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PhD proposal

Mechanobiology assisted by Surface Acoustic Wave (SAW) for medical diagnosis assistance

Keywords: Biosensors, Surface Acoustic Waves (Love and Rayleigh), Mechanobiology, Human cells, Microfluidics

Team 405 : Micro & Nanosystems

Institut Jean Lamour UMR 7198 CNRS – Université de Lorraine

Website: http://ijl.univ-lorraine.fr/recherche/departement-nanomateriaux-electronique-et-vivant-n2ev/micro-et-nanosystemes/

Contacts: Supervisor: Pr Frédéric SARRY, **E-mail** : frederic.sarry@univ-lorraine.fr

Co-supervisor: Dr Denis BEYSSEN **E-mail** : denis.beyssen@univ-lorraine.fr

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Project start: October 1st, 2018

Mechanobiology is an emerging field of science at the interface of biology and engineering. A major challenge in this field is understanding of mechanotransduction, i.e. the molecular mechanisms by which cells sense and respond to mechanical signals. This physical interaction will modify the mechanical properties of cells and tissues which contribute to the development of the cell, its differentiation and to the development of the disease. Hence, cell's viscosity and elasticity are important parameters that must be characterized. It has been shown that softer the substrate is, the smaller the spreading of cells is. To give an idea about the order of magnitude, the migration rate is close to 0.1 micron.min-1 on a 5 kPa stiffness gel (rigidity close to mammary tumour cells - MCF7) and reaches 0.5 micron.min-1 on a 70 kPa stiffness gel [1]. Cancer increases deformability and adhesion properties [2]. In 48 hours, Malaria cell stiffness increases by a factor of 10 [3]. There are different methods to characterize these properties such as rheology, dynamic mechanical analysis, AFM indentation, micropipette aspiration, etc. [4,5].

S.U. Senveli et al. conducted the most recent work in the field of surface acoustic wave (SAW) biosensors for the characterization of tumour cells. They coupled a surface acoustic wave (SAW) device to a microcavity and succeeded to analyse biological cells at the micron scale. They also managed to differentiate tumour cells in terms of elasticity modulus [6,7]. Using delay lines operating at 200 MHz, and exploiting the attenuation at the solid-cell interface, they were able to determine the elasticity of the cells. Moreover, we can note, the work of Stamp et al. [8] which demonstrated that dynamic stimulation of bone tumour cells (SaOs-2) with 159 MHz (Rayleigh-SAW) ultrasound accelerates the tissue healing process by stimulating cell migration and growth. They have developed a piezoelectric platform on a 128Y-X $LiNbO_3$ substrate coated with a SiO_2 layer. SAW appear to be a relevant an promising characterization method for the field of mechanobiology.

We propose to study the behaviour of different cells under mechanical stress. Our objective is to achieve a thorough understanding of the involved processes (modification of viscoelasticity, cytoskeleton structure, shear modulus,...) in order to opening up new possibilities for early diagnosis. To achieve this matter, we will develop a piezoelectric platform allowing the mechanical stimulation of the cells with Rayleigh waves (R-SAW) on one hand, and the detection of morphological, elastic, adhesion changes, etc… on the other hand, using SH-SAW or Love waves. Two approaches will be conducted, one static and the other dynamic.

The first approach will focus on the measurement using a Love wave (specific sensitive acoustic wave), which is a Shear Horizontal-SAW, confined in a guiding layer. The objective is to characterize the interaction between the biofluid/cell and the surface of the sensor. Comparative measurements between "healthy" and "tumour" cells will be made and will be compared to other types of cell assays. The cell will be placed without prior mechanical stimulation and we will detect the stiffness and adhesion differences between the cells.

The second approach is to mechanically stimulate the cell using a Rayleigh-SAW and to observe and measure, via Love waves, the reaction of the cell to this mechanical signal. This type of progressive wave (orthogonal vibrational component) will interact strongly with the biological medium. The dynamic approach should allow us to highlight the transduction difference of cells through the conversion of mechanical signal to biochemical signal. This can result in another cytoskeleton conformation, a change of adhesion, the activation of migration ... between "healthy" and « tumour » cells. It will also be very informative to observe in real time the response of the cell to stimuli. We will complete this analysis by using an imaging technique adapted to measurements on the living cells allowing to see, the cells distortion, reorganization of their cytoskeleton… First, a theoretical study (simulation) will be conducted using analytical and numerical methods, which will allow us to choose the piezoelectric substrate and the guiding layer to confine the Love waves. It will also be necessary to choose the geometry of the detection cell, design the microfluidic brick based on biocompatible polymer (PDMS) to dispense a single cell on the detection zone. Moreover, in order to work on the living (human cell ex-vivo) without temporal constraint, we will work on the design an acoustic thermoregulation brick (37 °C). A preliminary study [9] has allowed us to validate, on an equivalent piezoelectric device, the detection of a viscosity variation in a liquid medium (water-glycerol solution) using Love waves. Two multilayers structures will be used, ZnO/Quartz and ZnO/$LiNbO_3$.

This multidisciplinary project will be conducted in collaboration with two teams from our institute: "Nanomaterials for Life and Responsible Development" and "Nanoparticles and Health". The project includes three biologists-toxicologists (Luc Ferrari, Olivier Joubert, Bertrand Rhin) who have recently joined the lab.

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Team Micro & Nanosystèmes researchers involved in this doctoral project:

Professor Frédéric SARRY (Supervisor): Expertise on piezoelectric devices based on LOVE Surface Acoustic Waves (SAW) for the detection

Dr Denis BEYSSEN (Co-supervisor): Micro-fabrication skills (clean room), microfluidics assisted by Rayleigh acoustic waves. Development of elementary bricks for Lab on Chip ("microdroplet actuation", "mixing", "acoustic thermocycler").

Dr. Mourad OUDICH: Expertise in Numerical Simulation (Comsol Multiphysics Software) → acoustic and electromagnetic wave propagation phenomena in solid and fluid media.

Profile and skills

Master of Science or engineer in one or more of the following fields: Applied Physics, Acoustics in fluids and solids, Micro and Nanotechnologies, Biomedical Engineering, Biotechnology or related fields

For Master of Science: Master's degree with an average mark greater than 70% (14/20 in French system) and good ranking

For Engineers: good ranking

English level: Level B2 required or TOEIC > 800