Thesis project
Theme: flow / sensor technology
Thesis title:
Next generation in-situ sensor on-a-chip for cell-culture monitoring

Is an external organization involved? Yes, namely: Bi/ond (https://www.gobiond.com)
The thesis involves (select all that apply): experiment / design
Prerequisite courses and/or knowledge (e.g. software or programming languages):
Microfluidics, materials science, analytical techniques

Project description:

Organ-on-chips (OoCs) are micro-fabricated platforms that replicate the function and structure of human organs, enhancing the quality of in vitro testing, particularly in drug development[1, 2]. Despite the potential, OoC currently relies on fluorescent microscopy analysis, which requires labelling, thereby terminating the experiment. Thus, the need for label-free, continuous real-time analysis of cell viability parameters remains a critical challenge in advancing OoC models[1, 2].

Stimuli-responsive polymers have attracted great scientific interest in the field of chemical and biochemical sensors, due to their ability to change their physical and/or chemical properties in response to stimuli[4, 5]. In diagnostics, the development of stimuli-responsive microgel-based etalon sensors provide an optical response to a variety of stimuli such as temperature, pH and various biomolecules[6]. The microgels are made from pNIPAm (Poly(N-isopropylacrylamide)) thermo-responsive polymers, which are co-functionalized during synthesis to be responsive to other stimuli as well (e.g., pH, lactate, glucose and dissolved carbon dioxide (dCO_2)).

In this project you will develop an integrated metabolite-sensing platform designed for precise detection and monitoring of key metabolic indicators in cell cultures. The platform will utilize etalon sensors on substrates such as PDMS, glass, or silicon, designed to operate within an incubator environment at 37°C and high humidity. The aim is to integrate these sensors within Bi/ond's microfluidic chip, and enable real-time, non-invasive monitoring of biological samples on OoC. Resulting in **on-site analysis** of crucial parameters for applications in tissue engineering, screening, and precision medicine.

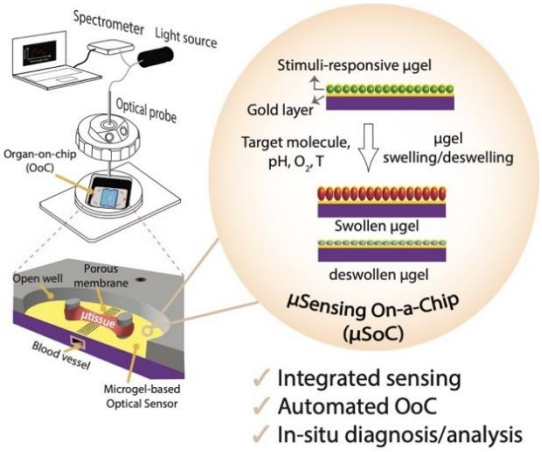

Fig. 1. In-situ sensing on organ-on-chip platforms using stimuli-responsive microgels.

The goal of this project is to:

1. **Develop a Metabolite-Sensing Platform:** Create an integrated system capable of accurately detecting in real-time analytes (glucose, lactate) and environmental conditions (pH and dCO_2) in OoC platforms, provided by Bi/ond. The challenge is to ensure minimal cross-reactivity and high sensitivity (**Fig. 1**).
2. **Evaluate Cross-Sensitivity and Enhance Selectivity:** Assess and mitigate cross-sensitivity issues of the etalon sensors by conducting simultaneous measurements of pH, dCO_2, and metabolites, enabling accurate detection of specific metabolic changes in the cell culture environment.

Supervisors, other staff involved, contact info:

Daily supervisors: Georgia Kontaxi (PhD student) (g.kontaxi@tudelft.nl)

Dr. Hanieh Bazyar (assistant professor) (h.bazyar@tudelft.nl)

Dr. Nikolas Gaio from Bi/ond

Ir. Tawab Karim from Bi/ond

Reference

1. Stefanie Fuchs et al. “In-Line Analysis of Organ-on-Chip Systems with Sensors: Integration, Fabrication, Challenges, and Potential”. In: ACS Biomaterials Science & Engineering 7.7 (2021), pp. 2926–2948. DOI: 10.1021/acsbiomaterials.0c01110.

2. Qasem Ramadan and Mohammed Zourob. “Organ-on-a-chip engineering: Toward bridging the gap between lab and industry”. In: Biomicrofluidics 14.4 (2020), p. 041501. DOI: 10 . 1063 / 5 .0011583.

3. Graham A. Clarke et al. “Advancement of Sensor Integrated Organ-on-Chip Devices”. In: Sensors 21.4 (2021), p. 1367. DOI: 10.3390/s21041367.

4. L. Hu, T. Shu, Y. Wan, C. Fang, F. Gao, and M. J. Serpe, “Recent advances in stimuli-responsive polymers for sensing and actuation,” Mol. Syst. Des. Eng. 6, 108–121 (2021).

5. S. Wellert, M. Richter, T. Hellweg, R. von Klitzing, and Y. Hertle, “Responsive microgels at surfaces and interfaces,” Zeitschrift für Physikalische Chemie 229, 1225–1250 (2015).

6. Y. Gao, X. Li, and M. J. Serpe, “Stimuli-responsive microgel-based etalons for optical sensing,” Rsc Advances 5, 44074–44087 (2015).