New nondestructive method for determining the composition of components in biological objects in express mode

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Abstract. The new method for determining the components composition and their concentration in the express mode in biological objects and liquid suspensions is proposed. This method is based on the Bloch equations solutions for the components of the magnetization vector in case of registration of the NMR signal using a modulation technique in a weak magnetic field. It has allowed to measure not only the relaxation constants $T_1$ and $T_2$, using which it is possible determine the deviation degree of the medium from the standard state, but also the concentrations of the components included in mediums composition, at the site of sampling by a compact NMR spectrometer.

1. Introduction

Currently, one of the urgent problems of applied physics is the development of fast and reliable methods for the express control of the condensed medium state [1–6]. Such studies are particularly in demand in determining the liquid state (various aqueous solutions, gasolines, oil, biological complexes or suspensions, etc.), as well as granular media (various salts, biological objects in the form of powders, etc.) in express mode [6–10]. To solve these problems, a large number of instruments have been developed, but most of them are mainly designed for research of a certain type of medium (for example, oil, motor oil, milk, etc.). It should also be noted that the sample with the researched medium after the measurements performed on some of such devices cannot be used for re-investigation on high-resolution spectrometers in stationary laboratories in order to confirm the result [1, 2, 4–7, 10–13]. This is because research using such devices can cause irreversible changes in the medium structure. In accordance with the latest requirements for rapid control methods, such changes are unacceptable.

One of the possible solutions to this problem is the small-sized nuclear magnetic spectrometer (relaxometer) considered in [1, 5, 6]. We can determine the degree of deviation from the standard state in the express mode using measured values of the relaxation constants $T_1$ and $T_2$. Experiments showed that the express method of control using a nuclear magnetic spectrometer (relaxometer) is very much in demand when carrying out various researches of condensed media, biological solutions and medical suspensions, environmental monitoring, and also in cases of product quality testing [1, 5, 6]. In addition, studies of various media conducted by the method of nuclear magnetic resonance (NMR) do not cause irreversible changes in their chemical composition and physical structure, unlike other express methods [1, 3, 5–9, 13–16]. Recently before conducting various researches, especially when working with biological solutions and suspensions, as well as acids, salts, it has increasingly become necessary to determine in express mode not only the medium state but also components concentration of which it is made (e.g., HCl, NaF, NaOH or FeCl3), acidity (pH), etc. Experiments have shown that this is especially important if the medium is used after prolonged storage, transport, container changes, etc.
In previously developed NMR spectrometer (relaxometer), registering of the NMR signal was possible only at the resonant frequency $f_p$ of the protons contained in the researched medium. It does not allow solving new tasks of express control.

2. **Compact NMR spectrometer and measurement methods**

To solve the considered new problems, we developed a new small-size design of the magnetic system of the spectrometer and a scheme for registering the NMR signal (figure 1)

![Figure 1](image-url) **Figure 1** Structural scheme of compact NMR spectrometer: 1 — permanent magnet; 2 — inserts; 3 — neutral for the placement and alignment of the magnets; 4 — adjusting screws; 5 — modulation coil; 6 — NMR signal registration coil; 7 — locking device for the container with the researched medium; 8 — container with the researched medium; 9 — RF generator; 10 — registration scheme; 11 — processing and control unit; 12 — oscilloscope

In the new design of compact NMR spectrometer by reducing the degree of inhomogeneity of the magnetic field more than tenfold and increasing the induction $B_0$ by several times in the registration coil placement area 6 S/N of the detected NMR signal is increased by 13 times. This made it possible to register the NMR signal at the resonance frequencies of the other elements nuclei, for example, sodium or chlorine. For mediums consisting only of elements containing nuclei with magnetic moments (for example, HCl, NaF, or ZnCl2) we have created a method that allows determining concentration of elements in a medium using amplitudes of the registered NMR signals from different nuclei.

However, the most significant result obtained on newly developed design is NMR signal registration with amount of "wiggles" (oscillating peaks) not less than six. This allows us to carry out many measurements with higher precision and to develop a new method for determining components concentrations of a mixture, which is formed by substances that not enter into a chemical reaction (e.g., fats, multicomponent medical suspensions, oils, gasoline, etc.). NMR signal from such mixtures due to specific of its registration with use of modulation technique is the total signal from each of the components.

In our new method for describing the registered NMR signal, we use solutions of the Bloch equations in a rotating coordinate system [16, 17].

\[
\begin{align*}
\frac{du}{dt} + \frac{u}{T_2'} + \Delta \omega \cdot v &= 0 \\
\frac{dv}{dt} + \frac{v}{T_2'} - \Delta \omega \cdot u &= -\gamma H_1 M_z \\
\frac{dM_z}{dt} + \frac{M_z}{T_1} - \gamma H_1 v &= -\frac{M}{T_1}
\end{align*}
\]

where $\Delta \omega = \gamma H_0 - \omega$ — field frequency deviation from resonance, $M = \chi_0 H$ — magnetization of the investigated medium in the magnetic field of the spectrometer, $v(t), u(t)$ — absorption and dispersion signals.

If case of using a modulation technique to detect the NMR signal in a weak magnetic field, the value of $H$ varies as follows:
where $H_0$ — constant magnetic field, $H_m$ — modulation coil field, $\omega_m$ — modulation frequency (figure 1).

In this case, the change in the frequency deviation of the field from the resonance in the system of Bloch equations, with allowance for (2), will have the following dependence:

$$
\Delta \omega = \gamma H_0 + \gamma H_m \sin(\omega_m t) - \omega
$$

One of the features of registering the NMR signal in a weak magnetic field using the modulation technique is that its registering should be performed only at the resonance frequency ($\omega = \omega_0 = \gamma H_0$). In this case (3) takes the following form:

$$
\Delta \omega = \gamma H_m \sin(\omega_m t)
$$

At the resonant registering frequency $\omega = \omega_0$, taking into account (4), the system of Bloch equations (1) takes the following form:

$$
\begin{align*}
\dot{u}(t) + \frac{u(t)}{T_2} + \gamma H_m \sin(\omega_m t)v(t) &= 0 \\
\dot{v}(t) + \frac{v(t)}{T_2} - \gamma H_m \sin(\omega_m t)u(t) - \gamma H_1 M_z(t) &= 0 \\
M'_z(t) + \frac{M_z(t)}{T_1} - \gamma v(t)H_1 - \frac{M}{T_1} &= 0
\end{align*}
$$

where $M = \chi_0 H_0 + \gamma H_m \sin(\omega_m t)$ — magnetization of the investigated medium in the magnetic field of the spectrometer, $\chi_0 = N(1 + 1) \mu^2 \frac{\mu_0}{3kT}$ — statistical nuclear magnetic susceptibility, $N$ — concentration of paramagnetic particles, $\mu$ — particle magnetic moment; $k$ — Boltzmann’s constant; $T$ — absolute temperature.

This system of equations is solved for $v(t), u(t)$ and $M_z(t)$ components, taking into account the initial conditions:

$$M_z(0) = \chi_0 H_0; \quad u(0) = v(0) = 0$$

The experimental researches carried out by us showed that the dependence of the line $G(t)$ of the registered NMR signal from the substance in a weak magnetic field when tuning the autodyne detector circuit to the maximum of the S/N ratio is described by the following relation:

$$G(t) = \sqrt{A v^2(t) + B U^2(t)},$$

where $v(t), U(t)$ — absorption and dispersion signals, $A, B$ — coefficients determining the contribution to the NMR signal of the absorption and dispersion signals.

The obtained solution (6), which is in good agreement with the experimental results, made it possible to develop a technique for simulating the detected NMR signal from the mixture, by dividing the received signal into signals from its constituent components. Following relation can represent the shape of the registered NMR signal $G_m(t)$ from the mixture:

$$G_m(t) = \sum_{i=1}^{k} V_i \cdot N_i \sqrt{A_i v_i^2(t) + B_i U_i^2(t)}$$

where $v(t), U(t)$ — absorption and dispersion signals, $A, B$ — coefficients determining the contribution to the NMR signal of the absorption and dispersion signals (m — mixture, i — mixture components).
Since in the experiment all NMR signals, both from the mixture and its components, are formed in the same fields $H_0$, $H_1$, and $H_m$, the solutions obtained for their components $v(t)$ and $U(t)$ from the Bloch equations (5), differ only in the relaxation constants. For the mixture itself, $T_1$ and $T_2$ can be determined using NMR signal detected from it. In addition, we know relaxation constants for one of the mixture components, because initially this mixture should be this component in its pure form. The relaxation constants of the remaining components of the mixture, as well as the volumes in which they are contained in the researched medium, are chosen so that (7) is satisfied, the temperature of the researched mixture is known. When relation (7) is fulfilled, through relaxation constants we can determine mixture components, as well as their relative concentrations through their volumes.

3. Results of the research and their discussion

Figure 2 shows, as an example, the NMR signals from sodium hydroxide NaOH registered on sodium in the new design of the NMR spectrometer.

![Figure 2](image1.png)

**Figure 2** The registered NMR signal from sodium hydroxide at $T = 291.3$ K: a) without accumulation; b) output of accumulation scheme

The analysis of NMR signals presented in figure 2 shows that when they are registered at the resonance frequency of sodium nuclei $\omega_{\text{Na}}$, signal-to-noise ratio more than 1.3. This makes it possible to perform the AFC on the resonance of sodium nuclei. However, it is impossible to carry out measurements of $T_1$ and $T_2$ with an error no more than 1.0% (which is necessary for unambiguously determining the medium state medium [1–4, 6, 8]) without usage of an accumulation scheme since the SNR < 3.0 (figure 2.a). In addition, there are noises at the peaks of the NMR signal. The subsequent accumulation of the NMR signal makes it possible to obtain a SNR > 10.0 (figure 2.b), which ensures measurement of $T_1$ and $T_2$ with the required accuracy. Moreover, the relative concentrations of protons and sodium in sodium hydroxide can be determined using ratio between their amplitudes $U_s$ in registered NMR signal.

Figure 3 shows, as an example, the possibility of determining the components and their concentrations in a mixture of two gasolines AI-95 and A-76 using developed by us method applied to registered NMR signal.
Figure 3 NMR signal line forms. Graph 1 corresponds to the experimental signal from a mixture of gasoline AI-95 and A-76 in the proportion of 75% to 25%. The NMR signal simulation: from pure gasoline AI-95 and A-76 - graphs 2 and 3, mixture of gasoline AI-95 and A-76 in a proportion of 75% to 25% - graph 4.

Comparison of the results of NMR signals simulation from gasoline AI-95 and A-76, as well as on their mixture, with experiment shows the reliability of proposed method. The calculated concentrations of gasolines AI-95 and A-76 in the researched medium are within the measurement error with the concentrations that we have used to prepare this mixture.

4. Conclusion
The obtained results shows that the usage of proposed by us method while carrying out researches in a new design of a small-size NMR spectrometer allows obtaining information on the composition of the medium at the site of sampling, and drawing a conclusion about its further use without additional measurements in a stationary laboratory. Earlier in [1, 5, 6], the measurement of $T_1$ and $T_2$ only provided information on the presence of deviation from the medium standard state and required its additional study in a stationary laboratory to make a reliable decision on the further use of this medium.

In addition, in the new design of the spectrometer, realization of the NMR signal registration from various nuclei with magnetic moments greatly expands its functional capabilities both in the number of possible researched mediums and in the information obtained about the state of the medium itself.

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