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Sensors

Dual-channel SPR biosensor for enhanced glioma relapse diagnostics: Blood cell aggregation as a biomarker for tumor malignancy

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Abstract. A biosensor based on the surface plasmon resonance (SPR) phenomenon has been developed for the express diagnosis of brain gliomas relapse by assessing blood cell aggregation indicators. The device features two optical channels, allowing for two studies to be performed simultaneously or enabling one channel to be used as a reference. This approach significantly increases biosensor sensitivity by reducing the impact of external factors. The optical excitation source is a *p*-polarized semiconductor laser with a 650 nm wavelength. The sensing elements were F1 optical glass plates with a refractive index of 1.61, with sputtered layers of chromium (5 nm) and gold (45…50 nm). As a result of the studies, a correlation was ascertained between the level of peripheral blood cell aggregation in patients and the degree of malignancy of gliomas. A statistically significant difference ($p \leq 0.05$) was found between the groups of conditionally healthy individuals and those with grade II-IV gliomas. A decrease in the shift of the SPR curve during blood testing indicates an increase in cell aggregation levels and a decrease in their electric charge on membranes. This trend gradually intensifies with the increasing degree of glioma malignancy, reaching minimal values in patients with grade IV gliomas, indicating changes in the physicochemical properties of cell membranes and a reduction in their electric charge.

Keywords: biosensor, surface plasmon resonance, brain glioma, blood cell aggregation.

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1. Introduction

Gliomas of the brain refer to a group of primary tumors that arise from the brain parenchyma. According to statistics, the incidence of this disease is 5–10 cases per 100,000 people [1]. Moreover, this pathology is the most common among primary brain tumors. Gliomas can be diagnosed in both children and adults, although certain types are characteristic of specific age groups. These tumors vary in growth rates and degrees of malignancy. The consequences of their development can differ significantly, depending on the tumor's location and type. However, any brain glioma, whether malignant or benign with active growth, leads to impaired brain function.

The manifestations of a glial brain tumor can vary widely depending on its location [2]. The most characteristic symptoms include persistent headaches that do not subside even after taking pain relievers; nausea, possibly with vomiting; seizures; paralysis of various body parts; coordination problems; memory issues; hallucinations; and personality changes. However, the same symptoms can occur with different types of brain tumors as well as other conditions. Therefore, when these symptoms appear, it is crucial to undergo an examination to determine the exact cause of these manifestations. As the tumor grows, it can affect neighbouring brain regions, exacerbating symptoms, and potentially leading to coma, paralysis, and respiratory disorders.

There are several classifications applied to glial tumors, differing by cell characteristics and degrees of malignancy [3]. Today, the WHO classification is used in medicine, which defines four grades of malignancy. Grade I tumors do not undergo malignant transformation and are classified as benign gliomas. Grade II tumors are considered "borderline" and are referred to as low-grade gliomas characterized by atypical cells but grow slowly, with a generally favourable prognosis. Grade II cells can transform into Grade III tumors that exhibit relatively rapid growth. The most aggressive are Grade IV gliomas that grow very quickly, whereas the prognosis in the presence of this tumor is unfavourable.

The prognosis upon diagnosing a brain glioma can vary significantly depending on the type of tumor. Patients can live for a long time with benign gliomas, whereas aggressive forms, namely diffuse brain gliomas or glioblastomas, are poorly responsive to therapy and have unfavourable outcomes. However, nowadays, medicine operates with methods that, even for aggressive brain tumors, can significantly extend life expectancy and improve quality of life, if not fully cure the disease. The most important task in these cases is early diagnosis.

Among modern methods, magnetic resonance imaging is the most informative for diagnosing brain cancer [4, 5]. Positron emission tomography, scintigraphy, and angiography of the head vessels are also used. Laboratory testing of cerebrospinal fluid is performed as well. Using these examinations, the presence, size, and location of the tumor can be determined, but it is impossible to accurately ascertain the tumor type. For a definitive diagnosis, cell samples must be taken from the tumor for histological laboratory analysis. The drawbacks of this method include the complexity and high invasiveness of obtaining material for analysis and the lengthy diagnostic process.

Surface plasmon resonance (SPR) sensors have become essential in cancer relapse diagnostics due to their high sensitivity and ability to monitor biomolecular interactions in real time [6–10]. These sensors work by detecting changes in light interaction at the sensor surface, allowing for precise, label-free detection of cancer-specific biomarkers. The SPR technology plays a crucial role in enhancing early cancer relapse detection, enabling timely interventions and personalized treatments, ultimately improving patient outcomes and reducing healthcare costs by promoting more effective disease management.

One of the most crucial parts of the SPR biosensors is the sensor surface, which plays a vital role in the overall sensing performance. Many studies have focused on the exploitation of smart sensing layers to implement more versatile applications [7, 11]. At the same time, some limitations of conventional SPR biosensors remained to date, namely the low sensitivity of direct label-free assays for small molecules, the limitations in multiplex analysis, fouling or instability of the SPR sensing surface when subjected to complex or harsh environments, the difficulty to perform continuous monitoring. Among various SPR sensors, the most commonly used are chip-SPR devices. These prism-based setups use a high refractive index prism covered with a metal film for implementing the total internal reflection of the incident light and exciting the surface plasmons. Several configurations of chip-SPR sensors are developed based on the variation of sensor parameters: angle-based systems, for instance, by Biacore instruments, BioNavis, Reichert Technologies; wavelength-based sensors and intensity-based sensors developed by Horiba, IBISWorld and Sierra Sensors [11]. Besides selectivity, sensitivity, linearity, reproducibility and stability, response time is a very important parameter. In this work, we present a system based on a dual-channel SPR biosensor used for express diagnostics of brain gliomas relapse.

2. Experimental details

2.1. SPR sensor

A biosensor “Plasmon” [12] has been developed at the V. Lashkaryov Institute of Semiconductor Physics of the National Academy of Sciences of Ukraine. It is based on the SPR phenomenon and employs a classical Kretschmann optical configuration [13] and angular scanning to determine the concentration of biomolecules or molecular complexes.

The main working principle of the biosensor involves irradiating the interface of two media with different refractive indices (n_1 and n_2, where $n_1 > n_2$) with a *p*-polarized electromagnetic wave from the side of the optically denser medium. As a result of mechanical scanning of the incident angles, the intensity of the reflected light is recorded, allowing for the detection and quantitative analysis of biomolecules adsorbed at the interface. The mathematical processing of the obtained data is performed using a specially developed algorithm.

The biosensor system is built based on a total internal reflection prism (*2*, Fig. 1) made of optical glass grade F1 (n = 1.61) [14].

The angle between the input face of the prism, where the laser beam enters and exits, and the working face with the installed gold-coated glass substrate (*3*, Fig. 1) is 65°, which corresponds to the excitation conditions of SPR for aqueous solutions with a refractive index close to n = 1.33. The prism also has an additional angle of 90°, which ensures the parallel course of the incoming (*1*, Fig. 1) and outgoing rays (*4*, Fig. 1).

For mechanical scanning of the incident angle of the *p*-polarized electromagnetic wave, a system with a stepper motor (*6*, Fig. 2) and a cable drive (*7*, Fig. 2) with a Kevlar thread (*8*, Fig. 2) is used [15]. This solution ensures uniform and stable rotation of the prism (*2*, Fig. 2) without the influence of the motor stepping, which enhances the accuracy and stability of the measurements.

A unique feature of the system is the use of a cable drive with a Kevlar thread, which provides tensile strength and the necessary elasticity for the uniform rotation of the sample block. This solution minimizes the influence of mechanical obstacles on the accuracy of measurements, reduces the cost of the device, and allows for

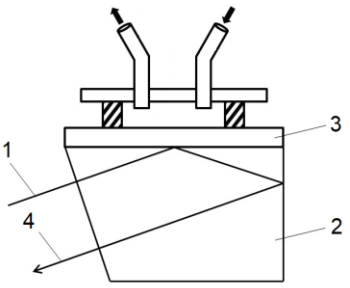

Fig. 1. Schematic presentation of the total internal reflection prism used in the biosensor “Plasmon” [14]. The components are as follows: *1* – input beam, *2* – prism, *3* – gold-coated glass substrate and *4* – output beam.

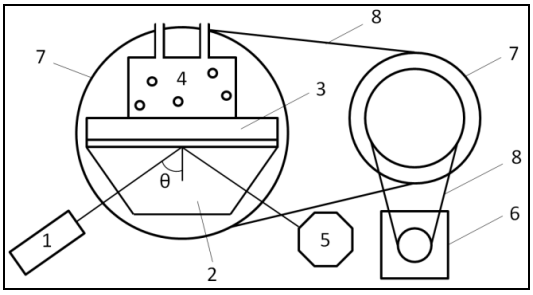

Fig. 2. Block diagram of biosensor "Plasmon" [15]. The components are as follows: *1* – semiconductor laser, *2* – prism, *3* – gold-coated glass substrate, *4* – measurement cell, *5* – photodetector, *6* – stepper motor, *7* – cable drive, *8* – Kevlar thread.

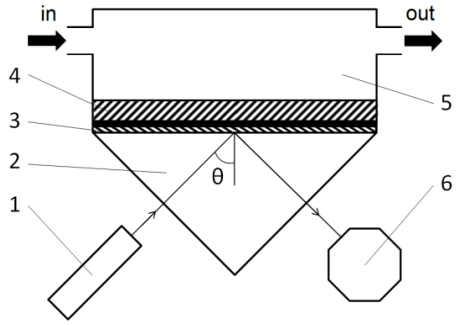

Fig. 3. Configuration of plasmon excitation in the biosensor "Plasmon" [16]. The components are as follows: *1* – semiconductor laser, *2* – prism, *3* – chromium adhesion layer, *4* – plasmon-supporting gold layer, *5* – measurement cell, and *6* – photodetector.

scanning angles up to 17°, enabling the investigation of layers with refractive indices ranging from 1.33 to 1.50.

Another problem that often arises when using biosensors is related to the stability of the plasmon-supporting gold layer (*4*, Fig. 3), which can become delaminated over time due to repeated washing or wiping when handling different samples that are passed through the measuring cell (*5*, Fig. 3). To avoid this, an additional adhesion layer of chromium (*3*, Fig. 3) is used between the sensing surface of the prism (*2*, Fig. 3) and the plasmon-supporting gold layer (*4*, Fig. 3) in the biosensor [16]. Chromium increases the adhesion of gold to glass, ensuring the stability and repeatability of measurements (Fig. 3). This approach minimizes distortion of the SPR curve and maintains its precise position even during prolonged studies.

The optical system of the biosensor is based on a *p*-polarized semiconductor laser with a 650 nm wavelength. The sensitive chips with the dimensions of 20×20×1 mm are made of F1 glass (n = 1.61), onto which the SPR gold layer is deposited.

After manufacturing, the chips are stored in a container filled with nitrogen to ensure their cleanliness until the sample investigation. The biosensor has two optical channels, allowing for two simultaneous studies or using one channel as a reference for differential measurements (Fig. 4).

This significantly increases the device sensitivity since most external factors that can affect the experiment performance and obtained results are excluded. For the analysis of peripheral blood cells, it is important that the sensor chips can be reused after rinsing with Ringer's solution. The interaction of surface plasmons with blood cells leads to a shift in the minimum of the SPR curve, which is recorded and processed by the biosensor. This allows for the assessment of the kinetics of blood cell aggregation and presents the results graphically on a computer monitor.

To increase the accuracy of measurements, an additional chromium adhesion sublayer is employed. It does not affect the SPR minimum that defines the working point while having a positive impact on the reproducibility of the results. The selected thickness of

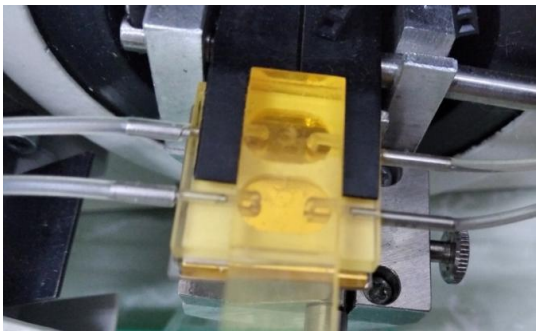

Fig. 4. External view of the dual-channel measurement cell of the SPR biosensor "Plasmon-6" placed above the gold film.

the chromium layer (2…8 nm) ensures maximal adhesion of the gold layer deposited on it and gives minimal absorption of laser irradiation. The thinner Cr layer does not increase the adhesion of the Au layer, while the thicker Cr layer (over 8 nm) significantly increases the absorption of laser irradiation, lowering the sensor sensitivity.

2.2. Materials

The object of the study was peripheral blood cells from patients in the neurosurgery department of the A.P. Romodanov Institute of Neurosurgery, National Academy of Medical Sciences of Ukraine, collected upon their admission to the clinic before treatment. Heparinized venous blood was taken from patients before the onset of treatment and was separated by centrifugation (3000 rpm for 10 min) into blood cellular components and plasma. The cell fraction was used to determine the minimum shift of the SPR curve, reflecting the degree of blood cell aggregation [17–19].

The patients were grouped among those without accompanying inflammatory diseases. The sizes of the gliomas were determined using the Siemens "SOMATOM CR" MRI scanner measuring their diameter and volume (in cm). Patients with hypoproteinemia, autoimmune diseases and so on that could affect blood

cell aggregation as well as those with conditions requiring the use of salicylates were excluded from the groups for investigation. Control blood samples were also analyzed, being collected from healthy individuals at a blood transfusion center. Besides, the comparison group included aggregation levels of blood cells from patients with moderate traumatic brain injury (TBI).

3. Experimental results

Activation of inflammatory processes in the body begins with a decrease in the electrical charge of blood cells, leading to increased aggregation. In a healthy organism, erythrocytes carry a negative charge and repel each other. The degree of aggregation rises with a reduction in the activity of gradient-forming membrane enzymatic systems and an increase in the concentration of acute-phase proteins in the blood plasma that are the markers of the inflammatory process (namely, fibrinogen, C-reactive protein, ceruloplasmin, sialic acids, immunoglobulins, *etc*.). This study demonstrates the relationship between the aggregation levels of peripheral blood cells in patients and the degree of malignancy of brain gliomas.

3.1. Diagnosis of the disease

To determine inflammatory processes, specifically those associated with oncology, the ratio of the SPR sensor responses to the deposition of red blood cells from the whole blood of patients on the surface of the gold film of the sensor was assessed. The estimations were carried out for both with the addition of deionized water and with the addition of an aqueous solution of verapamil, according to the methodology described in the work [17]. The studies were performed at room temperature. The SPR sensor response was defined as the difference between the angle positions of the minima of measured reflection characteristics (Fig. 5) for deionized water and the aqueous-blood mixture after the completion of the red blood cell deposition process.

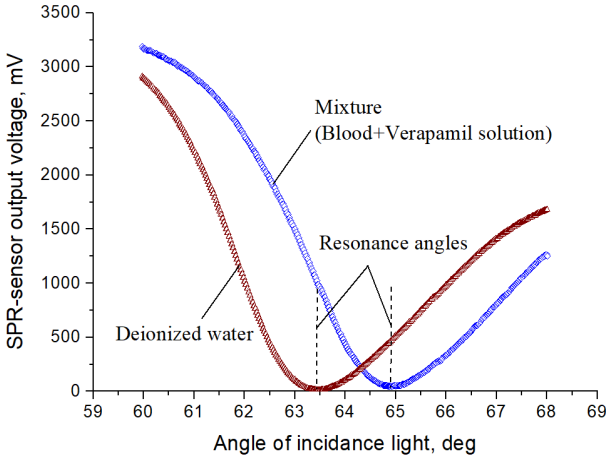

Fig. 5. Measured SPR sensor reflection characteristics for deionized water and the aqueous-blood mixture after the completion of the red blood cell deposition process.

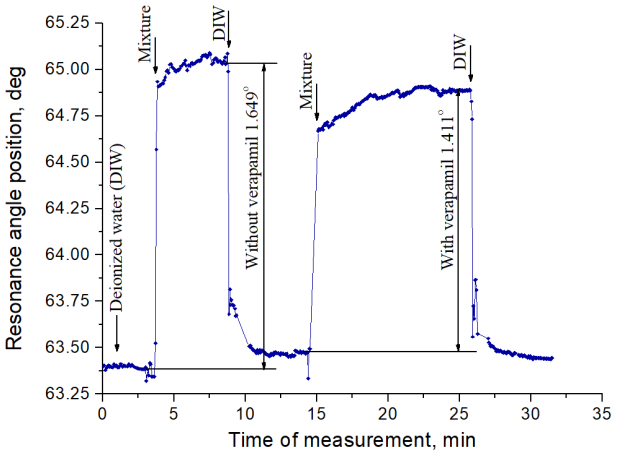

Fig. 6. Sensor response measured by the Plasmon-6 device showing the change of the minimum reflection characteristic over time during the sequential substitution of deionized water (DIW) with the corresponding aqueous-blood mixtures: without verapamil and with it.

According to the methodology [17] for measuring, the reflection characteristics and the sensor response minima changes over time, the sequential substitution of deionized water with the corresponding aqueous-blood mixtures was performed in the SPR sensor measurement cuvette with a volume of 70 μL, which ensured direct contact of the liquid with the surface of the gold film (Fig. 5). The substitution was performed manually using a 2 mL syringe.

To prepare the corresponding mixtures, 2 μL of water (or verapamil solution) and 2 mL of whole blood were taken. The dilution of verapamil was 1:10,000.

The deposition process was observed as an angular shift over time of the resonance minimum (Fig. 6). The completion of the red blood cell deposition process was determined by the change in the resonance angle, specifically when its value plateaued. For example, at the 25th minute of the sensorogram, the resonance angle value changes weakly, indicating the completion of the deposition process. The sensor response values were as follows: for the aqueous-blood mixture without verapamil – 1.649 degrees, and for the case with verapamil – 1.411 degrees. The response shows that the red blood cell deposition process with the application of verapamil was slower than without it.

Since the response for the case with verapamil was smaller in magnitude than without it, this indicates the initial stage of the inflammatory process.

3.2. Dependence of the SPR response on glioma grade

The examination of SPR parameters using blood cells revealed a statistically significant difference ($p \leq 0.05$) between the group of healthy individuals and neuro-oncological patients with gliomas II-IV grade of malignancy (Fig. 7). A decrease in the shift of the SPR curve during the examination of blood cells indicates an

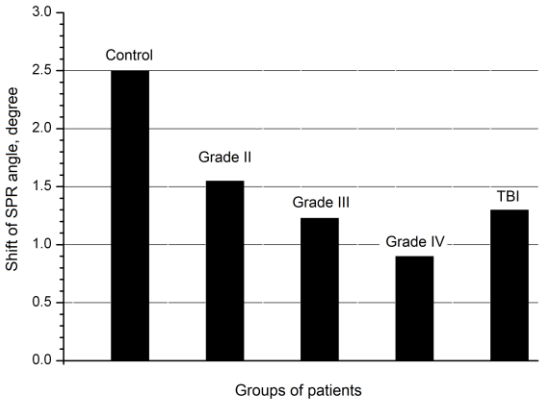

Fig. 7. Shift of the SPR curve during blood analysis of patients with different stages of glioma, control group, and patients with TBI.

increase in blood cell aggregation and a reduction in their electrical charge on the cell membranes. The trend towards decreasing SPR parameters for peripheral blood cells in patients with gliomas II-IV grade of malignancy, with the lowest values recorded for patients with high-grade gliomas (IV).

A decrease in SPR parameters when testing patients with gliomas indicates changes in the physicochemical characteristics of blood cell membranes, particularly a reduction in transmembrane potential, closely related to changes in the dielectric constant [20].

Fig. 8 illustrates a schematic representation of the erythrocyte layer deposited on the sensor chip. In Fig. 8a, the erythrocyte layer exhibits a low level of blood cell aggregation, characteristic of a healthy individual. In this case, erythrocytes densely fill the sensor surface, contributing to the maximum response of the SPR biosensor. In Fig. 8b, the erythrocyte layer from patients with brain glioma shows a high level of blood cell aggregation. The low electrical charge on the membranes of peripheral blood cells promotes erythrocyte clumping, leading to minimal contact with the sensor surface and, consequently, reduced response from the SPR biosensor.

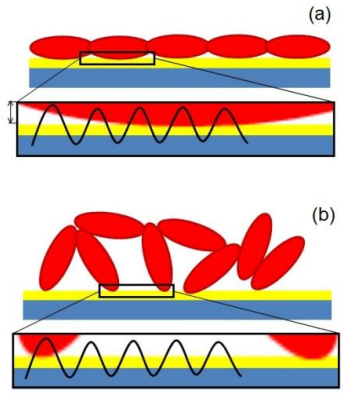

Fig. 8. Layers of erythrocytes formed on the sensor chip: *a* – healthy person, *b* – a person with a brain glioma.

4. Conclusions

Owing to the improved prism design, the use of a cable drive, and the additional adhesion layer of chromium, the "Plasmon" biosensor provides high-precision and sensitive measurements, making it an effective tool for the rapid diagnosis of brain gliomas relapse. The use of SPR in conjunction with a dual-channel optical system and a unique mechanical design significantly enhances the accuracy of the studies and reduces the influence of external factors.

The biosensor based on the phenomenon of surface plasmon resonance has been developed for the express diagnosis of brain glioma relapse. It has been ascertained that the degree of blood cell aggregation increases with the degree of malignancy and the cellular density of gliomas.

The results of the performed studies showed that the level of changes in the SPR parameters of peripheral blood correlates with the cellular density of gliomas, reflecting the malignancy of these tumors. Changes in SPR parameters in the blood cells of the studied patients may also serve as a predictive factor for the rate of glioma progression in the postoperative period, allowing for timely preventive measures against the recurrence of gliomas.

The strategy of these methods should focus on enhancing the transmembrane potential of blood cells to reduce their migration to the site of the removed tumor. Based on the correlations between changes in the SPR parameters in blood cells and their relationship with changes in cellular density in parenchymal organs, new opportunities arise for corrective influences on the tumor focus. This approach includes, alongside traditional chemotherapy methods, lifelong anti-inflammatory therapy.

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References

1. de Robles P., Fiest K.M., Frolkis A.D. *et al.* The worldwide incidence and prevalence of primary brain tumors: a systematic review and meta-analysis. *Neuro-Oncology*. 2015. **17**, No 6. P. 776–783. https://doi.org/10.1093/neuonc/nou283.
2. Nayak L., Deangelis L.M. Clinical Features of Brain Tumors, Part 3. *Blue Books of Neurology*. 2010. **36**. P. 54–70. https://doi.org/10.1016/B978-0-7506-7516-1.00003-7.
3. Smith H.L., Wadhwani N., Horbinski C. Major features of the 2021 WHO classification of CNS tumors. *Neurother.* 2022. **19**, No 6. P. 1691–1704. https://doi.org/ 10.1007/s13311-022-01249-0.
4. Kaifi R.A. Major features of the 2021 WHO classification of CNS tumors. *Diagnostics.* 2023. **13**. P. 3007. https://doi.org/ 10.3390/diagnostics13183007.

5. Delaidelli A., Moiraghi A. Recent advances in the diagnosis and treatment of brain tumors. *Brain Sci.* 2024. **14**. P. 224. https://doi.org/10.3390/brainsci14030224.
6. Jing J.-Y., Wang Q., Zhao W.-M., Wang B.-T. Long-range surface plasmon resonance and its sensing applications: A review. *Opt. Lasers Eng.* 2019. **112**. P. 103–118. https://doi.org/10.1016/j.optlaseng.2018.09.013.
7. Maheshwari R.U., Kumarganesh S., K V M S. *et al.* Advanced plasmonic resonance-enhanced biosensor for comprehensive real-time detection and analysis of deepfake content. *Plasmonics.* 2024. https://doi.org/10.1007/s11468-024-02407-0.
8. Kostyukevych K., Khrystosenko R., Zagorodnya S. *et al.* Molecular diagnostics based on surface plasmon angular spectroscopy. *Data Recording, Storage & Processing.* 2020. **22**. P. 14–30.
9. Klestova Z., Yushchenko A., Dremuch Yu. *et al.* Diagnostics of cattle leucosis by using a biosensor based on surface plasmon resonance phenomenon. *SPQEO.* 2019. **22**. P. 111–118. https://doi.org/10.15407/spqeo22.01.111.
10. Klestova Z., Yushchenko A., Blotskaya O. *et al*. Experimental and theoretical substantiation of the express method development for detection of enteroviruses in water by surface plasmon resonance method. *Innov. Biosyst. Bioeng.* 2019. **3**, No 1. P. 52–60. https://doi.org/10.20535/ibb.2019.3.1.163106.
11. Qu J.-H., Dillen A., Saeys W. *et al.* Advancements in SPR biosensing technology: An overview of recent trends in smart layers design, multiplexing concepts, continuous monitoring and in vivo sensing. *Anal. Chim. Acta.* 2020. **1104**. P. 10–27. https://doi.org/10.1016/j.aca.2019.12.067.
12. Dorozinska H.V., Dorozinsky G.V., Maslov V.P. Promising method for determining the concentration of nanosized diamond powders in water suspensions. *Funct. Mater.* 2018. **25**, No 1. P. 158–164. https://doi.org/10.15407/fm25.01.158.
13. Kretschmann E., Raether H. Radiative decay of non-radiative surface plasmons excited by light. *Z. Naturforsch. A.* 1968. **123**. P. 2135–2136. http://dx.doi.org/10.1515/zna-1968-1247.
14. *Patent No 46018, Ukraine*, CI G 01N 21/55. Method of detecting and determining the concentration of biomolecules and molecular complexes and device for its implementation. Shirshov Yu.M., Venger E.F., Prokhorovych A.V. *et al.* (2002). Appl. 22.10.1997. Publ. 15.05.2002. Bul. No 5.
15. *Patent No 57177, Ukraine*. CI G01N 21/55. Sensor for analysis of bio-chemical media. Ushenin Yu.V., Samoylov A.V., Khrystosenko R.V. No u201009975. Appl. 12.08.2010. Publ. 10.02.2011. Bul. №3.
16. *Patent No 76774, Ukraine*. CI G01N21/00 G01N21/55. Device for analysis of biochemical media. Dorozinsky G.V., Ushenin Yu.V., Samoylov A.V. *et al*. No u201209062. Appl. 23.07.2012. Publ. 10.01.2013. Bul. No 1.
17. Gridina N.Ya., Maslov V.P., Ushenin Yu.V. *et al.* Application of surface plasmon resonance phenomenon for early detection and determination of the drug concentration for treating the relapses of malignant tumors. *SPQEO.* 2020. **23**. P. 85–90. https://doi.org/10.15407/spqeo23.01.85.
18. Gridina N.Ya., Zhebrivska F.I., Morozov A.M. *et al.* The first experience of combined treatment of brain malignant gliomas by means of blocking membrane calcium channels. *Ukr. Neurosurg. J.* 2019. **25**. P. 43–50. https://doi.org/10.25305/168800.
19. Gridina N.Ya., Gupal A.M., Tarasov A.L., Ushenin Yu.V. Analysis of neurosurgical pathologies using Bayesian recognition procedures for indicators of surface plasmon resonance in the aggregation of blood cells. *Cybern. Syst. Anal.* 2020. **56**. P. 550–558. https://doi.org/10.1007/s10559-020-00271-4.
20. Shirshov Yu.M., Kostyukevych K.V., Khrystosenko R.V. *et al.* Analysis of forming blood elements using surface plasmon-polariton resonance model of transition layer. *Optoelectron. Semicond. Tech.* 2020. **55**. P. 136–150.

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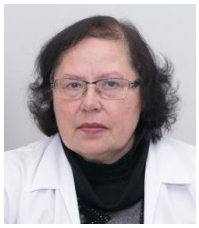

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Samoylov A.V.: conceptualization, methodology, validation, writing – original draft, writing – review & editing.
Khristosenko R.V.: investigation, data curation, validation, writing – review & editing.
Gridina N.Ya.: investigation, resources, formal analysis, writing – review & editing.
Dorozinsky G.V.: investigation, visualization, writing – review & editing.
Romanchuk V.V.: investigation, data curation.
Khomenkova L.Yu.: supervision, validation, project administration, writing – review & editing.

Двоканальний ППР біосенсор для вдосконаленої діагностики рецидиву гліом головного мозку: агрегація клітин крові як біомаркер злоякісності пухлин

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Анотація. Розроблено двоканальний біосенсор на основі явища поверхневого плазмонного резонансу для експресної діагностики рецидиву гліом головного мозку за показниками агрегації клітин крові. Прилад має два оптичні канали, що дозволяє проводити два дослідження одночасно або використовувати один канал як опорний. Такий підхід значно підвищує чутливість сенсора внаслідок зменшення впливу зовнішніх факторів. Джерелом оптичного збудження є *p*-поляризований напівпровідниковий лазер з довжиною хвилі 650 нм. Як сенсорні елементи використано пластинки з оптичного скла марки Ф1 ($n = 1.61$) з послідовно напиленими шарами хрому (5 нм) та золота (45…50 нм). Продемонстровано застосування біосенсора для виявлення гліом головного мозку та встановлено кореляцію між рівнем агрегації клітин периферичної крові пацієнтів та ступенем злоякісності гліом. Виявлено статистично значущу різницю ($p \leq 0,05$) між групами умовно здорових осіб та хворих на гліоми II-IV ступеня злоякісності. Встановлено, що зменшення величини зсуву кривої плазмонного резонансу зумовлене підвищенням рівня агрегації клітин та зниженням їх електричного заряду на мембранах. Ця тенденція поступово підсилюється із підвищенням ступеня злоякісності гліом, сягаючи мінімальних показників у хворих на гліому IV ступеня.

Ключові слова: біосенсор, поверхневий плазмонний резонанс, гліома головного мозку, агрегація клітин крові.