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**ELECTROMAGNETIC RESONANCE SPECTROSCOPY IN
MULTIFUNCTIONAL SENSOR TECHNOLOGY
(Potential Applications of Electromagnetic Resonance
Spectroscopy within the Infrastructure and Ecosystem of the
Smart Pharmacist's Office as a Multifunctional Sensor Technology,
Including Medical and Biological Applications, Based on the
Innovative Concept Proposed by Specialist Tatiana Gladilina)**

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Abstract

This article investigates an experimental technology for the non-contact measurement of the acidity level of liquid biological media intended for application within the infrastructure of a smart pharmacist's office, intelligent pharmaceutical storage systems, and smart manufacturing environments of pharmaceutical production facilities. Particular attention is devoted to the development of an innovative measurement system based on various electromagnetic sensor configurations designed to improve the accuracy, speed, and technological efficiency of acidity monitoring while reducing dependence on conventional contact-based measurement methods.

The study demonstrates that existing standard techniques for acidity determination require mandatory preliminary calibration of measuring equipment using reference buffer solutions, which substantially increases the duration of the measurement procedure and limits the implementation of real-time automated monitoring in intelligent pharmaceutical manufacturing systems. The necessity of developing alternative engineering solutions capable of minimizing calibration-related constraints while improving the operational efficiency of measurement technologies is therefore substantiated.

Particular attention is given to a comprehensive series of experimental investigations performed using distilled water, tap water, and model samples of synthetic gastric fluid with controlled physicochemical properties. Concentrated hydrochloric acid prepared under laboratory conditions was used to modify the acidity of the test samples. Experimental measurements were carried out employing several electromagnetic sensor configurations, including a planar

sensor design that demonstrated the highest levels of sensitivity, measurement accuracy, and technological potential.

The analysis of the experimental results, together with an extensive international patent survey, indicates that the application of a planar electromagnetic sensor for the non-contact determination of the acidity of liquid biological media represents a novel engineering solution that has not previously been reported for this class of measurement systems. The obtained results demonstrate the significant potential of the proposed technology for the development of intelligent autonomous devices for continuous acidity monitoring, including miniaturized capsule-based systems intended for monitoring gastric fluid acidity.

Special emphasis is placed on the comprehensive evaluation of the metrological characteristics of the proposed measurement system. The experimental program included investigations of sensor sensitivity to variations in acidity, electrical conductivity, temperature, chemical composition of the test media, and the presence of organic inclusions. In addition, the repeatability of measurement results was evaluated, the obtained data were compared with the readings of conventionally calibrated reference instruments, and the maximum permissible measurement deviations for the monitored parameters were determined.

The obtained results confirm the feasibility and technological potential of employing planar electromagnetic sensors as the foundation of a new generation of intelligent measurement systems intended for digital pharmaceutical technologies, automated quality control of biological fluids, and integration into smart pharmaceutical manufacturing infrastructures. The proposed technology provides a promising basis for the further development of highly accurate non-contact monitoring methods and advanced intelligent medical and pharmaceutical measurement systems.

Keywords: *Pharmaceutical sciences; electromagnetic resonance spectroscopy; sensor technology; Smart Pharmacist's Office infrastructure; Smart Pharmacist's Office ecosystem; critical quality factor; measurement system for key quality parameters of pharmaceutical products following manufacturing and throughout storage prior to use; calibration of measuring instruments using reference buffer solutions with pH values of 4 and 7; calibration procedures performed before pH measurements; autonomous capsule for continuous monitoring of gastric juice acidity in cattle; planar sensor providing optimal integration with adjacent capsule components due to its significantly smaller dimensions while offering higher sensitivity and measurement accuracy*

Introduction

The measurement of the concentration and composition of components in liquid media, in accordance with the methodology and engineering concepts developed and proposed by Tatiana Gladilina, encompasses a broad spectrum of liquid systems, including true solutions, dispersed systems such as emulsions and suspensions, and biological fluids including blood, milk, lymph, urine, and other physiological media. Owing to the high sensitivity of the proposed sensor configurations, the developed technology has significant potential for application in a wide range of scientific, medical, pharmaceutical, and industrial fields.

Potential applications include:

- pharmaceutical manufacturing processes for the production and quality control of medicinal products;

- laboratory and point-of-care analysis of biological fluids, including blood, milk, urine, lymph, and other physiological samples;
- medical, industrial, and food microbiology for monitoring microbial concentrations and detecting the presence of viruses, including coronaviruses.

Electromagnetic Impedance Measurement of Biological Tissues

At present, the measurement of the electrical impedance of biological tissues over a range of alternating-current frequencies is widely employed in clinical diagnostics as well as in biological and medical research.

For example, a significant increase in tissue impedance at low frequencies enables inflammatory processes to be detected at their earliest stages. Certain thyroid disorders can

be diagnosed through variations in the phase shift between electric current and voltage.

Electrical impedance mammography has proven to be an effective technique for the early detection of breast cancer. Similarly, measurements of skin impedance facilitate the diagnosis of dermatological disorders, including the identification of amelanotic malignant melanoma, and may also be applied for detecting areas of skin surface contamination by coronaviruses.

Endoscopic impedance measurements can also be employed for the diagnosis of pathological conditions affecting internal organs. Additional applications include non-invasive blood analysis, such as the assessment of elevated blood glucose levels, as well as the evaluation of the physiological condition of lymphatic fluid.

The application of electromagnetic resonance spectroscopy to all of the above-mentioned impedance measurement techniques has the potential to substantially improve measurement sensitivity, selectivity, and diagnostic performance.

Furthermore, the proposed sensor technology may enable the detection of coronaviruses in the human throat during the early stages of infection.

Application of Electromagnetic Resonance Spectroscopy in Biosensor Technologies

The term *biosensor* generally refers to a device in which biological materials – including enzymes, tissues, bacteria, yeast, antigens, antibodies, liposomes, organelles, receptors, DNA, and viruses, including coronaviruses – interact directly with the signal generated by the proposed electromagnetic sensor and produce a resonance response functionally associated with the presence and concentration of the target biological component.

Within the framework of the proposed technology, this approach establishes a fundamentally new method for obtaining information regarding the chemical composition of liquid media.

The presence of biologically active materials possessing highly specific recognition properties enables the selective identification of target compounds within complex

multicomponent mixtures without the need for additional analytical procedures involving chemical reagents, biological reagents, sample concentration, or other conventional preparatory operations. Consequently, the proposed approach represents a reagent-free analytical methodology based on electromagnetic resonance spectroscopy, providing a promising platform for next-generation non-contact analytical systems in pharmaceutical, biomedical, and biotechnological applications.

Приложение 1

Potential applications of electromagnetic spectroscopy in multifunctional Sensor Technology in medicine and biology

I. Measurement of the concentration and composition of components in liquids

These include mixtures of both solutions and dispersed systems: emulsions, suspensions, and biological fluids (blood, milk, lymph, urine, etc.). Due to the high sensitivity of the proposed design options for sensors, the proposed technology can be widely used:

1. In the pharmaceutical industry in technological processes for the production of medicines.

2. For laboratory and off-laboratory analyzes of biological fluids: blood, milk, urine, etc.

3. In medical, technical and food microbiology for monitoring the concentration of microorganisms and the presence of viruses, including the corona viruses.

II. Measurement of the electromagnetic impedance of biological tissues of the body
Currently, the measurement of the impedance of biological tissues at different frequencies of alternating current is widely used in diagnostics, as well as in biological and medical research. For example, a significant increase in tissue impedance at low frequencies can detect inflammation in the early stages. Some thyroid diseases are diagnosed by a change in the phase angle between current and voltage.

Electro – impedance mammography is an effective method for early diagnosis of breast cancer.

Measuring the impedance of the skin helps to diagnose skin diseases, for example, to detect unpainted malignant melanoma and also to identify foci of contamination of

the surface of the skin of the corona viruses. To identify the pathology of the internal organs, an endoscopic impedance measurement can be used. This also includes a non-invasive blood test, for example, for the presence of high sugar levels, and an analysis of the state of lymphatic fluid.

In all the fields of application of impedance measurements listed above, the technology of electromagnetic spectroscopy can contribute, significantly increasing the sensitivity of such measurements.

In addition, the use of these sensors can detect the presence of a corona of viruses in the throat of a person in the initial stages of infection

The use of methods and technologies of electromagnetic spectroscopy in biosensors

The term “biosensor” is usually understood as a device in which biological material: (enzymes, tissues, bacteria, yeast, antigens / antibodies, liposomes, organelles, receptors, DNA, viruses, including corona viruses), directly respond to the presence of a signal from of the proposed sensor and generates a resonant signal functionally associated with the presence and concentration of this component.

In this case, using the proposed device implements a fundamentally new way of obtaining information about the chemical composition of the solution. The presence of a biomaterial with unique properties in the solution allows high selectivity to determine the desired compounds in a complex mixture, without resorting to any additional operations associated with the use of other reagents, concentration, etc. (hence the name – analysis methods without chemical and biological reagents).

Appendix 2.

Methodology for Selecting the Operating Frequencies of Resonant Sensors

This methodology describes the initial stage required for the development of a monitoring system intended to determine the concentration of components within a test mixture.

For the purposes of this methodology, a **mixture** is defined as any combination of components in which one component predominates by volume and is regarded as the **reference solvent**, while the remaining

components are regarded as **target analytes** (reference dissolved components).

The concept of a *reference solvent* is not limited to a single liquid substance capable of dissolving other materials. It may also comprise a mixture of gaseous, liquid, or even solid substances (for example, a compound material) that serves as the base medium for the formation of solutions, suspensions, aerosols, foams, or other heterogeneous systems.

Accordingly, the target analytes may exist not only in dissolved form but also as suspended particles, bacterial colonies, aerosol droplets, gas bubbles within foams, or filler particles incorporated into composite materials.

Determination of the Optimum Operating Frequency for a Single-Component Monitoring System

Such a monitoring system is intended for technological processes in which the concentration of a single component may vary while the concentrations of all remaining components remain constant.

Preparation of Test Samples

Two samples shall be prepared with concentrations of the target component corresponding to the lower and upper limits of the expected concentration range.

Frequency Scanning

The prepared samples shall be scanned over the entire operating frequency range of the measuring instrument (in the present study, from **0.100 MHz to 170 MHz**).

During the frequency sweep, the measurement system records the variations in both:

- the amplitude of the current passing through the sample; and
- the phase shift between the measured current and the applied harmonic excitation voltage of stabilized constant amplitude.

Analysis of Measurement Results

Following completion of the frequency scan, several frequencies shall be selected at which:

- the difference between the measured current amplitudes of the investigated samples reaches its maximum values; and
- the difference between the corresponding phase shifts reaches its maximum values.

The selected frequencies constitute the initial design parameters for the development and fabrication of prototype resonant sensors.

Selection of the Optimum Sensor

The frequencies identified during the preliminary scanning stage should be regarded only as initial estimates.

To determine the optimum operating frequency for a single-component concentration monitoring system, each prototype resonant sensor shall subsequently be evaluated using at least ten test samples covering the entire anticipated concentration range of the target component, rather than only the two samples employed during the preliminary frequency selection stage. Following experimental evaluation of all prototype sensors, the most suitable sensor may be selected. Preference should be given to sensor designs that exhibit not only high measurement sensitivity but also a monotonic relationship between the measured response and the concentration of the monitored component, thereby facilitating subsequent calibration procedures.

From the standpoint of electromagnetic interference immunity, lower operating frequencies are generally preferable. In addition, practical mechanical and structural design constraints should be taken into account during the final sensor selection process.

Determination of the Optimum Operating Frequencies for a Two-Component Monitoring System

Such a monitoring system is intended for technological processes in which the concentrations of two target components may vary simultaneously, while the concentrations of all remaining mixture components remain unchanged.

Preparation of Test Samples

Two samples shall be prepared for each target component, with concentrations cor-

responding to the lower and upper limits of their anticipated concentration ranges. In addition, a reference sample shall be prepared in which both target components are completely absent.

These samples provide the experimental basis for determining the operating frequencies that maximize the sensitivity and selectivity of the resonant sensor system with respect to simultaneous variations in the concentrations of the two monitored components.

Frequency Scanning

The prepared samples shall be scanned over the entire operating frequency range of the measuring instrument (in the present study, 0.100 MHz to 170 MHz).

During the frequency sweep, the measuring instrument records the response of each sample by measuring:

- variations in the amplitude of the electric current passing through the sample; and
- variations in the phase shift between the measured current and the applied harmonic excitation voltage of stabilized constant amplitude.

The recorded amplitude and phase characteristics constitute the basis for the subsequent selection of the operating frequencies of the resonant sensors.

Analysis of Measurement Results

For each target component, the frequency scanning results shall be analyzed to identify:

- frequencies at which the differences in the measured current amplitudes between the investigated samples reach their maximum values;
- frequencies at which the differences in the measured phase shifts reach their maximum values; and
- frequencies, or frequency ranges, at which the sensor exhibits sensitivity to one target component while remaining substantially insensitive to the other.

The resulting frequency sets shall then be compared to determine the most appropriate strategy for selecting the operating frequencies of the resonant sensors. Depending on the comparison results, several alternative selection algorithms may be applied.

Case 1. Frequencies Exist That Are Selective to Only One Component

This represents the most favorable scenario for constructing a two-component concentration monitoring system.

If such selective frequencies exist for both target components, the selection of the operating frequencies is straightforward. Prototype resonant sensors should be designed to operate at frequencies where the sensitivity to one component is negligible while the sensitivity to the other component is maximized. At least one operating frequency should be selected for each target component.

If selective frequencies exist for only one of the two components, the operating frequency for that component should be selected where its sensitivity is maximal and the sensitivity to the other component is minimal or absent. For the second component, frequencies should be selected from its candidate frequency set where the difference in sensitivity between the two investigated components is greatest.

Case 2. No Fully Selective Frequencies Exist, but the Frequency Sets Differ

If no frequencies are completely selective for either component, yet the candidate frequency sets identified for the two components do not coincide, prototype resonant sensors should be designed using frequencies that provide the maximum difference in sensitivity between the investigated components.

Case 3. The Candidate Frequency Sets Coincide

This represents the most challenging scenario for developing a two-component concentration monitoring system.

If the candidate frequency sets for both components completely coincide, it is necessary to determine whether the proportional relationship between the amplitude variations or phase-shift variations remains identical at all frequencies.

If this proportional relationship is preserved throughout the entire frequency range, an additional frequency scan should be performed using different excitation voltage levels.

If no differences can be identified following repeated measurements, the investigated

components are likely to be indistinguishable by means of electrochemical impedance spectroscopy alone.

Nevertheless, prototype resonant sensors operating at several frequencies corresponding to the highest measurement sensitivity should still be fabricated and experimentally evaluated. Unlike the measuring instrument used during the preliminary scanning stage, a resonant sensor produces a more complex interaction with the investigated sample owing to the additional influence of its resonant electromagnetic field.

If testing demonstrates a change in the proportional sensitivity to concentration variations at even a single operating frequency, the development of a monitoring system capable of discriminating between the investigated components becomes fundamentally feasible. Furthermore, the greater the difference in sensitivity ratios between the components, the higher the selectivity of the resulting monitoring system.

Selection of the Optimum Resonant Sensors

The operating frequencies identified through the preliminary frequency-scanning procedure should be regarded only as initial design parameters.

To determine the optimum operating frequencies for a two-component concentration monitoring system, each prototype resonant sensor shall subsequently be evaluated using at least ten test samples containing different concentrations of the investigated components distributed across their anticipated operating ranges.

Following the experimental evaluation of all prototype sensors, the optimum sensor pair may be selected. Preference should be given to sensors that exhibit not only high sensitivity but also a monotonic relationship between sensor output and the concentrations of the monitored components, thereby facilitating subsequent calibration and quantitative analysis.

Lower operating frequencies are generally preferred because they provide improved immunity to electromagnetic interference.

In addition, practical mechanical, structural, and manufacturing constraints shall also be considered during the final selection of the resonant sensors.

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