New method for determining the composition of liquid media during the express control of their state using the nuclear magnetic resonance phenomena

N S Myazin¹, V V Davydov¹, V Yu Rud², V V Yushkova¹ and V I Dudkin⁴

¹Peter the Great St. Petersburg Polytechnic University, St. Petersburg 195251, Russia
²All-Russian Research Institute of Phytopathology, Moscow Region 143050, Russia
³Saint Petersburg University of Management Technologies and Economics, St. Petersburg 190103, Russia
⁴The Bonch-Bruevich Saint Petersburg State University of Telecommunications, St. Petersburg 191186, Russia
myazin.n@list.ru

Abstract. The processing of nuclear magnetic resonance (NMR) signals from various liquid media is an important step in monitoring their state. At the same time, the processing of NMR signals is quite a challenge during express control by NMR relaxometer. Therefore, the article substantiates the need to develop a new method for NMR signals processing. For this purpose, a universal mathematical model for describing the NMR signal from various media has been proposed. This model takes into account the features of recording signals using a modulation technique in a weak magnetic field. In addition, the article presents the results of calculations of the components concentrations in the studied mixtures of liquid media. Also these results are compared with the experimental data.

1. Introduction
At present one of the urgent tasks of applied physics is the development of reliable methods for performing express control of the condensed media state [1–7]. Express control methods are successfully used to solve various problems, such as environmental monitoring (especially water bodies) or quality control of fuel and motor oils [6–13]. In addition, they have become very popular for intermediate control during the production of drugs and biological solutions, as well as the quality of the finished product [3, 9, 11, 14-18].

There are many contactless methods (i.e. optical, ultrasonic, X-ray, electromagnetic) that allow conducting express control. However, not all of them are universal. This means that devices based on these methods are not suitable for the study of a large number of mediums. Therefore, different media may require different devices. Moreover, the main requirement for express control methods is that they should not change the physical structure and chemical composition of the studied medium. In other words, the method must be non-destructive. It is necessary to obtain confirmation on deviations in a given sample using high-resolution instruments in a stationary laboratory [7, 8, 13, 15, 19].

Results of numerous experiments have shown that the method based on the phenomenon of nuclear magnetic resonance (NMR) is the only one both universal and non-destructive [1–5, 11, 13, 14]. The only condition for the applicability of the NMR method is the presence of nuclei with magnetic moments in the medium [19–24, 31]. It should be noted that liquid media usually have hydrogen nuclei (protons) in their composition.
In papers [15, 25–28], we discussed in detail the various techniques used for recording the NMR signal. These papers show that express control of condensed media state can be carried out only using the modulation technique. For its implementation we have developed small-size NMR spectrometers and relaxometers [4, 11, 15, 25]. With their use, the times of the longitudinal \(T_1\) and transverse \(T_2\) relaxation of a condensed medium were measured. Moreover, NMR signals were recorded at the resonant frequencies of some nuclei [4, 11, 25, 26]. That information allows determining the deviation of the medium state from the standard one. The standard state of the medium is the state in which the ratio between the components, as well as the physical structure of the medium, is strictly observed. In this case, a series of measurements of the relaxation constants is carried out at different temperatures, thereby registering the relaxation constants corresponding to the standard ones.

However, the experience gained in conducting express control of various media, such as hydrocarbons or proteins, showed that this information may not be sufficient to make the right decisions about the future use of the medium. Often there are situations when it is necessary to establish what could have caused the deviations in the medium. One of the possible solutions to this problem may be the processing of the recorded NMR signal. This signal takes the form of damped non-periodic oscillation (“wiggles”). Since NMR signal depends on the composition of the medium, its processing may allow the determination of medium composition. The form and structure of this signal differs significantly from the classical NMR signals recorded using high-resolution pulsed NMR spectrometers and relaxometers. There are many theories based on the Bloch equations for describing NMR signals recorded in these pulsed devices. However, these theories cannot be used for NMR signals recorded in a weak magnetic field using a modulation technique. Various approximations are made in these theories. They do not correspond to the conditions of NMR signal registration in a weak field.

Therefore, we propose a mathematical model of the NMR signals recorded in a weak field, taking into account the previously established peculiarities [11, 25, 26]. Using this model, we develop a technique for “decoding” the structure of the NMR signal. That allows determining the state of the investigated medium and the concentration of medium components. Changes in concentrations may be one of the main reasons for the deviation of the medium state from the standard.

### 2. Mathematical model of the recorded NMR signal in a weak magnetic field

The motion of longitudinal and transverse components of the magnetization vector of the condensed medium in the NMR registration coil is described by Bloch equations [20–24]:

\[
\begin{align*}
\frac{dM_x(t)}{dt} + \frac{M_x(t)}{T_2} + \Delta \omega M_x(t) &= 0 \\
\frac{dM_y(t)}{dt} + \frac{M_y(t)}{T_2} - \Delta \omega M_y(t) + \gamma H_1 M_z(t) &= 0 \\
\frac{dM_z(t)}{dt} + \frac{M_z(t)}{T_1} - \chi_0 H_0 - \gamma H_1 M_z(t) &= 0
\end{align*}
\]  

(1)

where \(\Delta \omega = \omega_0 - \omega_{\text{nmr}}\) is the detuning of the NMR signal detection circuit frequency \(\omega_{\text{nmr}}\) from the magnetization precession frequency in the field \(H_0\) (\(\omega_0 = \gamma H_0\)), \(\gamma\) is the nucleus gyromagnetic ratio, \(\chi_0\) is the static nuclear magnetic susceptibility, \(H_1\) is the magnetic field of the detection coil, \(T_1\) and \(T_2\) are the times of longitudinal and transverse relaxation of a liquid medium, \(t\) is a time.

Papers [20–22] substantiate in detail the replacement of the components of the magnetization vector \(M_x\) and \(M_y\) \((1)\), as well as the transition to a rotating coordinate system. In a rotating coordinate system with new variables, equation (1) takes the following form:

\[
\begin{align*}
\frac{du(t)}{dt} + \frac{u(t)}{T_2} + \Delta \omega \cdot v(t) &= 0 \\
\frac{dv(t)}{dt} + \frac{v(t)}{T_2} - \Delta \omega \cdot u(t) &= -\gamma H_1 M_z(t)
\end{align*}
\]  

(2)
\[
\frac{dM_z(t)}{dt} + \frac{M_z(t)}{T_1} - \gamma H_1 v(t) = \frac{M}{T_1}
\]

where \( M = \chi_0 H \) is the magnetization of the studied medium in the magnetic field of the spectrometer, \( v(t) \) and \( u(t) \) are the absorption and dispersion signals.

If NMR signal registered in a weak magnetic field using modulation technique, the value of \( H \) changes as follows:

\[
H = H_0 + H_m \sin(\omega_m t)
\]  

(3)

where \( H_0 \) is a constant magnetic field, \( H_m \) is a modulation coil field, \( \omega_m \) is a modulation frequency.

Therefore, the change in the detuning of the circuit frequency from the resonance frequency in the system of Bloch equations (2), taking into account (3), will have the following form:

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

(4)

In this case, the Bloch equations (2) include a coefficient \( \gamma H_m \sin(\omega_m t) \), which have time dependency. The presence of this coefficient makes it impossible to use standard NMR spectroscopy methods to solve the equation (2). Therefore, in most of the papers the authors made the following approximation \( H_0 \gg \gamma H_m \sin(\omega_m t) \). Thus, assuming an insignificant effect of the modulation field on the magnitude of the magnetic field \( H_0 \). This allowed to perform an approximate solution of the Bloch equations and then introduce an additional member in their solution, which takes into account the modulation of the magnetic field.

The most accurate description of the NMR signal registered experimentally using modulation techniques was obtained in [21]:

\[
U(t) = U_0 \exp \left( -\frac{t}{T_2} \right) \cos \left( \omega_0 t + \frac{1}{2} \gamma \frac{dH}{dt} t^2 \right)
\]  

(5)

Taking into account (3), equation (5) takes the following form:

\[
U(t) = U_0 \exp \left( -\frac{t}{T_2} \right) \cos \left( \omega_0 t + \frac{1}{2} \gamma H_m \omega_m \cos(\omega_m t) t^2 \right)
\]  

(6)

Analysis of the obtained line shape using (6) shows that the recorded NMR signal does not depend on the value of the \( H_1 \) field. However, this parameter has a large impact on the signal being recorded using an autodyne detector. Figure 1 shows the recorded NMR signal from water at a temperature of \( T = 291.4 \) K and the result of fitting with function (6).

Figure 1. The NMR signal from water. The line 1 is the experimental data; the line 2 is the theoretical calculation of the line shape.
The calculation result presented in the figure 1 (the line 2) has a significant discrepancy to the experiment (the line 1). Such discrepancies with the experiment confirm the incorrectness of the use of (6).

The mathematical model of the registered NMR signal developed earlier by us [11, 23–29] allows reproducing the line shape up to 6 peaks with an error of about 3%. Using the result of the line shape calculation, we proposed a method for determining the composition of the liquid medium and the components concentrations of this medium.

Our further studies have shown that the accuracy of this technique may not be enough to make the right decisions on the use of the studied mixtures. Therefore, we have developed an addition to the previously proposed mathematical model [23–29]. This addition allows approximation of the NMR signals recorded during the express control of condensed media. In some cases, the use of the approximation allows reproducing experimental signals with high accuracy. In this addition to the mathematical model, we propose to “clamp” the experimental NMR signal between two envelopes. Envelopes have different attenuation coefficients. Figure 2 shows the approximation of the experimental NMR signal from water at a temperature \( T = 291 \) K.

![Figure 2. The NMR signal from water. The line 1 corresponds to the experimental data, the line 2 corresponds to the theoretical calculation of the line shape, and the lines 3 and 4 are the envelopes of the experimental signal.](image)

Based on our previous experimental results, as well as on results of other scientists, equations for the signal with two envelopes can be represented as follows:

\[
\begin{align*}
u(t) &= \frac{a \exp(-b t) + c \exp(-d t)}{2} \\
&+ \cos(g(t - t_0) + h(t - t_0)^2) \frac{a \exp(-b t) - c \exp(-d t)}{2},
\end{align*}
\]

where \( a, c \) are dimensionless parameters; \( b, d \) are attenuation coefficients (\( b \sim 1/T_2, \) \( d \) takes into account the inhomogeneity of the magnetic field \( H_0 \)); \( g \) is a parameter whose units of measurement are Hz, it takes into account the resonance frequency \( \omega_0 \); \( h \) is a parameter whose units of measurement are \( 1/s^2 \), it takes into account the modulation of the field; \( t_0 \) is used to correct the approximation in the time axis.

By selecting the coefficients \( b \) and \( d \), as well as the parameters \( a, c, g, h, \) and \( f \), the shape of the NMR signal line can be reproduced. Moreover, in this case, the fitting will be more accurate compared to the previously proposed mathematical model [25, 27, 28, 29]

3. Results and their discussion

Figure 3 shows, as an example, the result of comparing the line shapes (“wiggles”) of the recorded NMR signals with the fitting of their shapes.
Figure 3. The NMR signal from water (a) and mixture of gasolines AI-76 and AI-95 (b). The line 1 corresponds to the recorded NMR signal, the line 2 corresponds to the fitting of its shape, the lines 3 and 4 corresponds to the exponential envelopes.

Using the developed approximation it is possible to obtain a good agreement (see figure 3) between the experimental and calculated NMR curves.

The data obtained by approximation, as well as the previously proposed ratios in [11, 26, 29], allow us to determine the composition and components concentrations of various media. These can even be quite complex media, such protein compounds. Thus, this can be extremely useful in a variety of experiments, including long-term experiments.

For example, to study the molecular mechanism of protein-cell interaction it is necessary to determine the concentration of proteins in Eps13961 systems. Eps13961 proteins protect E coli cells from infection with bacteriophage X. These proteins are modified and unmodified, which determines their properties. The degree of modification depends on the ratio between their concentrations in the system, as well as on the presence of mChery and Venus coding proteins in the mixture. Thus, determining the concentration of Eps13961 proteins, mChery and Venus coding proteins, and water molecules in the mixture is an extremely important task. However, it is possible only on high-resolution spectrometers (fluorescent, NMR, EPR, etc.). This makes difficulties in some cases of carrying out research. Especially if medium should be preliminary checked before the experiments.

In order to confirm the method we have developed, a mixture of Eps13961 proteins has been studied. For the preparation of 100 ml of such mixture, 76 ml of Eps13961 protein, 6 ml of mChery protein, 8 ml of Venus protein and 10 ml of water were used. Figure 4 shows the NMR signal registered from this protein mixture in a small-size NMR relaxometer.
Figure 4. NMR signal line shapes. The line 1 corresponds to the experimental signal from the mixture. The lines 2 and 3 correspond to the result of calculation of NMR signals from mChery protein and water respectively. The line 4 corresponds to the result calculation of the mixture signal.

In figure 4, the NMR signals were calculated using the data obtained using our approximation technique, taking into account the peculiarities of NMR signal registration by an autodyne detector.

Using the methods developed by us \[19, 25, 26, 28\], the times of the longitudinal \(T_1\) and transverse \(T_2\) relaxation of the studied mixture were measured. It was established that they differ from the values of \(T_1\) and \(T_2\) corresponding to the standard state of this mixture. This means that other proteins, as well as water, may present in the investigated mixture. The calculated form of the NMR signal from the protein mixture (the line 4) coincided with the experiment (the line 1) only if the components Eps13961, mChery, Venus, and water were taken into account during the simulation of the medium, and their concentrations were 76%, 6%, 8%, and 10%, respectively.

In the small-size NMR relaxometer developed by us, the volume of the studied medium is 0.5 ml. Therefore, 0.5 ml of the mixture contains 0.38 ml of Eps13961 protein, 0.03 ml of mChery protein, 0.04 ml of Venus protein, and 0.05 ml of water.

This mixture was studied on a high-resolution spectrometer AVANCE III HD NMR (operating frequency 400 MHz). The obtained results confirmed the composition of the mixture and concentration of its components.

4. Conclusion
The mathematical model was supplemented by the use of approximation to describe the NMR signal. Based on the results of the experiments, it was found that the use of approximation allows us to bypass the restrictions on the use of this mathematical model \[25, 27–29\]. This significantly expands the possibilities of express control with the use of a small-size NMR relaxometer, especially in the study of biological solutions.

The results of the study of different media and their mixtures showed the reliability of the developed mathematical model and the validity of its use in express control.

5. References
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