Internship Proposal for a First-year Master's student

Metastable Phase Transitions in a Microfluidic Antisolvent Crystallizer

Duration: 3 months, starting as soon as possible in 2026

Salary ~660 EUR/month

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Context of the project: Practically water-insoluble (< 0.1 mg/mL) chemicals have been estimated to make up ~70% of the new drugs in development and ~40% of the approved drugs.[1] Therefore, the improvement of their bioavailability—though in competition with the stability—is expressly significant, giving rise to the research of more soluble (including amorphous) phases, cocrystals, and more dispersed morphologies.[2] The surface-to-volume ratio [3, 4] is an important factor, but, more substantially, it is the polymorphism [5, 6] that determines the stability, the crystal habit, the solubility, and the dissolution rate. Microfluidics enable rapid screening of mixing parameters while using minimum amount of material. Different phase transition behaviours (liquid-liquid phase separation, amorphous nano-precipitation, and crystallization) can be controlled by the mixing parameters.[7] Precise control of composition and steady-state conditions allow for thermodynamic understanding of the dynamics.[8, 9] Using fluorescent solutes, in situ fluorescence lifetime and spectral imaging microscopy offers a unique way to investigate the aggregation process.[10] Additional control over nucleation rate can be achieved by focusing a fs laser at the reaction frontier.[7] **The goal of this project is to identify conditions that yield different phase transition pathways and to characterize the aggregation dynamics using FLIM**.

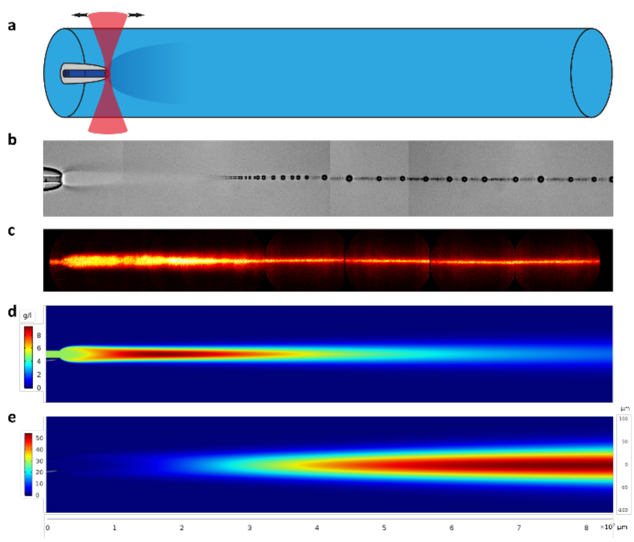

Figure 1. Metastable phase transition in a microfluidic antisolvent mixer. (a) Schematic of the coaxial microfluidic system. The solute solution is injected through the inner capillary into the antisolvent in the outer capillary. A laser can be focused at different places along the channel. **(b)** Liquid-liquid phase separation (LLPS) after mixing. **(c)** Fluorescence image of the LLPS. (**d**) Simulation of the solute concentration. (**e**) Simulation of the supersaturation.

Master 1 internship: The intern will participate directly in the microfluidic experiment and fluorescence characterization. The experiment will take 4 stages. First, measure the spectrum and solubility of a fluorescent molecule (tBZX) as a function of solvent composition. Second, map microfluidic conditions that yield different phase transition behaviours. Third, characterize representative phase transitions via FLIM and spectroscopy. Finally, explore laser-induced nucleation and laser fragmentation.

This work could be extended to a Ph.D. on laser-induced nucleation and fragmentation in microfluidics.

Candidate profile: Highly motivated candidates enrolled in a master's degree or equivalent, with a background in physics, chemistry, materials science or engineering. Prior experience in photophysics, microfluidics, and crystallization would be a strong plus.

Application procedure: Please email your CV to Zhengyu ZHANG (zhengyu.zhang@centralesupelec.fr) and Jeff Audibert (jaudiber@ens-paris-saclay.fr).

References

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[7] Zhang, Z. Laser-Induced Nucleation in a Coaxial Microfluidic Mixer. Université Paris Saclay (COmUE), Gif-sur-Yvette, Essonne, 2019, http://www.theses.fr/2019SACLN023.
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