

Post Doc position in Physics

Novel magnetic micro-swimmers in view of applications to nanomedicine (24 months)

Research unit: <u>INPHYNI laboratory</u> / Mixed research unit Université Côte d'Azur, National Centre for Scientific Research (CNRS)

Project summary:

General context.

Localized drug delivery to difficultly accessible zones of human organism is a key point for successful treatment of different severe deceases, such as cancer, ischemic heart decease or ischemic brain stroke. Classical therapeutics suffer from either pronounced side effects (when the injected drug affects healthy tissues) or low efficacy of the drug transport towards the target sites because of stagnation of blood circulation near these sites. Magnetic nanocarriers (nanoparticles or magnetic liposomes carrying the drug) guided along the vascular network by externally applied magnetic fields and releasing the drug directly at the target site (tumor tissue or blood clot) could in principle overcome these problems [1]. However, this technique does not allow an easy control over the displacement of the nanocarriers through a branched vascular network because of physical limitations associated to gradient magnetic fields. Shape anisotropy and/or flexibility of magnetic carriers can substantially improve the remote control over their motion through combination of their translational, angular or beating motion using a complex superposition of magnetic field gradients with 3D oscillating magnetic fields [2]. Such magnetic carriers are referred to as magnetic micro-swimmers. During last decades, various types of magnetic micro-swimmers have been designed with different swimming strategies developed. However, to the best of our knowledge, still none of them satisfy most of criteria imposed by clinical applications. Some of them are too large (microrobots of several millimeters size) to pass through blood vessels [3], others are fabricated using very sophisticated methods and/or at very small quantities incompatible with real applications [4].

Very recently, our research group at the Institute of Physics of Nice (INPHYNI, UMR 7010) have shown that ultrasmall magnetic nanoparticles (210 nm) can be rapidly displaced through a network of microfluidic channels by a simple combination of 2D rotating magnetic field with 1D magnetic field gradient (unpublished results). First, upon magnetic field application, magnetic nanoparticles self-assemble into elongated micron-sized aggregates; these aggregates are then involved into spinning by the rotating magnetic field and "roll" along the channel wall in a prescribed direction imposed by the sense of the magnetic field rotation and field gradient. Such rolling motion allows achieving speeds on the order of 1 mm/s, comparable with typical blood flow speed, and all this at very modest magnetic field intensity and frequency (B20.01 T, f=5 Hz), so that the swimming speed can be largely increased through increasing of B and f. At the first glance, this new swimming strategy is technically very simple, cost-effective and seems to respond to main requirements of the localized drug delivery application.

Objectives

The postdoc fellow will be in charge of extensive development of this swimming strategy going through the stages of fundamental understanding of physical mechanisms behind this swimming (through optical visualization of micro-swimmers trajectories in microfluidic network and, if possible, theoretical modeling of these trajectories) along with engineering of a remote control system allowing guiding of micro-swimmers along a prescribed trajectory through the branched artificial vascular network (fabricated through 3D printing at the hosting university). In collaboration with other researches of the hosting team, at the end of the postdoc project, it would become possible to realize preliminary experiments on drug delivery, controlled release and dissolution of the artificial blood clots using the magnetic swimmers with the drug molecules either bound to



the nanoparticle surface or incorporated into the magnetic liposomes. In general, the postdoc project is inscribed into a large research topic of the hosting team related to biomedical applications of magnetic nanoparticles, in which two associate professors, research engineers of the start-up Axlepios Biomedical and two PhD students are involved.

Candidate profile:

Experimental physicist or biophysicist. Required skills: Colloids; Biophysics; Microfluidics; Basic knowledges in hydrodynamics, electromagnetism and statistical physics.

Hosting Team and Supervision

The hosting team from Institute of Physics of Nice (INPHYNI, UMR 7010) has a broad experience in physicochemistry and industrial, environmental or biomedical applications of magnetic nanoparticle colloids. In particular, the **postdoc supervisors, Dr. Pavel Kuzhir (PK) and Dr. Guilhem Godeau (GG)**. PK is the head of the hosting team and is an expert in field-induced self-assembly (aggregation) of magnetic nanoparticles and microfluidic flows of magnetic dispersions (both from experimental and theoretical perspectives) [5,6]. GG is specialists in organic synthesis and surface/colloids functionalization [7,8]. The team has all the necessary equipment to conduct the experimental part of the project (materials, electromagnets, amplifiers, characterization tools – dynamic light scattering, zeta-sizer, magnetometer, 3D printing ...) and a free access to the clean room at INPHYNI (for microfluidic fabrication) and the university technological platforms (TEM, SEM, IR, TGA, ...). For the biomedical aspects of the project, the team plans to establish a tight collaboration with the biologists (G. Sandoz from the institute of Biology of Valrose – iBV, Nice) and neurosurgeons (Dr. L. Suissa, CHU Pasteur hospital, Nice).

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References:

1. Douziech-Eyrolles, L., Marchais, H., Hervé, K., Munnier, E., Soucé, M., Linassier, C., Dubois, P., Chourpa, I., 2007. Nanovectors for anticancer agents based on superparamagnetic iron oxide nanoparticles. Int J Nanomedicine 2, 541–550.

2. Bente, K., Codutti, A., Bachmann, F., & Faivre, D. (2018). Biohybrid and bioinspired magnetic microswimmers. Small, 14(29), 1704374.

3. A Oulmas, A., Andreff, N., & Régnier, S. (2018). 3D closed-loop swimming at low Reynolds numbers. The International Journal of Robotics Research, 37(11), 1359-1375.

4. Pauer, C., Du Roure, O., Heuvingh, J., Liedl, T., & Tavacoli, J. (2021). Programmable Design and Performance of Modular Magnetic Microswimmers. Advanced Materials, 33(16), 2006237.

5. Kuzhir, P., Magnet, C., Ezzaier, H., Zubarev, A., & Bossis, G. (2017). Magnetic filtration of phase separating ferrofluids: From basic concepts to microfluidic device. Journal of Magnetism and Magnetic Materials, 431, 84-90.

6. Orlandi, G., Kuzhir, P., Izmaylov, Y., Marins, J. A., Ezzaier, H., Robert, L., ... & Zubarev, A. (2016). Microfluidic separation of magnetic nanoparticles on an ordered array of magnetized micropillars. Physical Review E, 93(6), 062604.

7. Queiros Campos, J., Checa-Fernandez, B. L., Marins, J. A., Lomenech, C., Hurel, C., Godeau, G., ... & Kuzhir, P. (2021). Adsorption of organic dyes on magnetic iron oxide nanoparticles. Part II: Field-induced nanoparticle agglomeration and magnetic separation. Langmuir, 37(35), 10612-10623.

8. Queiros Campos, J., Boulares, M., Raboisson-Michel, M., Verger-Dubois, G., García Fernández, J. M., Godeau, G., & Kuzhir, P. (2021). Improved Magneto-Microfluidic Separation of Nanoparticles through Formation of the βCyclodextrin–Curcumin Inclusion Complex. Langmuir, 37(49), 14345-14359.