

**PhD thesis at the Doctoral School of Chemistry of Lyon**

***Sujet de thèse Ecole Doctorale de Chimie de Lyon***

**Preparation of nanoemulsions encapsulating sensitive biomacromolecules by  
premix membrane emulsification**

***Préparation de nanoémulsions encapsulant des biomacromolécules sensibles  
par émulsification membranaire avec prémix***

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**Keywords:** Membrane emulsification, formulation, sensitive biomacromolecules

**Abstract:**

Biomacromolecules are of high medical importance, e.g. the development of different RNA formulations is a major advance in the field of vaccines and therapeutics [1]. For administration, RNA-based actives are usually encapsulated in lipid nanoparticles. The nanoparticles are obtained by nanoprecipitation during which an ethanolic solution of a lipid mixture and an aqueous RNA solution are tightly mixed. The resulting suspensions are very dilute and require extensive concentration steps, which increases the production time and may compromise RNA stability. Other sensitive biomolecules are of high interest for therapeutics application (peptides, proteins,...) but need to be formulated to improve their stability or biodistribution.

The PhD thesis will investigate premix membrane emulsification [2, 3] as a new, gentle and scalable approach for the production of lipid nanoemulsions (LNE) encapsulating sensitive biomacromolecules like peptide and RNA. The expected benefits are to decrease (or even avoid) the use of solvents, to obtain more concentrated dispersions and to increase the stability of the biomolecules. In premix membrane emulsification, a coarse emulsion is first prepared, then this emulsion is passed through a porous membrane to homogenize the droplets. The technique uses low pressures and shear stresses which is advantageous for the processing of biomacromolecules.

The PhD thesis will be divided in different tasks. Task 1 will investigate the influence of the formulation (choice of lipids and additives, influence of biomolecule structure, etc) on the characteristics of the LNE obtained. Task 2 will focus on the membrane emulsification technique (influence of the membrane, operating conditions, etc). The LNE will be characterized by various complementary techniques to determine their size, charge, encapsulation efficiency,... The stability and integrity of encapsulated biomolecules will also be investigated. Depending on the results, biocompatibility of the formulations may finally be investigated via *in vitro* assays.

**Candidate profile:** Skills and knowledge in chemical engineering, chemistry, formulation, physicochemical analysis. Interest in transdisciplinary subjects. Motivated, curious, autonomous. A previous experience in experimental research is mandatory and preferably in an academic laboratory.

**Application:** Please send a resume and a letter of motivation (including references). Master 1 results (grade and rank) should also be provided to support the application. If Master 2 results are already available, please provide them too.

### Laboratory :

Laboratoire d'Automatique, de Génie des Procédés et de Génie Pharmaceutique, Laboratory of Automatic Control, Chemical and Pharmaceutical Engineering (LAGEPP), University Claude Bernard Lyon 1.

The PhD thesis will take place at the LAGEPP more specifically in the team of Pharmaceutical Engineering. LAGEPP is affiliated to the University Claude Bernard Lyon 1 and CNRS (UMR 5007). It includes around 40 professors and researchers and 40 PhD students. The Pharmaceutical Engineering team gathers strong pluridisciplinary competences (chemical engineering, formulation, physicochemical analysis, *in vitro* and *in vivo* evaluation,...) and works in collaboration with national and international research and development centers in industry or in academia. Especially, it has a national and international recognized expertise in the preparation of various colloidal forms using different techniques and the encapsulation of active substances for applications in medicine, diagnostics and cosmetics. The PhD student will work on the La Doua campus (UCBL, 69100 Villeurbanne).

### References

- [1] Brader M.L., Williams S.J., Banks J.M., Hui W.H., Zhou Z.H., Jin L. Encapsulation state of messenger RNA inside lipid nanoparticles. *Biophysical Journal*, 120 (2021) 2766–2770.
- [2] Alliod O., J.-P. Valour, S. Urbaniak, H. Fessi, D. Dupin, C. Charcosset, Preparation of oil-in-water nanoemulsions at large-scale using premix membrane emulsification and Shirasu Porous Glass (SPG) membranes, *Colloids and Surfaces A*, 557 (2018) 76-84
- [3] Nazir A., G.T. Vladislavjević, Droplet breakup mechanisms in premix membrane emulsification and related microfluidic channels, *Advances in Colloid and Interface Science*, 290 (2021) 102393