Sensitive and portable detection of nucleic acids *in vitro* through luminescent nanoparticle imaging: towards a new generation of diagnostic tests

The *in vitro* detection of pathogenic markers, either proteins or nucleic acids, is crucial for the diagnosis of numerous conditions, *e.g.* viral infectious diseases. Their efficiency relies on (i) their sensitivity, to identify pathogens at relevant concentrations, and (ii) their practicality, to allow their implementation possibly in a context with limited logistics. However, these requirements are difficult to fulfill simultaneously, notably in the case of viral DNA or RNA. The detection of nucleic acid for medical purposes relies mostly on amplification-based techniques, such as PCR or isothermal amplification, which –though sensitive (down to ≈10.000 cp/mL)- are costly and/or difficult to implement without specialized equipment and qualifications. We have developed the use of lanthanide-based nanoparticles (YVO_4:Eu) as reporters for biological imaging, *in vivo*[1] or *in vitro*[2,3].[4] The remarkable optical and chemical properties of these particles (high UV absorbance, large Stokes shift, photostability, colloidal stability in aqueous buffers, and easy functionalization) qualifies them for the detection of biomolecules at high sensitivities. We have thus designed optical instrumentation, which has enabled high-sensitivity detection of proteins on strip-based immunoassays (Lateral Flow Assays or LFA, Figure 1).

During this Master 2 internship, we propose to demonstrate the feasibility of amplification-free detection of DNA and RNA fragments on LFA. This work will thus involve (i) the development of methodologies for DNA/RNA hybridization on strip, (ii) the optical detection and analysis of nanoparticle signals in LFA, (iii) performance evaluation and comparison with conventional tests (sensitivity, concentration range, reproducibility) of these tests on model DNA and RNA fragments. The next step will be the adaptation of this method to physiological buffers in which actual tests may be performed (blood, serum, urine or saliva) whose optical and chemical properties may diminish the test sensitivity due to endogenous fluorescence and scattering and non-specific interactions. Altogether, these results aim at setting the basis for efficient, fast, *in vitro* diagnostic tests on strips, based on viral DNA/RNA detection. The internship is part of an interdisciplinary project, involving skills in biochemistry and biophysics, optics and imaging. It may be followed by a thesis project aiming at developing optical diagnosis tests, both for protein and nucleic acid detection, using either LFA or ultra-sensitive detection modalities for use in a medical environment.

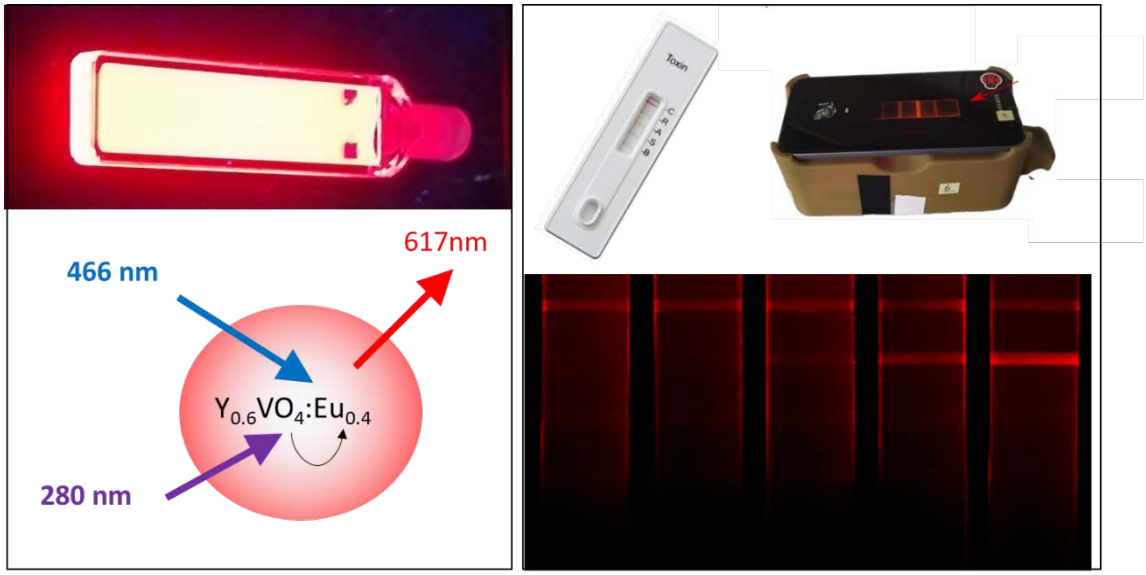

Figure 1. Left:nanoparticle luminescence under UV excitation. Right: Typical LFA test and a portable UV reader (top) and typical images of proteins (enterotoxins) detected with the reader (bottom).

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[1] Abdesselem et al. Biomed. Opt. Exp (2023)
[2] Mousseau et al. Nanoscale (2021)
[3] Mousseau et al. ACS Anal. Chem (2023)
[4] Preira et al. Patent WO2020/016308A1 (2020)