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DEVELOPMENT OF A SPIRAL-ELECTRODE CAPACITIVE BIOSENSOR FOR POINT-OF-CARE DIAGNOSIS OF LEUKOCYTOSIS AND LEUKOPENIA

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Keywords: dielectric sensing, cells sensor, spiral-electrode capacitive biosensor, point-of-care diagnosis, leukocyte quantification, gold-labeled CD45+ cells.
Abstract. Monitoring white blood cell counts is essential for diagnosing various medical conditions, including infections and leukemia. This paper proposes a high-sensitivity capacitive sensor featuring spiral-shaped copper electrodes for the detection and quantification of gold-labeled CD45+ cells. The sensor dimensions are 9.99 x 9.99 mm, integrated with a sensing chamber of 0.998 mm³ (9.99 x 9.99 x 0.01 mm). Simulation results demonstrate that the introduction of gold-labeled CD45+ cells alters the local dielectric properties, inducing a measurable shift in capacitance. The proposed device exhibits a near-linear response with a sensitivity of 17.288 fF per gold-labeled CD45+ cell. Given its cost-effectiveness and high precision, this sensor architecture offers a promising solution for point-of-care leukocyte quantification and the early diagnosis of leukocytosis and leukopenia.

РАЗРАБОТКА ЕМКОСТНОГО БИОСЕНСОРА СО СПИРАЛЬНЫМИ ЭЛЕКТРОДАМИ ДЛЯ ЭКСПРЕСС-ДИАГНОСТИКИ ЛЕЙКОЦИТОЗА И ЛЕЙКОПЕНИИ

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Ключевые слова: диэлектрическое зондирование, клеточный датчик, емкостной биосенсор со спиральным электродом, диагностика на месте оказания медицинской помощи, количественное определение лейкоцитов, меченные золотом Клетки CD45+.
Аннотация. Мониторинг количества лейкоцитов имеет важное значение для диагностики различных заболеваний, включая инфекции и лейкемию. В данной статье предлагается высокочувствительный емкостный датчик со спиралевидными медными электродами для обнаружения и количественного определения CD45+ клеток, меченных золотыми наночастицами. Размеры датчика составляют 9,99 × 9,99 мм, а объем чувствительной камеры – 0,998 мм³ (9,99 × 9,99 × 0,01 мм). Результаты моделирования показывают, что введение CD45+ клеток, меченных золотыми наночастицами, изменяет локальные диэлектрические свойства среды, вызывая измеряемый сдвиг емкости. Предложенное устройство демонстрирует почти линейный отклик с чувствительностью 17,288 пФ на одну CD45+ клетку, меченную золотыми наночастицами. Благодаря низкой стоимости и высокой точности предложенная архитектура сенсора представляет собой перспективное решение для экспресс-анализа количества лейкоцитов и ранней диагностики лейкоцитоза и лейкопении.

1. Introduction

The white blood cell (WBC) count is a critical biomarker for assessing an individual's health status. As a vital component of the body's defense mechanism, WBCs activate the adaptive immune system to eliminate pathogens and provide long-term protection [1-2]. The physiological range for a healthy adult typically spans from 5,000 to 10,000 cells/µL [2]. Deviations from this range often indicate underlying medical conditions: leukocytosis (elevated WBC count) is commonly associated with bacterial

infections and inflammatory responses, whereas leukopenia (reduced WBC count) may signal bone marrow deficiency or severe viral infections [3]. Consequently, routine monitoring of WBC levels is essential for the early diagnosis and prevention of systemic diseases. While traditional methods like microscopy remain prevalent [4-6], there is a growing need for advanced point-of-care testing to enhance healthcare outcomes. Recent studies on the dielectric properties of cancer cells have demonstrated that healthy cells exhibit higher permittivity compared to malignant ones, suggesting that dielectric analysis can be a viable tool for leukemia detection [7-9]. Furthermore, various research groups have implemented paper-based vertical flow assays for leukocyte counting. This technique captures white blood cells within a fibrous paper matrix and quantifies them by measuring the signal intensity of gold nanoparticles (AuNPs) attached to the cells. The selective labeling of leukocytes is achieved using anti-CD45 antibodies, which ensure the specific binding of AuNPs to the CD45+ cell surface [10]. Although paper-based methods offer significant convenience, the integration of coplanar capacitive sensors provides superior sensitivity and enables direct quantification without the need for complex signal intensity measurements.

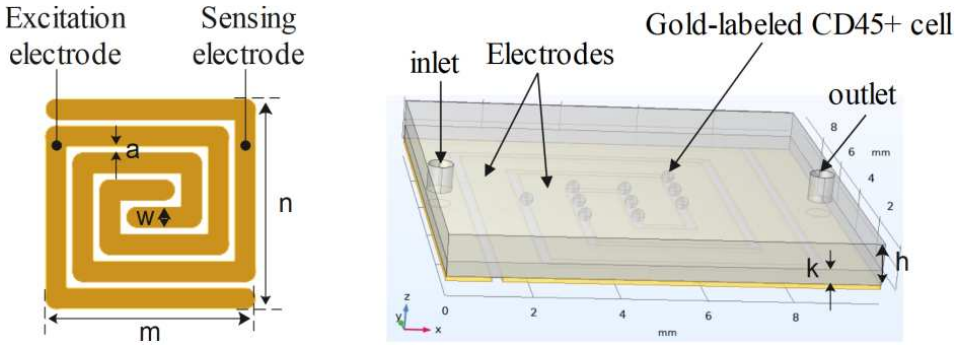
In this study, a capacitive sensor is proposed for the detection and quantification of white blood cells by labeling CD45+ cells with anti-CD45 antibody-conjugated gold nanoparticles (AuNPs). The sensor configuration features two capacitors with spiral-shaped electrodes positioned beneath the chamber: a sensing capacitor and a reference capacitor. The detection mechanism relies on the capacitance shift induced by the passage of these gold-labeled cellular complexes. As the cells traverse the sensing area, they alter the local dielectric environment, resulting in a measurable change in capacitance. By monitoring these variations, the presence and concentration of CD45+ cells can be accurately identified and estimated.

2. Theoretical Framework and Sensor Design

To prepare the gold-labeled CD45+ cell solution, gold nanoparticles are first conjugated with anti-CD45 antibodies. Upon exposure to the leukocyte sample, these functionalized nanoparticles specifically recognize and bind to the CD45 proteins expressed on the cell membrane. Consequently, the CD45+ cells become encapsulated by a gold nanoparticle layer, providing a distinct dielectric signature for capacitive detection.

The sensor geometry is illustrated in Figure 1, a. The sensing electrodes are made of copper with a thickness (t) and a width (w), separated by a gap (a). Figure 1, b show a plastic chamber with a height (k) is positioned directly above the electrodes to contain the gold-labeled CD45+ cell solution during the investigation. The gold-labeled CD45+ cell solution is injected into the chamber through the inlet and discharged via the outlet.

Figure 2 presents the top-down view of the sensor configuration, which consists of two capacitive elements: a reference capacitor and a sensing capacitor. The reference capacitor (C_1), positioned beneath the chamber containing pure water (without gold-labeled CD45+ cells), has a capacitance determined solely by the dielectric properties of the medium. In contrast, the sensing capacitor (C_2) is located under the chamber containing the target solution, where its capacitance is influenced by both the dielectric properties of the medium and the presence of gold-labeled CD45+ cells.



a b

Fig. 1. The design of the proposed capacitive sensing for detecting CD45+: a) design of sensor structure; b) capacitor sensor with CD45+ with AuNPs

Tab. 1. Dimensions of sensors

Symbol	Quantity	Unit (mm)
a	Gap distance between electrodes	0.25
w	Electrode width	1.03
t	Electrode thickness	0.1
n	Width of the sensors	9.99
m	Length of the sensors	9.99
k	Solution chamber height	0.01

Table 1 presents the dimensional specifications of the capacitive sensor shown in Figure 1. The chamber volume for the gold-labeled CD45+ cells was set at 0.998 mm³ (0.99 mm × 0.99 mm × 0.01 mm). For the simulation, each gold-labeled CD45+ cell was modeled with a radius of 7 μm.

The presence of gold-labeled CD45+ cells in the sensing chamber induces a capacitance mismatch between the sensing capacitor (C2) and the reference capacitor (C1). The differential capacitance, defined as (1), serves as a measurable indicator to detect and quantify the existence of gold-labeled CD45+ cells within the solution.

$$\Delta C = |C_2 - C_1|. \quad (1)$$

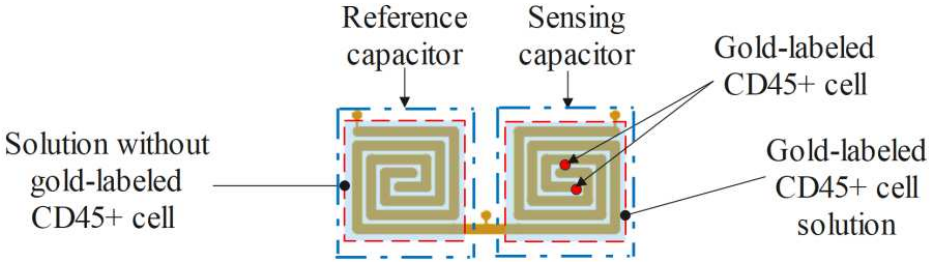


Fig. 2. The sensor shape are proposed for design and investigation

3. Simulations and Discussion

In this study, Comsol Multiphysics simulation software was employed to evaluate the sensor's performance. The electric field distribution within the sensor was analyzed by applying a voltage of 12 V between the excitation electrode and the sensing electrode. The sensor parameters were designed as outlined in Table 1. The simulated material parameters used in the model are summarized in Table 2.

The simulation results in Figure 3 illustrate the relationship between the output capacitance change and the number of gold-labeled CD45+ cells investigated within a

solution volume of 0.998 mm³. These results indicate that as the cell count increases from 1 to 10, the output capacitance exhibits a near-linear response, rising from 8 fF to 180.886 fF, respectively. The achieved sensitivity is 17.288 fF per gold-labeled CD45+ cell.

Tab. 2. Simulation parameters in the model

System component of the sensor	Material	Dielectric constant	Conductivity (S/m)
Chamber containing	Acrylic (PMMA)	3.0	-
Solution	Pure water	80	$5.\ 10^{-4}$
Cell	Gold-labeled CD45+ cell	5	41.10^{6}
Electrode	Copper	-	$5{,}96.10^{7}$

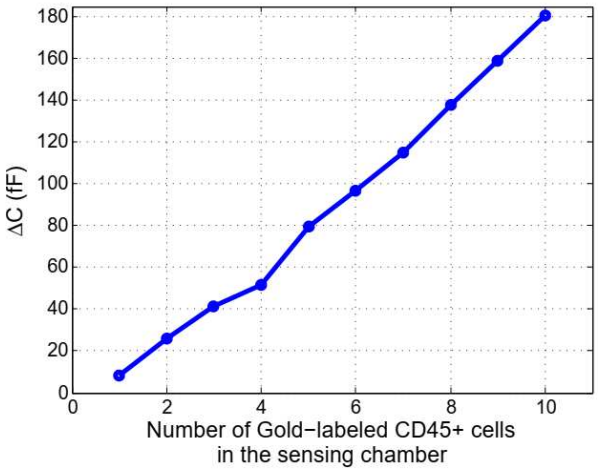


Fig. 3. The change in output capacitance corresponds to a change in the number of gold-labeled CD45+ cells

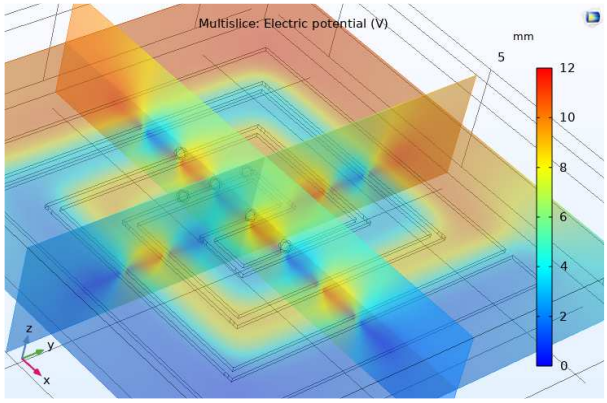


Fig. 4. Simulated image of the sensor

Figure 4 illustrates the electrostatic field distribution when gold-labeled CD45+ cells are introduced into the chamber above the sensor electrodes, alongside the simulation model of the sensor. The red regions represent higher voltage levels, while the blue regions indicate lower voltage levels. This electric field distribution demonstrates a significant interaction between the sensing electrodes and the gold-labeled CD45+ cells.

4. Conclusions

This study presents a capacitive sensor featuring a spiral-shaped electrode design with a footprint of 9.99 x 9.99 mm for the detection and quantification of gold-labeled CD45+ cells. The sensing chamber positioned above the sensor has a total volume of 0.998 mm³ (9.99 x 9.99 x 0.01 mm). To enhance measurement accuracy and stability, a reference capacitor structure was integrated to mitigate power supply noise and parasitic capacitance. The introduction of gold-labeled CD45+ cells into the chamber induces changes in the local dielectric properties, resulting in a measurable shift in the sensor's capacitance. This variation allows for the precise estimation of the cell count within the solution. The proposed sensor exhibits a sensitivity of 17.288 fF per gold-labeled CD45+

cell. The results demonstrate that this sensor architecture is cost-effective, highly sensitive, and well-suited for leukocyte quantification, thereby facilitating the diagnosis of clinical conditions such as leukocytosis and leukopenia.

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