

THE ABSTRACT OF DOCTORAL THESIS

a) Introductory Information:

- Author's name: Nguyen Thu Hang
- Thesis Title: Research and development of an organ-on-a-chip platform for assisted reproductive technologies based on microsystems
- Field of Study: Electronics Engineering Code: 9520203
- Name of the training institution: University of Engineering and Technology, Vietnam National University, Hanoi

b) Abstract Content:

Purpose and objectives of the thesis:

In assisted reproductive technologies, *in vitro* maturation (IVM) provides an important strategy for maturing oocytes outside the body. However, conventional IVM systems still have limitations in reproducing the dynamic and physiologically relevant microenvironment of the female reproductive tract. In addition, the efficiency of oocyte culture, handling, and selection remains highly dependent on manual procedures and the experience of embryologists. The dissertation aims to design, fabricate, and evaluate microfluidic systems for streamlining key steps in oocyte handling and IVM. The proposed system enables dynamic co-culture of oocytes and cumulus cells within a controlled microfluidic environment. This provides a more physiologically relevant platform for oocyte maturation while supporting automated handling, intelligent evaluation, and non-invasive selection in assisted reproductive technologies. Through these objectives, the dissertation seeks to improve the control, efficiency, reproducibility, and degree of automation of oocyte-related procedures in assisted reproductive technologies.

The experimental object of the dissertation is porcine oocytes, which are widely used as a relevant biological model in reproductive research due to their physiological and developmental similarities to human oocytes. By using porcine oocytes, the study provides an appropriate experimental basis for evaluating the feasibility and effectiveness of the proposed microfluidic systems. The results are expected to serve as a foundation for further optimization and future translation toward human-assisted reproductive applications.

Research methodology:

The research methodology employed in this study consists of theoretical analysis, finite element method (FEM)-based numerical simulation, microfluidic chip design and fabrication, experimental validation, biological evaluation, and AI-assisted image analysis. Theoretical analysis and FEM simulations were used to investigate microfluidic flow behavior, fluid–cell interaction, shear stress distribution, oocyte/cell trajectories, and dielectrophoretic effects, thereby supporting the optimization of chip structures, flow conditions, and electrical parameters.

The optimized devices were fabricated using standard soft-lithography and microfabrication techniques, and then experimentally validated with porcine oocytes as a relevant biological model. The proposed systems were evaluated for dynamic oocyte–cumulus cell co-culture, automated cumulus cell removal, and non-invasive oocyte selection. Their performance was assessed based on key technical and biological indicators, including oocyte survival rate, maturation rate, IVF outcomes after maturation, degeneration rate, denudation efficiency, processing throughput, and selection capability. In addition, image processing and artificial intelligence methods were applied to support more objective and intelligent assessment of oocyte quality. This integrated methodology provides a systematic

basis for evaluating the potential application of the proposed microfluidic platforms in assisted reproductive technologies.

Key results and conclusions:

This thesis developed an integrated microfluidic platform to support key steps in the *in vitro* maturation workflow, including single-oocyte trapping, dynamic culture, maturation monitoring, cumulus cell removal, and quality-based oocyte selection. By integrating microfluidics, organ-on-chip technology, artificial intelligence, and dielectrophoresis, the proposed system provides a more controlled, standardized, and automation-compatible approach for oocyte handling and assessment in assisted reproductive technologies.

The OvaOoC module enabled stable single-oocyte immobilization and dynamic oocyte–cumulus cell co-culture under controlled microfluidic conditions. Simulation and experimental results demonstrated favorable flow and shear stress distributions, with a trapping efficiency of 88,37%. Compared with conventional microdrop culture, the dynamic on-chip culture improved mass transport, microenvironmental regulation, and oocyte maturation performance. The integration of time-lapse imaging and deep learning further allowed automated and objective evaluation of cumulus expansion, reducing dependence on subjective morphological assessment.

For post-culture processing, the denudation module achieved a high cumulus cell removal efficiency of $95,94 \pm 0,94\%$ with superior throughput, while maintaining IVF outcomes comparable to conventional manual denudation. In addition, the DEP-integrated chip enabled label-free and non-invasive separation of normal and abnormal oocytes based on intrinsic dielectric properties, with good agreement between simulation and experiment.

Overall, the thesis demonstrates the feasibility of an integrated microfluidic platform for oocyte handling, culture, monitoring, denudation, and selection. These results contribute to the development of more efficient, standardized, and intelligent workflows for assisted reproductive technologies.

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PHD CANDIDATE

SUPERVISOR

Nguyen Thu Hang

Prof. Dr. Chu Duc Trinh

CONFIRMATION FROM THE TRAINING UNIVERSITY