PhD THESIS POSITION

Title:

Development of a new technology of concurrent 2-dimension separation for characterization of nanoparticles towards nanomedicine applications

Host Institution: Institut Galien Paris Saclay, UMR CNRS 8612, Team 'Proteins and nanotechnologies in analytical science' (PNAS)

https://www.umr-cnrs8612.universite-paris-saclay.fr/pres_eq4-uk.php

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The PhD position is granted by the *Agence Nationale de la Recherche* (ANR) for 36 months starting from the 1st of January 2024.

Project Description:

This project aims at developing a novel concept and prototyping in separation science, called microscale 2D magneto-electrography (2D-ME). This concept will allow two simultaneous orthogonal migration dimensions in the same microchannel: capillary electrophoresis (CE) under a high electric field and magnetophoresis under a powerful magnetic field gradient. This new concept is expected to be better adapted for size, charge and shape characterization of nano objects (e.g., functionalized nanoparticles).

Nanoparticles (NPs), including magnetic nanoparticles (MNPs) play important roles in diagnosis, drug delivery systems and nanomedicine. Particularly for MNPs, size is also a key parameter when using them as contrast agents in magnetic resonance imaging or tumor radio-sensitization, for magnetic hyperthermia dedicated to thermosensitive drug delivery or cancer treatment [1]. For each family of MNPs, there is often a co-existence of various subpopulations and interferences (especially in biological fluids) with overlapping physical properties, rendering challenging their fine separation and characterization. This requires qualified methods to well separate their subpopulations and characterize them, in order to improve their synthesis to obtain the desired MNPs quality, which is mandatory for biomedical applications and drug delivery systems.

Recently, particular attention has been paid to anisotropic MNPs with elongated shapes such as nanorods or nanochains as they exhibit improved magnetic properties for magnetic resonance imaging and magnetic hyperthermia in comparison to their spherical counterparts [2]. Such anisotropic MNPs are also featured by a higher blood circulation time and a prolonged retention in tumor sites compared to spherical NPs, as well as improved interaction with cells thanks to their cylindrical shape. It is however very challenging to separate and characterize anisotropic NPs using conventional separation approaches.

From this urgent need, the first 2D-ME prototype to be developed in microfluidic format will be used for resolute charge, size and shape characterization of spheric MNPs and nanorods serving as innovative drug carriers. 2D-ME will also explore and control the nanometric heterogeneity as well as their interactions with biomolecules (e.g., blood proteins) to improve NPs synthesis and the quality of nanomedicine.

This interdisciplinary project covers microfluidics, instrumentation, (bio)analytical chemistry, and nanoscience. This project will be supported by the complementary expertise of partners from Institut Néel (for magnetic field design modeling and micro-magnet parterning) and the Inorganic Colloids team of laboratory Physico-chimie des Electrolytes et Nanosystèmes InterfaciauX (PHENIX, Sorbonne university, for synthesis and characterization of magnetic nanoparticles).

The PhD student will develop the 2D-ME system and protocols for pre-concentration, separation and characterization of tailored spheric MNPs synthesized by PHENIX. The 2D-ME system in microfluidic format will be developed, with the strong support of our group in purpose-made microfluidic and electrokinetic instrumentation [3, 4]. The PhD student, in close collaboration with Institut Néel, will try to propose different ways to combine the magnetic and electric fields in a

microchannel to carry out 2D-ME of standard MNPs. The PhD student will then demonstrate the applicability of the developed system and methodology for separation of magnetic nanorods provided by PHENIX and monitoring their interaction with human plasma proteins to evaluate their behavior under biological conditions.

QUALIFICATION

• You are highly motivated to work at the boundary between microfluidics, instrumentation, bioanalytical chemistry and nanoscience.

• You have a master's degree or equivalent (obtained within 4 years) in either Instrumentation or Analytical Chemistry / Nanoscience / Microfluidics

• You have practical experience in microfluidics and/or instrumentation and/or microfabrication, with a good sense of analytical chemistry

• Good knowledge about biochemistry and nanoparticles is advantageous.

• You have strong communication and presentation skills in English (verbal and written)

• You enjoy working independently and challenging scientific obstacles with an optimist aptitude.

Send your application by e-mail before the 1st of October 2023 to thanh-duc.mai@universite-paris-saclay.fr and claire.smadja@universite-paris-saclay.fr **including your CV, motivation letter and recommendation letters from your previous supervisors / professors.**

Refs:

[1] N.V.T. Nguyen, C. Smadja, M. Taverna, J.M. Siaugue, E. Secret, S. Elmousli, H.L.T. Nguyen, T.D. Mai, Electroosmotic flow modulation for improved electrokinetic preconcentration : application to capillary electrophoresis of fluorescent magnetic nanoparticles, Anal. Chim. Acta, 1161 (2021) 338466.

[2] S.E. Mousli-Saada, Elaboration de nanoparticules magnétiques anisotropes et étude de leurs voies d'internalisation cellulaire (PhD thesis), PHENIX - PHysicochimie des Electrolytes et Nanosystèmes InterfaciauX, https://theses.hal.science/tel-03884548 (2022)

[3] N.V.T. Nguyen, C. Smadja, M. Taverna, H.L.T. Nguyen, S. Descroix, T.D. Mai, On-line dual-stage enrichment via magneto-extraction and electrokinetic preconcentration: a new concept and instrumentation for capillary electrophoresis, Anal. Chim. Acta, 1255 (2023) 341141.

[4] T. Liénard--Mayor, J.S. Furter, M. Taverna, H.V. Pham, P.C. Hauser, T.D. Mai, Modular instrumentation for capillary electrophoresis with laser induced fluorescence detection using plug-and-play microfluidic, electrophoretic and optic modules, Anal. Chim. Acta, 1135 (2020) 47-54.