THE ABSTRACT OF DOCTORAL THESIS

a) Introductory Information:

- Author's name: Phan Hoang Anh
- Thesis Title: "Research and Development of a Lab-on-a-Chip (LoC) Device for the Detection and Quantification of Lung Cancer Cells"
- Field of Study: Electronics Engineering Code: 9510302.01
- Name of the training institution: University of Technology, Vietnam National University, Hanoi

b) Abstract Content:

Purpose and Objectives of the Thesis:

Lung cancer is currently one of the leading causes of death worldwide, accounting for the highest percentage of cancer-related deaths. Early detection of circulating tumor cells (CTCs) plays a crucial role in timely diagnosis, prognosis assessment, and treatment monitoring. However, the greatest technical challenge lies in the extreme scarcity of CTCs in peripheral blood, with a ratio of only about 1 to 10 cells per million white blood cells, making their isolation and detection extremely difficult. To address this issue, the thesis focuses on developing an integrated Lab-on-a-Chip (LoC) platform that combines magnetic separation, impedance measurement, and machine learning techniques to automate the process of isolating, detecting, and counting A549 lung cancer cells.

The main research objectives of the thesis include three key tasks: designing and fabricating a microfluidic chip with an optimized magnetic separation structure for effective CTC capture; developing an impedance measurement system capable of real-time cell detection and counting; and applying machine learning algorithms to accurately classify cell signals from background noise. The specific research subjects are A549 lung cancer cells, MRC5 normal cells, and superparamagnetic Fe3O4 magnetic nanoparticles surface-functionalized with EpCAM-specific aptamers for selective binding to target cells. Research methods used:

The research methodology employed in this study consists of:

In terms of methodology and theoretical basis, the thesis applies a multidisciplinary approach, combining numerical simulation and experimentation. COMSOL Multiphysics software was used to simulate physical fields including magnetic fields, hydrodynamic flow, and electric fields. The microfluidic channel structure was designed in a serpentine configuration with integrated cavities to create a high magnetic field gradient under the

influence of an external permanent magnet, optimizing cell capture. Additionally, a spiral channel structure is integrated to utilize inertial lift force and Dean flow, helping to arrange cells into a single stream and maintain a stable distance before entering the sensor region.

The device fabrication process is performed using microelectromechanical systems (MEMS) technology. The gold electrode system is fabricated on a glass substrate using photolithography and wet etching, while the microfluidic channel is molded from PDMS (polydimethylsiloxane) material based on an SU-8 mold. The channel size is optimized at 30 μm to ensure sensitivity for impedance measurement and avoid clogging. The impedance measurement circuit system is designed based on Lock-in Amplifier technology to collect both the real and imaginary components of the cell impedance signal, helping to eliminate noise and improve accuracy.

Key results and conclusions:

The results of the magnetic separation efficiency study show a clear dependence on magnetic particle size. Simulation results predict capture efficiencies of 80%, 94%, and 100% for magnetic particles with sizes of 1.36 μm, 3.00 μm, and 4.50 μm, respectively. Actual experimental results showed that the effective capture efficiency increased gradually with particle size, reaching 77.6%, 82.0%, and a maximum of 88.4% with 4.50 μm particles. Notably, the system achieves very high sample purity, averaging approximately 99.1% when testing the separation of A549 cells from a mixture containing HeLa control cells, confirming the high specificity of the aptamer-based method.

For detection and quantification capabilities, the microfluidic impedance sensor system operates stably and can clearly distinguish the characteristic signal peaks of cells (bipolar type) from background noise. Under optimal operating conditions at 3V voltage and 100 kHz frequency, combined with a dynamic thresholding algorithm, the system achieves a counting accuracy of up to 94.7% compared to manual counting via video. The system's processing speed reaches approximately 101 events/second, equivalent to counting over 6000 cells/minute. Furthermore, the comparison of signal amplitude and signal-to-noise ratio (SNR) shows that the system can clearly distinguish between A549 cancer cells and MRC5 normal cells, with signals from MRC5 being 4-6 times higher than those from A549 at high frequencies (150-200 kHz).

Another important contribution of the thesis is the successful application of machine learning models to signal and image processing. The YOLOv8 image segmentation model achieved an mAP@0.5 accuracy of 99.5% in quantifying the degree of particle coverage on

cells. For impedance signal classification, models such as Isolation Forest and OneClassSVM were implemented, with OneClassSVM achieving an F1-score of 0.790, demonstrating a good balance between cell signal recognition and noise removal. Additionally, the YOLOv5 object detection model applied to cell counting in microfluidic droplets also achieved high accuracy with a Precision of 97.5%.

In summary, the thesis contributed a complete technological solution, from chip design and fabrication to the integration of measurement systems and intelligent data processing. The developed LoC system has the advantages of being compact, low-cost, highly automated, and non-invasive, offering great potential for future point-of-care cancer screening applications. The results achieved not only hold scientific significance in elucidating the microfluidic-electromagnetic interaction mechanism but also lay the practical foundation for developing "made in Vietnam" biomedical devices to serve the community.

Hanoi, on month year 2025

RESEARCH STUDENT **SUPERVISOR**

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