Cellular Impedimetric Sensor Platform for point-of-care and drug screening applications.

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Application Deadline : *May, 10th 2015*

- **Supervisors**

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- **Domain and scientific context**

This PhD concerns the development of Lab-On-a-Chip systems dedicated to medical diagnosis and drug screening. Indeed, the development of personalized medicine and Point-Of-Care (POC) diagnostic tools addresses a strong social demand related to the steady increase in the number of elderly, and is one of the key issues that the health industry will have to urgently address in near the future. Fluidic microsystems enable the manipulation of small volume of liquids, and thus the reduction of analysis time and cost, while offering enhanced portability. Due to their dimensions, they enable analyses at the single cell level and offer numerous prospects for medical diagnostics and drug screening.
A growing interest in the field of drug screening is the exploitation of the physical properties (dielectric for example) of the cellular sample in order to perform drug screening assays.
Key-words : *Impedance spectroscopy, Lab-on-a-Chip, cells, cancer.*

- **Objectives of the PhD**

Despite the development of automatic analysis in videomicroscopy applied to biological assays, this technique remains time-consuming and requires high storage and computer capacities. An alternative approach is to monitor impedance variations induced by changes in cell phenotype. Indeed, multi-frequency Electrical Impedance Spectroscopy (EIS) can be used to study and characterize cells present on, between or in the vicinity of measurement electrodes, depending on the electrode arrangement used. Such measurements can determine the presence, morphology, attachment, growth and migration of a given cell-type. They therefore have potential benefit in a wide range of applications including fundamental biological assays for chemotaxis, wound healing and drug screening. The impedimetric cellular sensing method was probably pioneered by Giaever and Keese[1]. Using this approach, various authors have successfully investigated cell spreading, as well as the morphological and functional status of cells[2,3]. Recently, some companies have commercialised such systems[4]. However, they remain at the macro-scale and a large amount of cells are necessary to obtain accurate signals. Thus, this method is not yet adapted for the high-throughput screening assays necessary in drug screening.
We aim to investigate thoroughly the design of a versatile impedimetric sensing platform and to then incorporate suitably designed impedimetric cellular sensing systems into microfluidic devices in order to make the systems fully automatic, quantitative, and sensitive to fine cell changes.

[1] Giaever, I., and Keese, C. R. (1984) *Proc Natl Acad Sci U S A 81*, 3761-4
[2] Wegener, J., Keese, C. R., and Giaever, I. (2000) *Exp Cell Res 259*, 158-66
[3] DePaola, N., Phelps, J. E., Florez, L., et al. (2001) *Ann Biomed Eng 29*, 648-56
[4] *xCELLigence System*, Roche

- **Research program and scientific approach**

The present research will be thorough and systematic in its approach to developing an optimally-designed cellular impedance sensing system and to then integrate it within microfluidic systems appropriate for a range of given applications. Our primary objective here is to quantify cellular coverage.
The PhD project will be divided into three main tasks:

- First a bibliographic review of the possible impedimetric approaches will be carried out
- Then we will investigate the design of the electrodes in terms of sensitivity (shape, size, layout; electrode materials, fabrication methods and resultant surface topography).
- Finally, we will investigate the integration of these optimised designs into a microfluidic environment and ensure its compatibility with lens-free imaging

- **Integration inside the laboratory, collaboration(s)**

The student will join two INL groups: the Biomedical Sensors and the Lab-On-Chip-Instrumentation teams attached to the Biotechnology/Health Department of INL. He (or she) will have access to the infrastructures of the Nanolyon technological platform in terms of Micro/Nanofabrication and cell Biology, and also to the impedimetric characterization equipments of both groups.
Collaborations: Centre de Recherche en Cancérologie de Lyon.

- **Profile of the candidate (prerequisite)**

The candidate should possess a Master in one of the following fields: Micro-Nanotechnologies, Physics, Chemistry or Electronics.
Experience of or a strong interest in microfluidics and biology will be welcome.

- **Skills developed during the PhD**

The skills developed during the PhD involve bioimpedance measurement and modelling, micro-nanofabrication, cell biology, numerical simulations, design and preparation of microfluidic systems.