storage, transportation, change of container or other influences that can change its state. [1 - 5].

Chemical analysis of such solutions is difficult and time consuming task, because a complete analysis needs much expensive chemical reagents [6, 7].

Currently one of the most precise analytical techniques for studies of condensed matter is a nuclear magnetic (NMR) spectroscopy [2, 3, 5, 8]. Method of NMR spectroscopy is successfully applied to inorganic chemistry, solid-state physics, as well as for the study of biological objects, including farmaceutico [1, 6, 7]. Unlike infrared spectroscopy (IR), NMR spectroscopy allows scientists to obtain more complex information about molecular structure and the chemical composition of the studied compounds. High resolution of NMR allows using it for the study of intermolecular and intramolecular dynamics in liquid media. That allows us to determine the rate constants of chemical reactions and relaxation [1 - 5, 8, 9].

NMR spectroscopy received the most practical application for protons (^1H , ^2H), and nuclei of carbon - 13 (^{13}C), fluorine - 19 (^{19}F), phosphorus - 31 (^{31}P), lithium - 7 (^7Li), sodium – 23 (^{23}Na), boron - 10



(^{10}B), nitrogen - 15 (^{15}N) and etc. The only condition for the NMR spectroscopy application is the presence in substance of nuclei with non-zero magnetic moment, because for the study the sample is placed in a strong magnetic field B_0 with a high homogeneity degree (no less than 10^{-3}). Currently, most of the produced NMR spectrometers based on the detection signal of the NMR pulse techniques (spin echo Hannan and Carr - Purcell, etc.). In pulse NMR spectrometers, a magnetic system with at least 7 T B_0 is used (operating frequency not lower than 300 MHz). In high-resolution NMR spectrometers the magnitude of the magnetic field changes, in this case, the fields with induction of not lower than 11 T are used. In addition, for studies of substances with complex structure, especially liquid media (for example, biological fluids), BRUKER has developed an NMR spectrometer with a superconducting magnet with an operating frequency of 1.82 GHz.

Most laboratories are not equipped with a spectrometer or analyzer for full research of environments, as these devices require special maintenance and such studies are expensive. This problem occurs not only on research, but also in environmental monitoring sampling in the "manual" (biological and liquid media), especially in hard to reach places of waterbodies [1 - 3, 5].

In this situation, methods of express-controls that allow scientists to determine the state of the medium at the site of sampling are most important. But recently the methods of express-monitoring were required that the study should not change the chemical composition and physical structure of the taken substance. This is necessary to obtain confirmation of identified abnormalities in the study of the substance with high resolution devices in stationary laboratories (for example, when the customs control or quality assurance of products), as well as to establish of possible causes this deviation. Using the method of nuclear magnetic spectroscopy, which satisfies this requirement, is one of the solutions.

But as the NMR spectrometer should be easy to carry and self-powered (rechargeable batteries), the NMR signal needs to be registered in a weak magnetic field ($B_0 \leq 0.1$ T - operating frequency is above 4.2 MHz). Because basically the weight and size of the NMR spectrometer are determined by the design of the magnetic system and service its devices, the registration of the spectrum of the investigated medium using pulse techniques in this case is impossible [1- 3]. All this creates a lot of features in the study.

2. Features of the study of biological fluids and liquids in low magnetic fields.

The main parameters of condensed matter, which can instantly set changes in its aggregate state (temperature increase, the appearance in it of other substances dissolved or not), are the times of the longitudinal T_1 and transverse T_2 relaxation [6 - 9].

The longitudinal relaxation time T_1 is determined by the interaction of the spin magnetic moments of nuclei with their surroundings (hence its second name is spin-lattice) and characterizes the substance containing the nucleus [6 - 9].

Transverse relaxation time T_2 is determined by the interaction of the spins (on each spin effects field created by neighboring nuclei being different for different spins matter), so its second name is spin-spin. It describes the time during which the broken phase matching of nuclei precessional rotation, ie, decreases the nuclear magnetization vector transverse component of the material [6, 7].

Knowing the temperature of the investigated medium it is possible to compare the measured values of relaxation times T_1 and T_2 with a base and then conclude its state [4, 5, 8 - 12].

The measurement of two relaxation constants is needed because in water, alcohol and dairy liquids are repeatedly embodiments with various mixtures of hazardous substances, in which T_2 is as the initial medium at the most a temperature range [1 - 3, 5 - 7]. Simultaneous measurement of T_1 and T_2 eliminates the error in determining the state of investigated medium.

Another feature of the study is that the registration of the NMR signal is supplied from a small volume of the test medium. Therefore, recording the NMR signal may not be possible with all of nuclei with magnetic moments. The main condition for registration of the NMR signal is the sensitivity of the substance to a method of NMR should be not below 10. This is because rapid control is carried out in

a wide range of ambient temperature. When the temperature is more than 283 K the magnetic field changes. At signal-to-noise ratio is less than 1.3 it is quite difficult to configure the spectrometer device reception of the NMR signal on the resonance for measurements in automatic mode is. Therefore, the detection scheme is the NMR signal should have a high sensitivity and high gain that is hard.

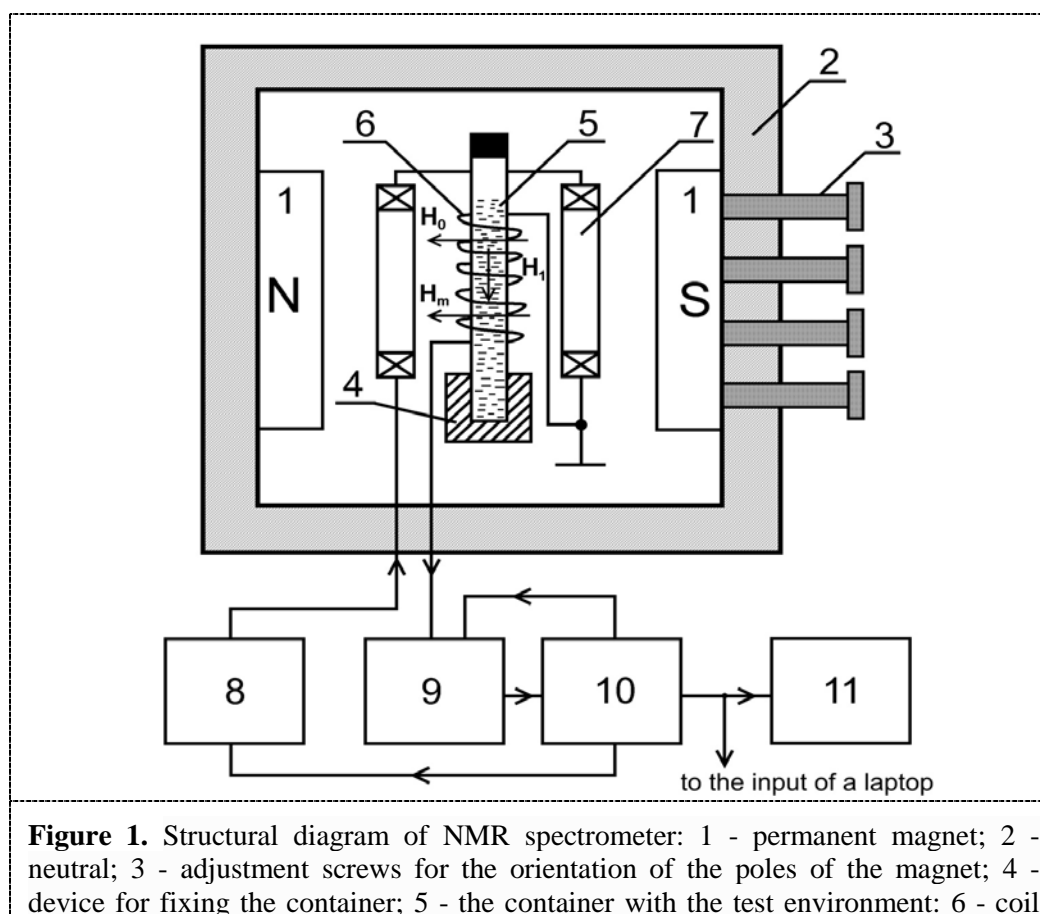
Measurement of the relaxation constants T_1 and T_2 of biological fluids and liquids are made using modulation techniques for registration of the NMR signal. Therefore, in contrast to the stationary spectrometers, other than adjusting the frequency of reception of the NMR signal f_{NMR} on resonance, it is necessary to provide automatic adjustment of frequency f_m and amplitude H_m field modulation B_0 and generation level (H_1 field) of registration scheme of the NMR signal to the maximum signal-to-noise ratio. Otherwise, the measurement of T_1 and T_2 in automatic mode will not be possible.

Compact nuclear magnetic spectrometer and the experimental results.

On the basis of previous studies, we have developed a design of compact NMR spectrometer. Its structural scheme is presented in Fig. 1.

In this design of the NMR spectrometer the distance between the poles of the magnets 1 is 12 mm, magnetic induction $B_0 = 62$ mT, the heterogeneity of $0.5 \cdot 10^{-3} \text{ cm}^{-1}$, the frequency of reception of the NMR signal for the protons $f_{\text{NMR}} = 2614$ kHz.

Registration of the NMR signal in such a weak magnetic field B_0 was carried out using the developed design of the low variance generator (autodin) 9, connected to the reception coil 6, which allowed us to record the NMR signal in the above-described magnetic system, from the volume of 0.2 ml and less. It was ensured that the low variance generator circuit is made on the basis of modern JFET with drain detection of the NMR signal and its further amplification. Such a scheme provides stability to operate in a wide frequency range with good rejection of common mode noise.



reception of the NMR signal; 7 - modulation coil; 8 - RF generator; 9 - generator low variance (autodin); 10 - device processing and control; 11 - oscilloscope.

Fig. 2.a presents the recorded NMR signal at the output autodin. The NMR signal is registered in wide bandwidth (10 kHz) with modulation frequency of the magnetic field $f_{\text{mod}} = 50$ Hz.

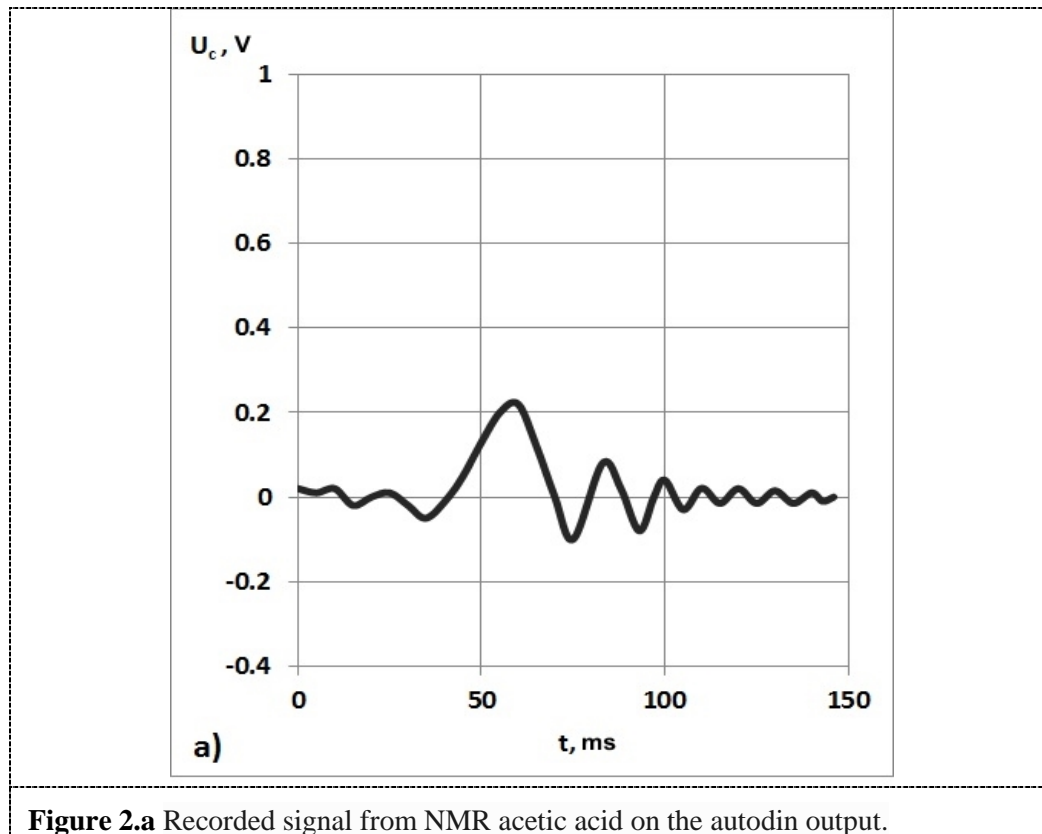
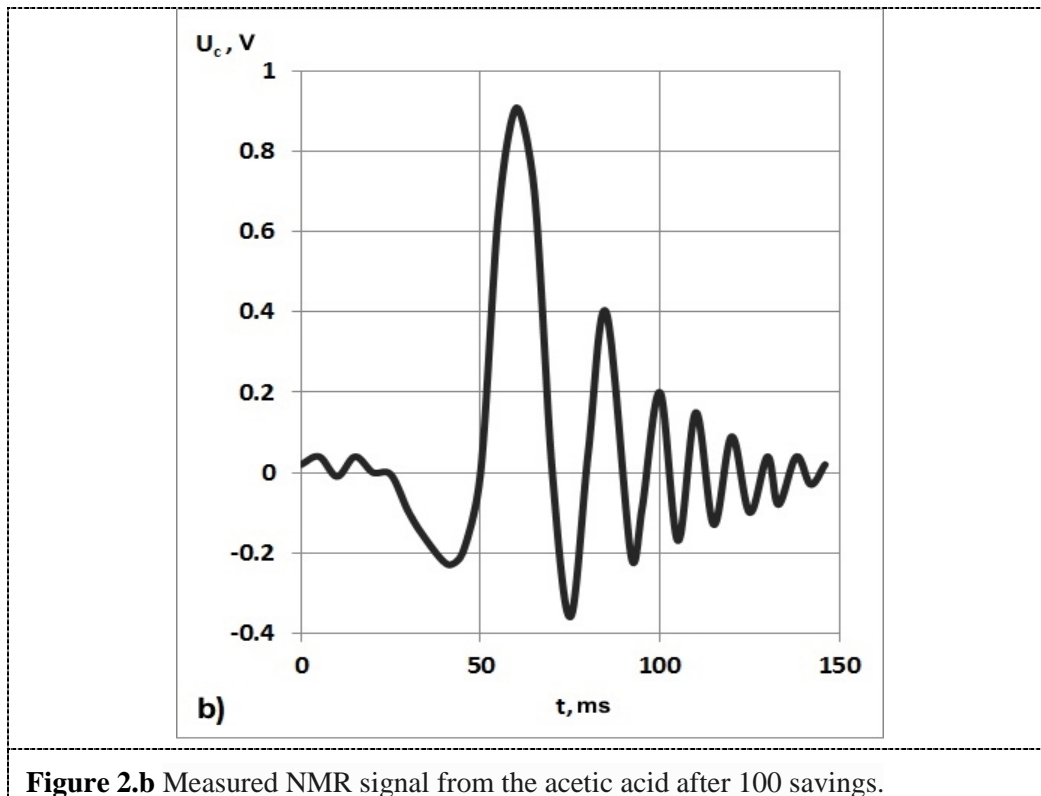


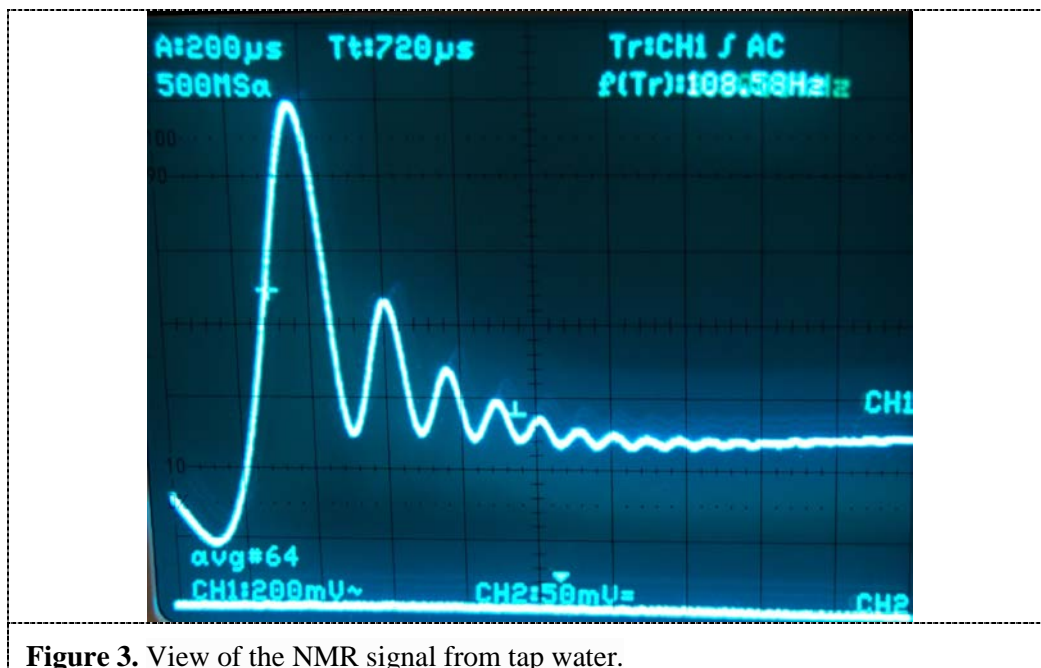
Figure 2.a Recorded signal from NMR acetic acid on the autodin output.

Determination of relaxation constants T_1 and T_2 using detectable NMR signals is discussed in detail in [1 - 3, 8]. Registered NMR signal (Fig. 2.a) despite the signal-to-noise ratio ≈ 4 does not allow measurement of T_1 and T_2 with an accuracy of 0.5 % [1 - 5]. Therefore, in the processing device and based on the STM32 microcontroller was implemented consistent scheme of accumulation of the NMR signal. The scheme is set to 100 and 1000 savings. This is due to the fact that the NMR signal can be registered in such fields not only protons, but also in the nuclei of fluorine - 19 (^{19}F), phosphorus - 31 (^{31}P), lithium - 7 (^7Li), sodium - 23 (^{23}Na), boron - 10 (^{10}B). But the attitude they SNR will be lower due to lower sensitivity to NMR method than that of protons.

Fig. 2.b presents the NMR signal at the output of the accumulation circuit. The line shape of the NMR signal obtained after accumulation allows the measurement of T_1 and T_2 with an accuracy of 0.5 %.



In Fig. 3 as an example of the detected NMR signal from tap water at $T = 283$ K without the use of circuits of accumulation is presented.



Modulation method of the NMR signal registration has a limitation on the application that is associated with the transversal relaxation time T_2 of condensed matter [2, 3, 5]. In environmental monitoring, especially when working with biological fluids T_2 may be above the limit of measurement

[6, 7]. In this case, the registration of the NMR signal will be impeded and the measurement impossible. Therefore, the developed NMR spectrometer has a breakpoint, allowing submitting the recorded NMR signal to the input of a personal computer. According to the observed NMR signal on the computer monitor it is possible to estimate the transversal relaxation time T_2 . That will allow us to know the presence of impurities in a biological solution.

4. Conclusion

The peculiarities of the NMR signal reception in weak magnetic fields in the design of compact NMR spectrometer allowed us to perform measurements of the relaxation constants at ambient temperatures from 276 to 313 K with an error of $< 1\%$ in the following ranges: T_1 – from 1 ms to 20 s, T_2 – from 0.5 ms to 2.0 s. The measuring time of the two relaxation constants does not exceed 10 seconds. In addition, it is possible to tune of the NMR frequency for the different types of nucleus, which allows establishing their presence in the medium and their relative concentration. This feature fundamentally distinguishes the developed spectrometer by existing small NMR relaxometry for measuring T_2 of only one nuclei type [1-3, 5].

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