PROGRAMME INTITUTS ET INITIATIVES

Appel à projet – campagne 2021

Proposition de projet de recherche doctoral (PRD)

IUIS - Institut univ d'ingénierie en santé

Intitulé du projet de recherche doctoral (PRD): Portable electromagnetic and microfluidic lab-on-chip using magnetic nanoparticles for immunological multipathogens detection such as SARS-Cov-2 using saliva

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Unité de Recherche :
Intitulé : Group of electrical engineering-Paris (GeePs)
Code *(ex. UMR xxxx)* : UMR 8507

École Doctorale de rattachement de l'équipe (future école doctorale du.de la doctorant.e) : **ED391-SMAER**

Doctorant.e.s actuellement encadré.e.s par la.e directeur.rice de thèse (préciser le nombre de doctorant.e.s, leur année de 1e inscription et la quotité d'encadrement) : Une doctorante (Rania SHAHBAZ) inscrite en 2019, 30%

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Code *(ex. UMR xxxx)* : Inserm U1135 - CNRS ERL 8255

École Doctorale de rattachement : **ED394-Physiologie,Physiopathologie Thérapeutique**
Ou si ED non Alliance SU :

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Co-encadrant.e :

NOM : Prénom :
Titre : Choisissez un élément : ou HDR ☐
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Unité de Recherche :
Intitulé :
Code *(ex. UMR xxxx)* :

École Doctorale de rattachement : **Choisissez un élément :**
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Description du projet de recherche doctoral *(en français ou en anglais) :*

Ce texte sera diffusé en ligne : il ne doit pas excéder 3 pages et est écrit en interligne simple.

Détailler le contexte, l'objectif scientifique, la justification de l'approche scientifique ainsi que l'adéquation à l'initiative/l'Institut.

Le cas échéant, préciser le rôle de chaque encadrant ainsi que les compétences scientifiques apportées. Indiquer les publications/productions des encadrants en lien avec le projet.
Préciser le profil d'étudiant(e) recherché.

Électronique et électromagnétisme, capteurs et instrumentation de mesures, avec des notions en biologie et modélisations.

Très motivé et ouvert d'esprit pour travailler sur un sujet de recherche pluridisciplinaire de développement d'un dispositif portable de tests immunologiques avec un fort impact sociétal en santé publique.

Merci d'enregistrer votre fichier au format PDF et de le nommer :
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PhD subject at Sorbonne University,
IUIS (Institut Universitaire d'Ingénierie en Santé), 2021

Portable electromagnetic and microfluidic lab-on-chip using magnetic nanoparticles for immunological multipathogens detection such as SARS-Cov-2 using saliva

Context:

The detection and quantification of one or more biological agents has become essential to anticipate a possible health threat (epidemic or pandemic), environmental or other contextual threats (bioterrorism, chemical and biological weapons). In this area, one of the main objectives is to facilitate this detection with a sensitive, reliable, portable and low cost lab-on-chip system.

The present COVID-19 pandemics caused by the SARS-Cov-2 virus illustrates how important it is to develop sensitive diagnostic assays that could be widely used in the population, preferably avoiding the need for blood samples. Saliva testing would be particularly convenient, but also medically-relevant, as COVID-19 is mainly a respiratory condition primarily inducing mucosal (IgA mediated) immunity.

The biological analysis based on high sensitivity magnetic measurements is a new type of immunological diagnosis using magnetic nanoparticles (MNP) as markers [1-8]. This new method of analysis involves the coupling of antibodies or antigen proteins to MNP. The specific binding of the antibody to its antigen will be assessed by the detection of MNP of various sizes and also different magnetic properties. Thanks to their extractability and sortability, MNP are suitable for the examination of biological samples, serving as markers for biochemical reactions [2, 7, 8].

Up to now, the final detection step is mainly carried out by the ELISA colorimetric method, fluorescence-based techniques or markings with radioelements. The standard enzymatic detection used in the ELISA method has a limited sensitivity (approximately 100 ng/ml) and a relatively long measurement time (approximately 10 min). This method as well as the fluorescent methods have a limited dynamic range and require the use of transparent materials and non-colored and non-fluorescent media. The use of radioactive markers is also problematic because of the regulations on radiation protection. Therefore, the immunoassays which detect the analyte by means of MNP constitute a very promising alternative with a sensitivity already obtained of 6ng/ml in a macroscopic system (10x23x7 cm3) using coaxial cylindrical coils and an ABICAP reservoir for the sample [2, 6-8].

The MNP covered on their surface with a biocompatible streptavidin layer can be specifically linked to analytes (proteins, viruses or bacteria), figure 1. Among the available magnetic techniques, the new technique based on the principle of frequency mixing has a definite advantage by making possible to quantify MNP with a very broad dynamic [8]. By studying the characteristics of the response signal (amplitude and phase) at a well-defined frequency, non-linear and specific signatures of different types of MNP can be discriminated.

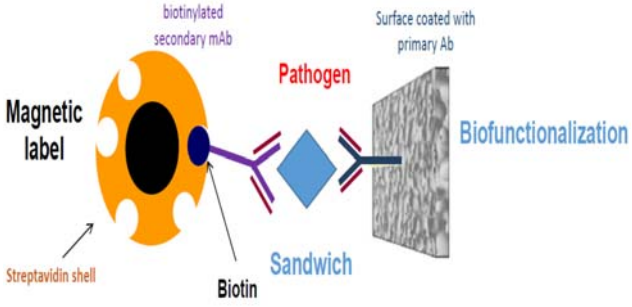

Figure 1 : Detection principle with antigen-antibodies association for the immunlogical detection using MNP.

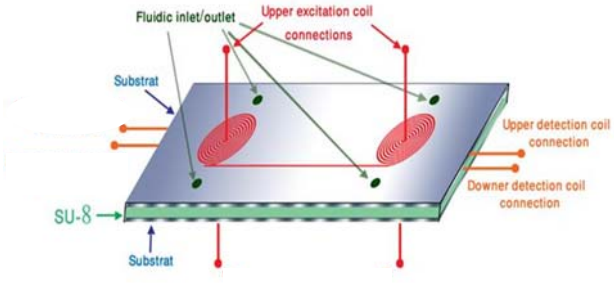

Figure 2 : Schematic view of the planar magnetic sensor with microcoils integration within a SU-8 microfluidic structure.

For this research project, contacts and collaboration have been established between GeePs, CIMI and other SU laboratories (LISE and PHENIX) and the "Institute of Bioelectronics" in Juelich (Germany). A miniaturized structure of planar and multilayer microcoils associated with a suitable microfluidic structure has been designed and realized (Figure 2, see in references the French-German patent issued in 2019 with extension to USA in progress). A bench of magnetic measurements, with frequency mixing and synchronous detection techniques coupled to a microfluidic bench was also set up [1, 3-5].

Besides the team led by Guy GOROCHOV at CIMI has a great expertise in the field of immune / microbe interactions mediated by IgG and IgA antibodies (11-13). The GOROCHOV team also has the ability (14) to engineer human recombinant anti- SARS-Cov2 antibodies that could be used within the framework of this program in order to capture SARS-Cov2 antigens. He is supported by ANR and Sorbonne University by iCOVID program

This joint PhD project between CIMI and GeePs fits in perfectly with the Alliance Sorbonne University's scientific policy to support activities of the SU institutes and initiatives and particularly the IUIS (University Institute for health Engineering) for the development of interdisciplinary biomedical research. This project combines the complementary scientific and medical skills and knowledge of the involved teams [1-14] on an important international public health issue with high sanitary, economic and social impacts.

Objectives:

The ultimate goal of this medical and engineering PhD project is to perform portable magnetic immunoassay and multipathogen sensing on a chip. Detection of pathogens such as SARS-Cov-2 in human samples, mainly saliva but also urine and blood will be achieved using the experimental knowledge and facilities at CIMI. A microsystem using MNP markers in a microfluidic channel as microliter sample holder will be developed. Fully integrated planar excitation and sensing microcoils will be deigned and fabricated on both sides of a suitable microfluidic chip with multiple micro-analysis reservoirs with optimized size and shape. Analytical and numerical multiphysics modeling and simulations (Electromagnetic, thermal, microfluidic and biochemical reaction) of the magnetic detection and actuation will make possible to optimize the parameters of the integrated microcoils. These models will also make possible to evaluate the performances of the microsystem in terms of sensitivity and specificity.

The MNP will be synthesized by PHENIX to get mono-core, multi-core and core-shell nanoparticles with different sizes and magnetic properties. They will be compared also with other commercially available MNP in innovative microfluidic structures in collaboration with LISE laboratory. These MNP will be characterized according to their non-linear magnetic responses. They will be surface-coated and functionalized with so-called "detection" antibodies or antigen proteins for the specific detection of the analyte in collaboration with CIMI. The surface of the fluidic channel in the microsystem will be functionalized by grafting with appropriate capture biological entities in collaboration with CIMI. The magnetic actuation will be tested as an analyte detection trapping technique based on magnetic relaxation time measurements. Compared to current techniques, the operational speed of this new method will allow access to real-time measurements. C-Reactive Protein (or CRP) will serve as the first biological proofing entity before extending the application to other specific and relevant biochemical entities such as procalcitonin (PCT) and SARS-Cov-2 spike antigen for human or animal medical diagnosis.

Expected results:

This PhD thesis consolidates activities of GeePs and CIMI in innovative bio-testing methods and microsystems for immunological applications. A real-time measurement of the concentration of viruses such as SARS-Cov-2, bacteria and proteins and a test of their functionality based on the interaction of the antigen-antibody becomes possible. The results will have high public health impacts with a portable, fast, ergonomic and cost-effective multipathogens detection system and lead to technological transfers to companies, which develop Point-of-Care (POC) biological analysis systems.

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French-German European patent: (Extension to USA in progress)

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