Name of the IDIL Master Internship:
Nanothermometers for intracellular temperature measurements

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Sujet de Master IDIL :
(2 pages maximum, incluant : contexte, objectifs et méthodes proposés, résultats attendus, faisabilité) / (*including: context, proposed objectives and approaches, expected results, feasibility)*

Context:

Temperature is one of the basic physical parameters in the life activities of organisms, affecting various biochemical reactions and physiological activities in cells, such as gene expression, energy metabolism, neurotransmitter release, and immune reactions.[1,2] Despite recognizing the fundamental involvement of temperature in biochemical changes, the specific molecular mechanisms by which cells produce and use heat remain largely unknown, which has driven research on intracellular temperature measurements over the past decade. Traditional temperature recording technologies like thermocouples, thermistors, or thermal imaging are robust and reliable but are inappropriate for *intracellular* thermometry or *in vivo* body temperature mapping. In contrast, luminescence thermometry, which allows sub-millimeter spatial resolution, is highly attractive for temperature monitoring and imaging. Up to day, several types of luminescent materials have been proposed for intracellular temperature sensing, including organic molecules, polymers, carbon dots, quantum dots, N-vacancy nanodiamonds, and trivalent lanthanide ion-doped hybrid nanomaterials.[3] However, the intracellular/*in vivo* temperature monitoring by using luminescent nanoprobes is still in its infancy and highly challenging.

Objectives:

The objectives of this Master's internship consist in designing ratiometric luminescent nanothermometers based on silica nanoparticles incorporating organic fluorophores or lanthanide complexes to monitor the intracellular thermal dynamics. Fluorophores and lanthanide complexes are chosen for their absorption in the visible range and emission in the visible or near-infrared domain (biological window). After synthesis, characterizations, and property studies, the efficiency of these nano-objects as nanothermometers will be assessed through temperature measurements of:

(i) Microglia cells, which are immune cells of the central nervous system. They rapidly adapt to pathophysiological conditions through immune activation and inflammation. For instance, spinal cord injury induces microglial cells to move to the injury site and transform into an amoeboid form with phagocytic functions, a process known as "microglial activation." The exact nature of this activation is not fully understood, and factors like aging and temperature modulation within the cells during activation and their role in inflammation remain unknown. For this reason, temperature monitoring inside the microglia cells under external *stimuli* inducing their activation, as well as investigation of microglia response upon their heating from inside are highly challenging. This work will be done in collaboration with F. Perrin (Inserm MMDN) and L. Ulman (IGF CNRS)

(ii) cardiomyocytes, which are the muscle cells that make up the heart tissue. They are responsible for the contraction and relaxation of the heart, which pumps blood throughout the body. The temperature will be measured inside these cells under electrical stimulation. This work will be provided in collaboration with Dr. A. Lacampagne (PhyMedex, Montpellier)

Methods:
Nanothermometers will be designed on the base of mesoporous silica nanoparticles loaded with luminescent organic fluorophores and/or lanthanide complexes. These nanoparticles will be functionalized with biomolecules/polymers to ensure their biocompatibility and their phagocytosis by cells. These nanoparticles will exhibit temperature dependent luminescence in the near infrared region making them self-calibrated and biologically compatible nano-thermometers, where the luminescence can be used as a signal allowing remote and local measurements of temperature with high sensitivity, high thermal resolution (0.1 °C) and in short acquisition time (<10 μs).

Expected results:
(i) Design of biocompatible nanothermometers with optimized thermal sensitivity working in the near infrared spectral region.
(ii) Investigation of thermal dynamic of microglia cells during their activation *in vitro*. Identification of activated and non-activated microglia states by cell's temperature. Identification of stimuli and ageing tendency impacting the thermal dynamic
(iii) Investigation of intracellular temperature of cardiomyocytes under electrical simulation

Feasibility/Preliminary results: The preliminary results proving the feasibility of our approach have been done in our team on silica nanoparticles containing lanthanide complex working as temperature nanoprobes in the visible region.[4]

References:

1 Nano Lett. **2022**, 22, 14, 5698.
2 Chemical Engineering Journal **2024**, 490, 151645.
3 Nanomaterials **2023**, 13, 2904
4 Nanoscale,2023,15, 14409