Non-Newtonian coflows in a coupled microfluidic-electrospinning setup

Aim of the project

The aim of this project is to develop and study a microfluidic electrospinning (MFES) process for the fabrication of polymer fibers. The technological and scientific objectives are (1) the development of a coupled microfluidic-electrospinning setup compatible with polycaprolactone (PCL) and its solvents; (2) the characterization of the coflow in the microfluidic device and of the produced fibers; (3) a detailed investigation of the relationship between microfluidic and electrospinning operating conditions and the properties of the generated fibers.

Context

Electrospun fibers are commonly used in tissue engineering applications as a way to mimic the fibrous nature of native tissues. Polycaprolactone is commonly used in bone and tendon tissue engineering [1]. To improve the outcomes of cell culture and differentiation on electrospun PCL scaffolds, the addition of mineral (hydroxyapatite nanoparticles) or organic (growth factors) components is explored, but current setups do not always offer sufficient control to ensure a reproducible spatial distribution of these additives. Microfluidic devices appear as a promising technology for micro/nanofiber production since it provides tools to manipulate fluids at the microscale. In a microchannel with multiple inlets, internal and sheath fluids meet at a junction and, under certain conditions, form a liquid thread [2]. Microfluidic spinning consists in triggering the cross-linking of such threads by a chemical reaction, photopolymerization or solvent exchange, thereby forming micron-scale fibers [3]. This technique offers fine control but yields large single fibers and cannot be used for scaffold production. By combining microfluidic and electrospinning in a single platform (Fig 1a), one could prepare fluid threads with the desired gradients in polymer/nanoparticles/ growth factor radial gradients in the channel before the flow reaches the nozzle of the electrospinning setup. The idea of combining microfluidic and electrospinning is not new, but remained largely unexplored since the pioneering work of Srivastava et al in 2007 [4]. Later studies mostly focused on fiber repulsion in the case of multijet spinning or on emulsion-based electrospun fibers [5]. To the best of our knowledge, no systematic study of the fibers generated by coupled MFES approach was reported in the literature.

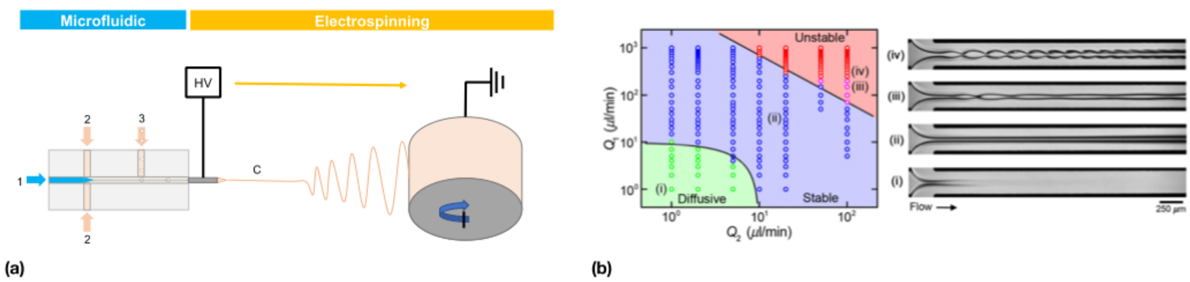

Figure 1 (a) Sketch of the MFES platform. (b) Phase diagram representing the stability of Newtonian fluid threads [Cubaud].

Scientific approach

Recent research has extended the study of microfluidic coflows, initially limited to immiscible fluids and the generation of emulsions, to miscible fluids and the stability of liquids threads. For Newtonian fluids, regions of fluid thread stability have been identified and can be mapped in a 2D phase diagram (Fig 1b) in pressure- as well as flow-rate-controlled configurations [6]. The PCL solutions used for electrospinning exhibit non-Newtonian behavior [7]. **We aim at exploring (experimentally and numerically) the coflow behavior of non-Newtonian polymer solutions in microfluidic devices.** Several geometries, from simple cross junctions to devices including 3 or more inlets, will be used to generate core-shell fibers. The main objectives of this parametric study are (1) to **define regions associated with the formation of stable fluid threads** and the relevant governing parameters, taking into account the rheology of polymer solutions (2) to **study the variations of relevant properties of the fluid threads**, such as their diameter and, when relevant, core-shell structure.

At such small scales the main numerical challenges for two-phase flows, particularly within T-junctions, are related to the fluid rheology, the role of surface tension between the two fluids, and to the identification of the relevant time scales of the coupled problem (advection, polymer elasticity, diffusion…). We propose to investigate this issue using Basilisk, an open-source solver designed for fluid dynamics, and developed at the d'Alembert Institute (Sorbonne University). Basilisk implements a **geometric Volume of Fluid (VoF) approach to accurately describe interfacial flows**, combined with quad/octree Adaptive Mesh Refinement (AMR) to efficiently capture the details of multiscale problems [8,9]. These characteristics make Basilisk a suitable tool for the problems encountered in microfluidics, as already demonstrated in many publications [10]. **The main concept is integrating data exchange between the experimental setup and numerical simulations** to benefit both aspects of the project. This dual approach, combining both numerical and experimental studies of the same problem, holds significant value in providing complementary insights and validating the accuracy of the findings across different methodologies.

Experimentally, a main limit to MFES approach is the compatibility issue between the most commonly used material for microchannels, polydimethylsiloxane (PDMS), and organic solvents. Many solvents, including the dichloromethane used to prepare polycaprolactone (PCL) solutions for electrospinning, make PDMS swell, provoking leaks and loss of control on the process. MFES has long been regarded as limited to water- or ethanol-based polymer solutions, which is very restrictive. However, alternative microfluidic materials have been investigated, opening new perspectives for microfluidic manipulation of organic solvents. **To prevent solvent-induced PDMS swelling, we selected perfluoropolyether** (PFPE), which is compatible with most solvents. PFPE fabrication by replica molding is readily available at BMBI [11].

We will then **use the PFPE-MFES coupled device to produce fibers**, which will be characterized. In this phase again, the goal is to understand to what extent the structure of the flow in the microfluidic channel determines the properties of the generated fibers. Apart from the fluid solutions, the operating parameters that will be tuned include flow rates, voltage, and distance to the collector. Fibers will be characterized by optical and electronic microscopy. The main features of interest are the fiber diameter, its core-shell structure. The inclusion of hydroxyapatite nanoparticles is considered, and the spatial distribution of particles will be quantified. Finally, **scaffolds composed of electrospun fibers** will be fabricated. The biological evaluation of these scaffolds is out of scope of the current PhD project but we plan to explore this aspect in future projects.

Risk management

The exploration of the behavior of non-Newtonian fluids in a microfluidic junction can be performed with PCL and its solvent or with other water- and ethanol-based complex fluids. Prototypes of MFES devices based on a PDMS chamber and a metal-coated glass slide have already been built, successfully coupled with electrospinning and can be replicated with PFPE using routine protocols. If rectangular cross-section channels are found unsuitable for MFES, circular cross-section PFPE channels will be directly 3D-printed.

Numerical approaches in micro fluids often involve simplifications and assumptions about the physical system and without proper validation against experimental data, there is a risk of using inaccurate models at such small scales. Furthermore, sensitivity analyses appear necessary both to understand the physics of the problem and to ensure that uncertainties in input parameters, coupled to model assumptions, do not significantly impact the relevance of the simulation results. In order to achieve the necessary dialogue between experimental and numerical approaches, the motivation to address both will be a selection criterion for the PhD candidate to be recruited. However, depending on his/her abilities and preferences, the priorities may be readjusted during the project.

References

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Description of the consortium

BMBI (T. Baudequin and A. Le Goff) has expertise on experimental methods (microfluidics and electrospinning) and tissue engineering. The PhD candidate will benefit from the microfabrication platform, an equipped microfluidic station with high-speed camera, and two electrospinning setups. **Institut Jean Le Rond d'Alembert** (J. M. Fullana and S. Popinet) has expertise on numerical methods. The PhD candidate will benefit from the numerical resources and expertise available within the Dalembert research group,

Research program

The research program is summarized on the Gantt chart below.

Project	Trimester											
	1	2	3	4	5	6	7	8	9	10	11	12
Experimental study of non-Newtonian coflow (BMBI)												
Literature review, definition and characterization of sample fluids												
Definition of the experimental study												
Generation of the experimental database (thread shape and stability)												
Simulation of microfluidic coflow (JLRA)												
Definition of the numerical study												
Implementation of numerical methods												
Generation of numerical database of thread behavior												
Analysis of thread properties, dialogue between experiments and simulations												
Fiber production and characterization (BMBI)												
Technological development of the MFES platform												
Generation and characterization of fiber batches												
Analysis of fiber properties, dialogue between experiments & simulation												
Writing of the manuscript												